REVIEW

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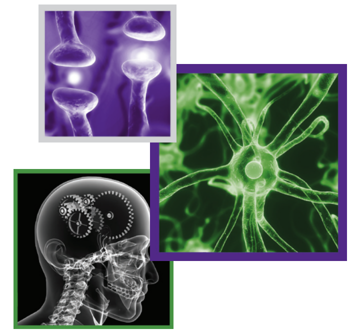
Neurodegenerative Disease Management



Prevention of falls in Parkinson's disease: a review of fall risk factors and the role of physical interventions

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Practice points

- A three-step clinical tool assessing falls in the past year, freezing of gait in the past month and gait speed can be used to accurately identify level of fall risk in the next 6 months.
- Freezing of gait, impaired balance and impaired cognition are commonly identified, potentially remediable fall risk factors.
- There is emerging evidence to support fully supervised challenging balance exercises performed in groups or individually to reduce falls.
- There is limited evidence for minimally supervised, home-based exercise programs for fall prevention.
- Improvements in mobility and physical activity can be achieved without increasing falls.
- Physical interventions aimed at reducing falls need to be tailored to level of fall risk, as well as fall history (e.g., multiple or injurious falls) and presenting risk factors (e.g., cognitive impairment).

SUMMARY Falls in people with Parkinson's disease (PD) are frequent and recurrent events with devastating and widespread consequences. Despite this, understanding of the predictive and explanatory value of fall risk factors, as well as the development and testing of interventions aimed at reducing falls, are in their infancy. This review focuses on fall prediction and risk factors that are potentially remediable with physical interventions. We show that falls can be predicted with high accuracy using a simple three-step clinical tool. Evidence from recently published randomized controlled trials supports the implementation of balance-challenging exercises in reducing falls. Larger scale trials utilizing technologically advanced monitoring methods will further elucidate those interventions most likely to be cost effective according to individual risk factor profiles.

KEYWORDS
• balance • exercise • falls • fall risk factors • freezing of gait • mobility • Parkinson's disease

Extent of the problem

Parkinson's disease (PD) is a complex, progressive multisystem disease presenting with a wide range of motor, cognitive and emotional impairments. Falls in people with PD are frequent and recurrent events, with 45–68% of people falling annually [1–4] and two-thirds of these falling recurrently [5]. These fall rates are double those reported for the general older population, and although the risk of falls increases with disease duration [6], falls are common even early in the disease [7,8]. The resulting injuries [9], activity limitations [10], pain [11], loss of independence [11,12], fear of falling [13,14], reduced quality of life [15–17] and high levels of caregiver stress [18] mean that the consequences

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of falling are both devastating and widespread. The incidence of hip fracture is reported to be four times that for older persons of the same age without PD [19] and the costs associated with falls resulting in fractures are considerable [12]. With the number of people affected by PD expected to almost double between 2005 and 2030 [20], falls among people with PD are set to become a major health challenge.

Scope of the review

Despite the looming enormity of the problem of falls in PD, the development and testing of interventions aimed at reducing falls in this population is in its infancy. In this review we will first provide an up-to-date overview of motor and non-motor risk factors for falls in PD, focusing on both fall prediction and risk factors that are potentially remediable with physical interventions. Physical interventions for the purpose of this review include exercise, motor learning interventions and behavioral strategies to increase physical activity. We will then review evidence from systematic reviews and recent randomized controlled trials of physical interventions designed to prevent falls in people with PD. On the basis of this summary, we will provide up-to-date evidence-based guidance for fall prevention, identify unmet challenges and present future directions for research.

Predicting falls

Prospective studies investigating fall prediction in PD have proposed that previous falls [1–2,10,21–22], increased disease severity [10,23], freezing of gait [2,7], reduced mobility [7,24], poor balance [2,7,25] and reduced leg muscle strength [2] predict falls. However, some of these studies have either used univariate analysis [24,25] or overfitted multivariate models [1,7,10,23]. Moreover, some predictors are not consistently demonstrated across studies and can be time consuming to evaluate in clinical practice. One consistent finding is that the best predictor of a future fall in people with PD is a previous fall [21].

A clinical prediction rule regarding fall risk in PD enables the absolute probability of future falls to be estimated after a brief assessment of predictors [26] and can guide clinicians' decision-making. A recent study investigated the ability of fall risk factors (including fall history, disease severity, freezing of gait, mobility, balance, leg muscle strength, cognition and fear of falling) to predict falls in people with PD [3]. A simple clinical fall prediction tool was developed based on logistic regression analysis of a sample of 205 individuals with PD and internally validated in this sample. A positive fall history, a history of freezing of gait and reduced gait speed were found to be the best predictors of falls, and these predictors were used to develop the fall prediction tool which showed high discrimination (area under receiver-operating characteristic curve of 0.80) [27]. The tool permits quick identification of an individual's absolute risk of falling based on the weights of each of the three risk factors **(Figure 1)** [3]. Individuals identified to be at low, moderate or high risk of falls have a 17, 51 or 85% probability, respectively, of falling in the next 6 months, and the clinician can communicate this information to the patient and explore options for fall prevention.

While a previous history of falls is the most consistent predictor of fall risk in PD [21], it does not provide information to guide assessment and intervention strategies for preventing subsequent falls. Therefore, understanding the contribution of potentially remediable motor and non-motor risk factors to falls is a critical consideration in the development of fall prevention programs for people with PD. The following section will examine recent evidence on this topic.

Fall risk factors

A large number of fall risk factors for PD have been proposed, but many of these risk factors are inconsistently identified across studies [1–4,10,21–23,28–38]. Reasons that may contribute to this inconsistency include: the relatively small sample size of many studies, the different factors investigated in each study and the methods used to determine risk factors. The most robust method is to determine risk factors from the relative risk or odds of falling in individuals with or without the risk factor [39]. However, some studies have sought to identify risk factors by using between-group comparisons of fallers and non-fallers.

Fall risk factors may be considered as non-remediable (i.e., fixed) or potentially remediable with medical, surgical or physical intervention; the latter is the focus of this review. Fixed risk factors include: prior fall history [1–3,10,21–23,28–29], greater disease severity [2,4,10,21–23,28,30–33,38] and longer disease duration [1,3,30,32–33,38]. Factors such as age [3,21–23,30,33,38] and gender [2–3,21–22,30,33,38] have not been shown to be associated with falls in PD. Although increased levodopa dose appears to be associated with increased fall

Name:
Medical record number:
Date:

Assessing the probability of falling in people with Parkinson's disease				Score
Step 1	Ask your patient: Have you fallen in the past 12 months?	Yes = 6	No = 0	
Step 2	Ask your patient: Have you experienced freezing of gait in the past month?	Yes = 3	No = 0	
Step 3	Time your patient walking over the middle 4 m of a 6 m walkway at a comfortable pace: >3.6 s to walk 4 m = 'yes'	Yes = 2	No = 0	
			Total score	

Total score	0	2–6	8–11
Probability of falling in next 6 months	Low (17%)	Moderate (51%)	High (85%)
Tick appropriate box	☐	☐	☐

Figure 1. Three-step clinical prediction tool for assessing the probability of falling in the next 6 months in people with Parkinson's disease. The timed walking test is performed 'on' medication. Reproduced with permission from Movement Disorders, © 2013 Movement Disorder Society.

risk [2,31,33], deep-brain stimulation [33,38] and polypharmacy [22,23] have not been found to be consistent fall risk factors.

A number of fall risk factors may be potentially remediable with physical interventions (Table 1). Recent prospective studies of moderately large sample sizes investigating fall risk across physical and cognitive domains have found that freezing of gait [2,28,34], impaired balance [2,34] and cognitive impairment [2,28,34] are the risk factors most consistently associated with falls. Other common but inconsistently reported fall risk factors for people with PD that are potentially remediable with physical interventions include poor mobility [2,7,24,29–30,32,35,37,40–47], reduced leg muscle strength [2,7], difficulty performing daily activities [1,4,7,29–33,42,44,46–47], depression [1,4,30–31,33,42] and fear of falling [14,22,31–33,35,40,42,48].

There is emerging evidence that impulsivity may also contribute to fall risk in PD and is more prevalent in the postural instability and gait disorder (PIGD) subtype [86,87]. Impulsivity and perceived fear of falling appear to be opposite factors but have in fact a complex relationship with fall risk in healthy older people [88,89]. Similarly, there is a proportion of people with PD who fall frequently, despite demonstrating low fear of falling [90,91].

Many of the potentially remediable fall risk factors outlined above are amenable to physical

Table 1. Fall risk factors in Parkinson's disease that are potentially remediable with physical and/or cognitive interventions.

Risk factor	Yes (identified to be a fall risk factor)		No (identified to not be a fall risk factor)		Evidence for remediation†
	Prospective	*Retrospective*	*Prospective*	*Retrospective*	
Parkinson's disease symptoms					
Freezing of gait	**Camicioli and Majumdar (2010)** [28] **Latt *et al.* (2009)** [2] **Paul *et al.* (2013, 2014)** [3,34] Cole *et al.* (2010) [40] Gray and Hildebrand (2000) [49] Kerr *et al.* (2010) [7] Matinolli *et al.* (2011) [29]‡	**Contreras and Grandas (2012)** [31] **Lim *et al.* (2008)** [32] **Matinolli *et al.* (2007)** [33] Robinson *et al.* (2005) [42] Schaafsma *et al.* (2003) [47]			Balance exercises + lower limb strengthening + cueing strategies [50] Physiotherapy [51]§ Dance [52] Cued gait training [53]¶ Cued treadmill training [54]
Balance & mobility					
Anticipatory balance with change in base of support (includes mobility, i.e., gait speed, Timed Up & Go, sit-to-stand)	**Latt *et al.* (2009)** [2]# **Paul *et al.* (2013, 2014)** [3,34] Cole *et al.* (2010) [40] Foreman *et al.* (2011) [24]†† Kerr *et al.* (2010) [7] Mak and Pang (2010) [45]‡ Matinolli *et al.* (2011) [29]‡,# Smulders *et al.* (2012) [43]‡	**Balash *et al.* (2005)** [30] **Lim *et al.* (2008)** [32] **Mak and Pang (2009)** [35] **Parashos *et al.* (2013)** [38]‡‡ Dibble *et al.* (2008) [41] Koller *et al.* (1989) [46] Latt *et al.* (2009) [44] Plotnik *et al.* (2011) [37]# Robinson *et al.* (2005) [42]§§ Schaafsma *et al.* (2003) [47]	**Ashburn *et al.* (2001)** [22] **Latt *et al.* (2009)** [2]# Foreman *et al.* (2011) [24]†† Mak and Pang (2009) [48]‡ Matinolli *et al.* (2011) [29]‡,# Wood *et al.* (2002) [1]	**Contreras and Grandas (2012)** [31] Ashburn *et al.* (2001) [4] Plotnik *et al.* (2011) [37]# Robinson *et al.* (2005) [42]§§	Aerobic exercise [55] Balance exercises [50,56] Exercise and/or motor training [57] Lower limb strength exercises [50,58] Physiotherapy [51,59,60]§ Behavioral training for motor tasks [61] Dance [52,62] LSVT®BIG [63] Tai Chi [58] Nordic walking [64] Overground gait training [55,64] Robotic gait training [65,66] Treadmill training [66–68] Cued gait training [50,53,62] Cued treadmill training [54] Cued sit-to-stand retraining [69]

†Ideally, risk factors should be established based on the relative risk or odds of falling [26,39]; these studies are listed in bold text. Other studies listed have identified risk factors using between group comparisons of fallers and nonfallers. The interventions listed have been shown to have a positive impact on the relevant fall risk factor. This evidence was extracted from meta-analyses within relevant systematic reviews and from well-designed randomized controlled trials (PEDro rating [83] ≥6/10) [84] with at least 15 participants per group.

‡These studies [10,29,43,45,48] investigated recurrent fallers (≥2 falls) versus nonrecurrent fallers (0–1 fall).

§This systematic review [51] had a broad classification of physiotherapy which included multiple modalities of intervention, some of which are not prescribed by physiotherapists.

¶Effect of intervention only in individuals who have freezing of gait [53].

#Timed Up & Go (and cadence) [2] was a fall risk factor or associated with falls, but gait speed (and gait variability [37]) was not a fall risk factor or not associated with falls.

††Timed Up & Go when 'off' was associated with falls, but Timed Up & Go when 'on' was not associated with falls.

‡‡Results reported from this study are based on the multivariate model reporting hazard ratios [38].

§§Sit-to-stand was associated with falls, but Timed Up & Go was not associated with falls.

¶¶Anteroposterior sway on floor was associated with falls, but functional reach, sway on foam and mediolateral sway on floor were not associated with falls.

##Functional reach was associated with falls, but sway was not associated with falls.

†††Effect of dual-tasking on gait speed was not associated with falls. Effect of serial subtraction of 3's on gait variability and incoordination was associated with falls, but serial subtraction of 7's was not.

‡‡‡Subset of UPDRS-II was associated with falls, but Schwab and England score was not associated with falls.

§§§MMSE scores and FAB scores ≤17/18 were determined to be fall risk factors using modified poisson regression [34], but MMSE and FAB scores were not found to be fall risk factors using logistic regression [3].

¶¶¶Semantic fluency was associated with falls, but delayed recall was not associated with falls [38].

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Risk factor	Yes (identified to be a fall risk factor)		No (identified to not be a fall risk factor)		Evidence for remediation[†]
	Prospective	*Retrospective*	*Prospective*	*Retrospective*	
Anticipatory balance without change in base of support (functional reach, postural sway, Romberg's test, tandem stand, single leg stand)	**Latt *et al.* (2009)** [2] **Paul *et al.* (2013, 2014)** [3,34] Kerr *et al.* (2010) [7][¶¶] Matinolli *et al.* (2011) [29][‡]	**Balash *et al.* (2005)** [30] **Matinolli *et al.* (2007)** [33] Ashburn *et al.* (2001) [4][##] Dibble *et al.* (2008) [41]	**Ashburn *et al.* (2001)** [22] Kerr *et al.* (2010) [7][¶¶] Mak and Pang (2010) [45][‡]	**Lim *et al.* (2008)** [32] **Mak and Pang (2009)** [35] Ashburn *et al.* (2001) [4][##] Robinson *et al.* (2005) [42]	Balance exercises [56,70] Lower limb strength exercises [58,70] Physiotherapy [51][§] Tai Chi [58]
Balance & mobility (cont.)					
Reactive balance (Pull test, Push & Release test)	**Paul *et al.* (2014)** [34]	Koller *et al.* (1989) [46] Robinson *et al.* (2005) [42] Schaafsma *et al.* (2003) [47] Valkovic *et al.* (2008) [71]	**Latt *et al.* (2009)** [2] Foreman *et al.* (2011) [24] Mak and Pang (2010) [45][‡] Wood *et al.* (2002) [1]		Robotic gait training [65]
Dual-tasking		Ashburn *et al.* (2001) [4] Plotnik *et al.* (2011) [37][†††]	**Ashburn *et al.* (2001)** [22]	Plotnik *et al.* (2011) [37][†††] Smulders *et al.* (2012) [43][‡]	Dance [52]
Composite measures (Tinetti assessment, Berg Balance scale, Continuous Physical Function Performance scale)	Foreman *et al.* (2011) [24] Kerr *et al.* (2010) [7] Wood *et al.* (2002) [1]	**Contreras and Grandas (2012)** [31] Dibble *et al.* (2008) [41]			Balance exercises [56,72] Balance + flexibility + functional exercises [73] Lower limb strength exercises [72] Physiotherapy [51][§] Dance [52,62] Robotic gait training [65,66]

[†]Ideally, risk factors should be established based on the relative risk or odds of falling [26,39]; these studies are listed in bold text. Other studies listed have identified risk factors using between group comparisons of fallers and nonfallers. The interventions listed have been shown to have a positive impact on the relevant fall risk factor. This evidence was extracted from meta-analyses within relevant systematic reviews and from well-designed randomized controlled trials (PEDro rating [83] ≥6/10) [84] with at least 15 participants per group.
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[¶]Effect of intervention only in individuals who have freezing of gait [53].
[#]Timed Up & Go (and cadence) [2] was a fall risk factor or associated with falls, but gait speed (and gait variability [37]) was not a fall risk factor or not associated with falls.
[††]Timed Up & Go when 'off' was associated with falls, but Timed Up & Go when 'on' was not associated with falls.
[‡‡]Results reported from this study are based on the multivariate model reporting hazard ratios [38].
[§§]Sit-to-stand was associated with falls, but Timed Up & Go was not associated with falls.
[¶¶]Anteroposterior sway on floor was associated with falls, but functional reach, sway on foam and mediolateral sway on floor were not associated with falls.
[##]Functional reach was associated with falls, but sway was not associated with falls.
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[‡‡‡]Subset of UPDRS-II was associated with falls, but Schwab and England score was not associated with falls.
[§§§]MMSE scores and FAB scores ≤17/18 were determined to be fall risk factors using modified poisson regression [34], but MMSE and FAB scores were not found to be fall risk factors using logistic regression [3].
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Risk factor	Yes (identified to be a fall risk factor)		No (identified to not be a fall risk factor)		Evidence for remediation[†]
	Prospective	*Retrospective*	*Prospective*	*Retrospective*	
Physical activity					
Physical activity levels	Matinolli *et al.* (2011) [29][‡]	**Matinolli et al. (2007)** [33]	**Paul *et al.* (2013)** [3] Gray and Hildebrand (2000) [49]	Robinson *et al.* (2005) [42]	Cued gait training [74] Multifaceted behavior change program [75]
Perceived effort to complete tasks	**Ashburn *et al.* (2001)** [22]	Ashburn *et al.* (2001) [4]			
Activities of daily living					
Difficulty or assistance with ADLs (Schwab & England, UPDRS-II, Rivermead Motor assessment)	**Matinolli *et al.* (2011)** [29][‡] Kerr *et al.* (2010) [7] Wood *et al.* (2002) [1]	**Balash *et al.* (2005)** [30] **Contreras and Grandas (2012)** [31] **Lim *et al.* (2008)** [32] **Matinolli *et al.* (2007)** [33] Ashburn *et al.* (2001) [4] Koller *et al.* (1989) [46] Latt *et al.* (2009) [44] Robinson *et al.* (2005) [42][‡‡‡] Schaafsma *et al.* (2003) [47]	Gray and Hildebrand (2000) [49]	Robinson *et al.* (2005) [42][‡‡‡]	Exercise [76] Balance exercises [73] Flexibility exercises [73] Functional exercises [73] Physiotherapy [51,59–60,77][§] Health education [77]
Use of walking aid	Gray and Hildebrand (2000) [49] Matinolli *et al.* (2011) [29][‡]	**Matinolli *et al.* (2007)** [33]			
Physiological					
Hand RT, foot RT			**Latt *et al.* (2009)** [2] Kerr *et al.* (2010) [7]		Aerobic exercise + overground gait training [55]
Visual acuity			Cole *et al.* (2010) [40] Kerr *et al.* (2010) [7]	Matinolli *et al.* (2007) [33]	
Visual contrast	**Latt *et al.* (2009)** [2]				
Proprioception	**Paul *et al.* (2013)** [34]		**Latt *et al.* (2009)** [2] Kerr *et al.* (2010) [7]	Koller *et al.* (1989) [46]	

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Risk factor	Yes (identified to be a fall risk factor)		No (identified to not be a fall risk factor)		Evidence for remediation†
	Prospective	*Retrospective*	*Prospective*	*Retrospective*	
Vibration sense			Kerr *et al.* (2010) [7]	Koller *et al.* (1989) [46]	
Touch sense	Kerr *et al.* (2010) [7]		**Latt *et al.* (2009)** [2]		
Knee extensor strength	**Latt *et al.* (2009)** [2] **Paul *et al.* (2013, 2014)** [3,34] Kerr *et al.* (2010) [7]				Lower limb strength exercises [58,78] Tai Chi [58] Treadmill training [68]
Knee flexor strength	**Latt *et al.* (2009)** [2]		Kerr *et al.* (2010) [7]		Lower limb strength exercises [58] Tai Chi [58]
Ankle dorsiflexor strength	**Latt *et al.* (2009)** [2]		Kerr *et al.* (2010) [7]		
Leg extensor muscle power		**Allen *et al.* (2010)** [36]			Leg muscle power training [79]
Cognition					
Global cognitive impairment (carer rated, MMSE)	**Camicioli and Majumdar (2010)** [28] **Latt *et al.* (2009)** [2] **Paul *et al.* (2013)** [3]§§§ Smulders *et al.* (2012) [43]‡ Wood *et al.* (2002) [1]	**Contreras and Grandas (2012)** [31]	**Paul et al. (2013)** [34]§§§ Cole *et al.* (2010) [40] Mak and Pang (2010) [45]‡ Matinolli *et al.* (2011) [29]‡	**Matinolli *et al.* (2007)** [33] Koller *et al.* (1989) [46] Plotnik *et al.* (2011) [37] Robinson *et al.* (2005) [42] Schaafsma *et al.* (2003) [47]	Cognitive training [80]
Executive function (FAB, Brixton, digit span, Trail Making)	**Latt *et al.* (2009)** [2] **Paul *et al.* (2013)** [34]§§§		**Paul *et al.* (2013)** [3]§§§	**Lim *et al.* (2008)** [32] Plotnik *et al.* (2011) [37]	Cognitive training [80,81]
Attention	**Allcock *et al.* (2009)** [23]	**Plotnik *et al.* (2011)** [37]	Smulders *et al.* (2012) [43]‡		Cognitive training [81]
Central processing speed (cognitive RT)	**Allcock *et al.* (2009)** [23]			Plotnik *et al.* (2011) [37]	Cognitive training [80,81]
Mental fatigue				**Lim *et al.* (2008)** [32]	

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Table 1. Fall risk factors in Parkinson's disease that are potentially remediable with physical and/or cognitive interventions (cont.).

Risk factor	Yes (identified to be a fall risk factor)		No (identified to not be a fall risk factor)		Evidence for remediation†
	Prospective	*Retrospective*	*Prospective*	*Retrospective*	
Cognition (cont.)					
Semantic fluency		**Parashos *et al.* (2013)** [38]‡‡,¶¶¶			
Memory				**Parashos *et al.* (2013)** [38]‡‡,¶¶¶ Plotnik *et al.* (2011) [37]	Cognitive training [81]
Visuoperception				Plotnik *et al.* (2011) [37] Robinson *et al.* (2005) [42]	Cognitive training [81]
Psychological					
Worry, fear of falling (FES-I, ABC-scale, single questions)	**Ashburn *et al.* (2001)** [22] **Paul *et al.* (2013)** [3] Cole *et al.* (2010) [40] Mak and Pang (2009) [48]‡	**Lim *et al.* (2008)** [32] **Mak and Pang (2009)** [35] **Matinolli *et al.* (2007)** [33] Contreras and Grandas (2012) [31] Rahman *et al.* (2011) [14] Robinson *et al.* (2005) [42]	Matinolli *et al.* (2011) [29]‡ Mak and Pang (2010) [45]‡	Plotnik *et al.* (2011) [37]	Balance exercises [56,72] Lower limb strength exercises [72] Robotic gait training [65] Cued gait training [53]
Depression	Wood *et al.* (2002) [1]	**Balash *et al.* (2005)** [30] **Matinolli *et al.* (2007)** [33] Ashburn *et al.* (2001) [4] Contreras and Grandas (2012) [31] Robinson *et al.* (2005) [42]	**Ashburn *et al.* (2001)** [22] Mak and Pang (2009) [48]‡ Mak and Pang (2010) [45]‡	Mak and Pang (2009) [35] Plotnik *et al.* (2011) [37]	Balance exercises [56] Physiotherapy [77] Alexander technique [82] Health education [77]
Anxiety		Ashburn *et al.* (2001) [4]	**Ashburn *et al.* (2001)** [22]	Plotnik *et al.* (2011) [37]	

†Ideally, risk factors should be established based on the relative risk or odds of falling [26,39]; these studies are listed in bold text. Other studies listed have identified risk factors using between group comparisons of fallers and nonfallers. The interventions listed have been shown to have a positive impact on the relevant fall risk factor. This evidence was extracted from meta-analyses within relevant systematic reviews and from well-designed randomized controlled trials (PEDro rating [83] ≥6/10) [84] with at least 15 participants per group.
‡These studies [10,29,43,45,48] investigated recurrent fallers (≥2 falls) versus nonrecurrent fallers (0–1 fall).
§This systematic review [51] had a broad classification of physiotherapy which included multiple modalities of intervention, some of which are not prescribed by physiotherapists.
¶Effect of intervention only in individuals who have freezing of gait [53].
#Timed Up & Go (and cadence) [2] was a fall risk factor or associated with falls, but gait speed (and gait variability [37]) was not a fall risk factor or not associated with falls.
††Timed Up & Go when 'off' was associated with falls, but Timed Up & Go when 'on' was not associated with falls.
‡‡Results reported from this study are based on the multivariate model reporting hazard ratios [38].
§§Sit-to-stand was associated with falls, but Timed Up & Go was not associated with falls.
¶¶Anteroposterior sway on floor was associated with falls, but functional reach, sway on foam and mediolateral sway on floor were not associated with falls.
##Functional reach was associated with falls, but sway was not associated with falls.
†††Effect of dual-tasking on gait speed was not associated with falls. Effect of serial subtraction of 3's on gait variability and incoordination was associated with falls, but serial subtraction of 7's was not.
‡‡‡Subset of UPDRS-II was associated with falls, but Schwab and England score was not associated with falls.
§§§MMSE scores and FAB scores ≤17/18 were determined to be fall risk factors using modified poisson regression [34], but MMSE and FAB scores were not found to be fall risk factors using logistic regression [3].
¶¶¶Semantic fluency was associated with falls, but delayed recall was not associated with falls [38].
LSVT®BIG is a physical and occupational therapy program based on the Lee Silverman Voice Treatment method [85].
ABC-scale: Activities of balance confidence scale; ADL: Activities of daily living; FAB: Frontal assessment battery; FES-I: Falls efficacy scale-international; MMSE: Mini-Mental State Examination; RT: Reaction time; UPDRS-II: Unified Parkinson's Disease Rating Scale, Part II (Activities of Daily Living).

interventions [51,92] or cognitive rehabilitation, although the evidence for cognitive rehabilitation is much weaker [93]. However, it is only in recent times that studies have been designed to determine the effect of physical interventions on falls as an outcome. The results of these studies will be considered in the next section.

Effect of physical interventions on falls

Two systematic reviews [57,92], including one meta-analysis [57], have investigated the effect of physical interventions on falls. The meta-analysis [57] of two trials [53,70] showed no effect of physical intervention on proportion of fallers compared with usual care, although it should be noted that Nieuwboer *et al.*'s trial [53] was not designed to reduce falls but rather to monitor falls as a potential adverse effect of a home-based cueing intervention. The other review [92] included four randomized controlled trials published as full-length papers [53,70,72,94] and three published as abstracts. Many of these trials were underpowered to detect an effect on falls and meta-analysis was not undertaken due to poor and variable reporting of falls. The authors concluded that there was no difference in falls when physiotherapy was compared with no intervention; however, a trend towards a reduction in the number of falls with physiotherapy was noted.

Further information can be gained by examining recently published (2010–current) randomized controlled trials. Our search yielded four studies: three studies tested physical interventions with a primary or secondary aim of reducing falls [56,58,72] and one study monitored falls as adverse events in the context of an interventions designed to increase physical activity [75]. All four studies **(Table 2)** recorded falls prospectively using falls diaries [56,58,72,75] over periods ranging from 15 weeks to 24 months. Only two studies [58,72] analyzed falls using a recommended method of statistical analysis [95] that accounts for the non-normal distribution of falls and adjusts for the non-independence of fall events in individuals and follow-up time. The quality of the studies was moderate to high, based on Physiotherapy Evidence Database (PEDro) scores of 6–8 out of 10 [83].

An important aim of physical interventions for people with PD is to improve mobility and activity. However, there is concern that an overall increase in physical activity could render the individual at higher risk of falls due to increased exposure to physical activity or moving at a faster pace. In line with the results of Nieuwboer *et al.* [53], van Nimwegen *et al.* [75] showed that a 2-year behavioral coaching program aimed at increasing physical activity achieved this outcome without increasing fall risk.

The three studies explicitly aiming to reduce falls implemented exercise interventions designed to address either single or multiple physical fall risk factors. Two trials [56,58] compared exercises that challenged balance with a control group performing exercises that did not challenge balance. Li *et al.* [58] reported a significant reduction in falls in a group undertaking fully supervised Tai Chi classes twice a week for 6 months compared with control stretching exercises. In addition, the reduction in falls remained significant at the 3-month follow-up. This trial included a second active exercise intervention – that is, resistance training – and found no difference in fall rates between the resistance training and the Tai Chi group during the 6-month intervention, but significantly fewer falls in the Tai Chi group compared with the resistance training group at the 3-month follow up. The comparison between the two active groups should be interpreted with caution, since the resistance training exercises appear to have been delivered at a less than optimal dose. Furthermore, a comparison of fall rates in the resistance training group compared with the control stretching exercises group was not presented.

Smania *et al.* [56] reported a reduction in falls in a group undertaking fully supervised balance-challenging exercises three times a week for 7 weeks, compared with control exercises. However, the actual number of falls and the distribution of falls were not reported, and a statistical method accounting for the frequent and recurrent nature of falls in this population as well as the non-normal distribution of falls was not utilized.

Only one trial to date has reported a parallel economic analysis [72,97]. Goodwin *et al.*'s underpowered trial of group-based plus home-based exercise targeting balance and strength reported a non-significant 32% reduction in falls and a non-significant reduction in healthcare costs in the exercise group compared with the control group. Nevertheless, analysis of the uncertainty around the estimates of healthcare costs suggests that there is >80% probability that the exercise intervention is a cost-effective strategy relative to usual care. This finding highlights the need for further well-designed, large-scale trials to examine both efficacy and cost-effectiveness with a thorough analysis of not only falls, but injuries and fractures associated with falls.

The inconsistent findings across trials are likely attributable to: the characteristics of participants; variations in fall definitions, fall reporting periods and statistical analyses; as well as the type and dose of exercise and the extent of supervision provided. It is noteworthy that the two trials demonstrating significant effects focused on a single risk factor – that is, impaired balance – with all intervention being facility-based and fully supervised, either individually [56] or in a group [58]. In contrast, the trial with nonsignificant findings [72] included only participants at high risk of falls (reporting two or more falls in the past year), used exercise to address several physical risk factors, and the majority of the prescribed exercises were performed unsupervised at home.

Insights into mechanisms underlying physical interventions

One method of gaining insight into the mechanisms underlying the effects of physical interventions designed to reduce falls is to consider the coinciding effects on falls and physical fall risk factors. The picture that emerges with respect to balance outcomes shows some consistency. The two trials targeting balance [56,58] that produced significant reductions in falls also showed significant improvements in balance in favor of the exercise group, and these improvements were maintained during follow-up periods of 4 and 12 weeks. In Li *et al.*'s Tai Chi study [58], it is noteworthy that over 70% of the participants in the Tai Chi group continued to attend classes during the follow-up period, suggesting that maintenance of effects may be reliant upon continued exercise.

A consistent improvement in balance confidence or fear of falling was shown in all three trials measuring these outcomes [53,56,72]. Smania *et al.* [56] showed improvement in balance confidence in line with the significant reduction in falls in favor of the exercise group. Goodwin *et al.* [72] showed a reduction in fear of falling with a corresponding increase in recreational physical activity in favour of the exercise group, while Nieuwboer *et al.* [53] showed a reduction in fear of falling in line with a corresponding improvement in mobility in the cueing group. Therefore, these studies suggest that while a reduction in fear of falling is not consistently accompanied by a decrease in falls, it does appear to be accompanied by an increase in mobility and physical activity without increasing falls. These observations require confirmation with direct regression analyses.

There is little information available regarding outcomes for other key physical risk factors in fall prevention trials. Despite the prominence of freezing of gait as a significant risk factor for falls, freezing of gait was only assessed in one small study [94] without any noticeable effect on this gait disorder or on falls. Although freezing of gait was reduced in freezers in the Nieuwboer *et al.* cueing trial [53], there was no overall effect on falls; however, this study was not powered to find an effect on falls in subgroups. Similarly, although muscle strengthening exercises were delivered in three trials [58,70,72], no evidence of a link between improvement in muscle strength and falls reduction was identified.

Unmet challenges & future directions

Fall prevention interventions are typically classified according to a taxonomy [98], which includes nine intervention categories: exercise, medication, surgery, management of urinary incontinence, psychological, environmental/assistive technology, social environment, knowledge/education, and other interventions. Interventions are considered as single interventions (e.g., exercise), multiple interventions (e.g., exercise plus medication) or multifactorial interventions (multiple interventions linked to each individual's specific risk profile based on assessment of risk factors). To date, only single interventions as defined above – that is, exercise [56,58,70,72,94], medication [99–101], environmental [102] and education [103] interventions – have been trialed in people with PD. No interventions other than exercise [56,58] have been reported to significantly reduce falls, apart from a small trial showing a reduction in falls with the use of a central cholinesterase inhibitor in frequent fallers without freezing of gait [99]. It is possible that multiple interventions or multifactorial interventions may be more effective than single interventions, and trials addressing these possibilities are needed. While no trials have evaluated the efficacy of cognitive training, two small randomized controlled trials have shown improvements in elements of cognition with training [80,81], which may influence fall rates, but this remains to be tested in a large-scale trial powered to detect an effect on falls.

Some of the identified gaps in the evidence to

Table 2. Randomized controlled trials (2010 to current) of physical interventions delivered to people with idiopathic Parkinson's disease reporting falls as a primary outcome, a secondary outcome or an adverse event.

Study (year)	PEDRO score	Population				Intervention			Fall outcomes				Ref.
		Inclusion criteria (H&Y)	*Group (n)*	*Age (years)*	*Disease duration (years)*	*Type*	*Dose (min, frequency, weeks)*	*Delivery (location, method, supervision)*	*Fall reporting (definition†; method, period)*	*Outcome(s) and/or statistical test(s)*	*Between group differences (95% CI) during intervention period*	*Between group differences (95% CI) during follow-up period*	
Goodwin *et al.* (2011)	7/10	>1 fall in the last 12 months, independently mobile indoors	E: 64	72 ± 9	9.1 ± 6.4	Strength and balance exercises including walking	60, 3, 10	Facility, group + home, individual 33%	1, 2; prospective, week -10–20	Number of falls: Negative binomial regression adjusted for baseline falls	IRR: 0.68 (0.43–1.07)	IRR: 0.74 (0.41–1.33)	[72]
			C: 66	70 ± 8	8.2 ± 6.4	No training			1, 2; prospective, week 0–39		OR: 0.70 (0.28–1.74)		
Li *et al.* (2012)	7/10	At least one score ≥2 for ≥one limb for tremor, rigidity, postural stability, or bradykinesia items in UPDRS III; ability to stand unaided and walk with or without an assistive device	E: 65	68 ± 9	8 ± 9	Tai chi exercises designed to challenge balance and gait	60, 2, 26	Facility, group 100%		Proportion of fallers: Logistic regression adjusted for baseline faller status			[58]
			C1: 65	69 ± 8	8 ± 9	Resistance exercises	60, 2, 26	Facility, group 100%	Number of falls: Negative binomial regression		Tai chi vs resistance exercise IRR: 0.47 (0.12–1.00)	Tai chi vs resistance exercise IRR: 0.40 (0.18–0.88)*	
			C2: 65	69 ± 9	6 ± 5	Stretching exercises	60, 2, 26	Facility, group 100%			Tai chi vs stretching IRR: 0.33 (0.16–0.71)**	Tai chi vs stretching IRR: 0.31 (0.14–0.67)**	

†Fall definition: 1: Unintentional/unexpected change in position, 2: Person comes to rest on lower level, 3: Not as a result of a major intrinsic event or overwhelming hazard.
‡Near fall: defined as an occasion on which an individual felt that they were going to fall but did not actually do so.
§Between group difference not reported, except as effect size, Mann–Whitney U test.
¶Between group difference not reported.
*p <0.05; **p < 0.01; ***p < 0.001.
H&Y: Hoehn and Yahr disease stage; NR: Not reported; NS: No significant between group difference; PIGD: Postural instability gait disorder; UPDRS: Unified Parkinson's Disease Rating Scale.

Table 2. Randomized controlled trials (2010 to current) of physical interventions delivered to people with idiopathic Parkinson's disease reporting falls as a primary outcome, a secondary outcome or an adverse event (cont.).

Study (year)	PEDRO score	Population				Intervention			Fall outcomes				Ref.
		Inclusion criteria (H&Y)	*Group (n)*	*Age (years)*	*Disease duration (years)*	*Type*	*Dose (min, frequency, weeks)*	*Delivery (location, method, supervision)*	*Fall reporting (definition†; method, period)*	*Outcome(s) and/or statistical test(s)*	*Between group differences (95% CI) during intervention period*	*Between group differences (95% CI) during follow-up period*	
Smania *et al.* (2010)	6/10	H&Y stage 3–4, able to rise from chair or bed independently	E: 33	68 ± 7	10.4 ± 4.8	Anticipatory and reactive balance exercises in standing with/ without a change in base of support, and walking including obstacle avoidance	50, 3, 7	Facility, individual 100%	1, 2, 3; prospective, week -4–11	Number of falls: Mann–Whitney U	Effect size: -0.45** Compared intervention with baseline period§	Effect size -0.40** Compared follow up to baseline period§	[56]
			C: 31	67 ± 7	8.6 ± 5.4	Exercises that did not challenge balance	50, 3, 7	Facility, individual 100%					
van Nimwegen *et al.* (2013)	8/10	H&Y stage 1–3, sedentary lifestyle	E: 299	65 ± 8	5.0 ± 5.5	Multifaceted behavioral change program designed to increase physical activity using motivational strategies and ambulatory feedback	30, up to 70 sessions over 104 weeks	Facility and home, individual and group supervision NR	1, 2; prospective, week 0–104	Proportion of fallers: descriptive	E: 184 (62%) participants fell; C: 191 (67%) participants fell¶	NR	[75]

†Fall definition: 1: Unintentional/unexpected change in position, 2: Person comes to rest on lower level, 3: Not as a result of a major intrinsic event or overwhelming hazard.
‡Near fall: defined as an occasion on which an individual felt that they were going to fall but did not actually do so.
§Between group difference not reported, except as effect size, Mann–Whitney U test.
¶Between group difference not reported.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
H&Y: Hoehn and Yahr disease stage; NR: Not reported; NS: No significant between group difference; PIGD: Postural instability gait disorder; UPDRS: Unified Parkinson's Disease Rating Scale.

Table 2. Randomized controlled trials (2010 to current) of physical interventions delivered to people with idiopathic Parkinson's disease reporting falls as a primary outcome, a secondary outcome or an adverse event (cont.).

Study (year)	PEDRO score	Population				Intervention			Fall outcomes				Ref.
		Inclusion criteria (H&Y)	*Group (n)*	*Age (years)*	*Disease duration (years)*	*Type*	*Dose (min, frequency, weeks)*	*Delivery (location, method, supervision)*	*Fall reporting (definition†; method, period)*	*Outcome(s) and/or statistical test(s)*	*Between group differences (95% CI) during intervention period*	*Between group differences (95% CI) during follow-up period*	
van Nimwegen *et al.* (2013) (cont.)			C: 287	66 ± 7	5.5 ± 4.6	General physiotherapy program promoting safety of movements, according to the evidence-based physiotherapy guideline [96]	30, up to 70 sessions over 104 weeks	Facility and home, individual supervision NR					

†Fall definition: 1: Unintentional/unexpected change in position, 2: Person comes to rest on lower level, 3: Not as a result of a major intrinsic event or overwhelming hazard.
‡Near fall: defined as an occasion on which an individual felt that they were going to fall but did not actually do so.
§Between group difference not reported, except as effect size, Mann–Whitney U test.
¶Between group difference not reported.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
H&Y: Hoehn and Yahr disease stage; NR: Not reported; NS: No significant between group difference; PIGD: Postural instability gait disorder; UPDRS: Unified Parkinson's Disease Rating Scale.

date may be clarified when results from recently completed large trials [104–106] and those currently underway [107,108] become available. Of note is the virtual reality (V-time) trial [108], which is investigating a multiple integrated intervention (walking on a treadmill combined with systematically increasing cognitive and physical challenge in a virtual environment) targeting both physical and cognitive risk factors compared with treadmill training alone. This trial points to the potential of technology-based interventions for fall prevention, as evidenced by a number of pilot studies in this domain [109,110]. The PDSAFE trial [111] (currently in pilot phase) is aiming to recruit 600 participants, which makes it by far the largest fall prevention trial in PD to date. The intervention to be tested is multifactorial and targeted at individual risk factors. It uses a home-based format of implementing an intensive exercise program tailor-made to the individual and supported by DVD and iPad technology to optimize adherence. A significant advantage of such a large trial is the ability to have sufficient power to test *a priori* hypotheses regarding the impact of the intervention on subgroups classified according to factors such as fall history, disease severity, cognition or motor phenotype. For example, retrospective falls data suggest that the tremor dominant phenotype is associated with reduced risk of falls [38]. Finally, in light of the increasing number of randomized controlled trials, it is timely that a Cochrane systematic review is planned to investigate interventions for preventing falls in people with PD [112].

As risk factors identified in prospective falls studies in people with PD are also likely to be influenced by the heterogeneity of this population, studies with larger sample sizes are required to tease out the risk factor profile of identified subgroups. While a meta-analysis of risk factors for falls could be considered in the future, at this stage only one prospective study in people with PD [3] would meet the inclusion criteria as recently published in community-dwelling older people [113]. A more parsimonious solution could be achieved by researchers in the field collaborating to identify key risk factor measures and agreed methods of recording falls, facilitating the development of a falls database for pooling data. Even those patients identified to be at low risk of falls have some risk and further research is required to identify predictors of first-time falls. Another approach with potential to add further insights is the implementation of longitudinal studies designed to assess risk factors over time and analyze the emergence of fall behavior at critical time points, such as conversion from non-faller to infrequent faller, or infrequent faller to frequent faller.

Currently, identification of risk factors, mobility and physical activity typically relies upon physical assessments tested on one occasion while the patient is 'on' medication and/or participant recall. In addition, the use of monthly falls diaries with routine monthly telephone follow-up is considered best practice for prospective monitoring of falls [98]. Since there are limitations to these methods of assessment, the development of reliable, valid, technology-based assessment methods is a key priority [114,115]. Research teams are exploring wearable sensors with the potential to accurately detect freezing of gait [116,117] and falls [118] in everyday settings, and deliver a cue to prevent the event. These possibilities are currently being investigated as part of an EU-funded project CUPID [119].

Prevention strategies according to level of fall risk

Due to the complex and progressive nature of PD and the multiple factors potentially contributing to falls, it is tempting to suggest that fall prevention be informed by a complete fall history and full assessment of all potential fall risk factors. However, this approach is unlikely to be sustainable and evidence from the general older population suggests that single interventions targeting common risk factors (e.g., impaired balance) are as effective as multifactorial interventions linked to the individual's risk profile [120,121]. A quick and easy method to establish absolute risk of falling in clinical or community settings is to use the three-step clinical prediction tool described earlier **(Figure 1)**. This information can then be used to direct management strategies.

• Strategies to manage high risk of falls

For individuals identified to have a high risk of falls, a detailed fall history including circumstances and consequences of falls, as well as reports of near-falls, will provide information regarding likely triggers for falls. While pharmacological interventions and deep-brain stimulation surgery have limited impact on falls [122,123], it is recommended that medical review be undertaken to ensure optimal medical management of both motor (e.g., freezing of gait) and non-motor (e.g, orthostatic hypotension, cognitive impairment and depression) risk factors for falls, as well as consideration of common age-related fall risk factors such as polypharmacy and visual impairment. In addition, an assessment of potentially remediable risk factors such as freezing of gait, impaired mobility, impaired balance, reduced leg muscle strength and environmental risk factors is recommended (Table 1). Other risk factors such as cognitive deficits and fear of falling may also be amenable to intervention, and will impact on delivery and uptake of intervention. Therefore, identification of these risk factors allows clinicians to modify their approach based on the individual's known cognitive abilities and on whether the individual's self-reported level of fear of falling corresponds to actual fall risk [89,90].

Informed by the results of these evaluations and the patient's goals, the healthcare professional can identify and discuss with the patient interventions that are likely to be effective based on current evidence. Intervention for those at high risk of falls is likely to include avoidance of high-risk activities (e.g., walking and turning on a slippery surface while talking on the phone) and targeted physical interventions. Interventions such as suitably supervised challenging balance exercises and/or strategies to manage and reduce freezing episodes should be considered. Consideration should also be given to the acceptability of the interventions to the patient, as well as the timing of the proposed interventions. In the older population, it is recommended that interventions be introduced sequentially, rather than simultaneously [124].

• Strategies to manage low risk of falls

Fall prevention is often not addressed in the early stages of the disease when risk of falls is lower than at later stages. Yet, the strongest evidence to date is for the delivery of a single intervention (balance-challenging exercise) directed at individuals with lower disease severity and fall risk [58]. It is possible that deliberate targeting of balance may be a critical strategy for reducing falls in the longer term. Group-based or minimally supervised balance exercises are more likely to be sustainable than fully supervised individual exercise, and patients should be encouraged and supported in exploring community-based options that are acceptable to them. While the evidence to date has explored exercise programs designed specifically for people with PD, it may be that more general fall prevention programs are suitable for those with low fall risk.

There is little evidence to guide the approach to patients with moderate risk of falls. If on brief screening, key significant risk factors such as freezing of gait and/or poor cognition and/or impulsiveness are evident; or there is a history of multiple falls, an injurious fall, or dizziness or syncope resulting in a fall, then it would appear logical to manage as previously described for those at high risk. Otherwise, these individuals can be treated as low risk in the first instance. It is important to be mindful that people with PD are likely over time to move from one level of risk to another, so regular monitoring of falls and fall risk should be in place. Some cognitively intact individuals will be able to monitor their own risk using the three-step tool.

Conclusion & future perspective

This review shows that falls in people with PD can be predicted with high accuracy using a simple three-step clinical tool and that fully supervised balance-challenging exercise are effective in reducing falls. The key points emerging from this review are shown in the Practice Points, and it is notable that physical interventions that have successfully increased mobility and/or physical activity have done so without increasing falls. Nevertheless, despite considerable evidence for remediation of fall risk factors with physical interventions [51,57,92], as summarized in Table 1, there is limited evidence of translation of these improvements into prevention of falls. Falls are clearly complex and the majority probably result from interaction of multiple risk factors, including motor and non-motor PD-specific impairments, as well as comorbidities and age-related fall risk factors. Larger scale trials are required to determine the efficacy and cost–effectiveness of multifactorial fall prevention interventions and to elucidate those interventions most likely to be effective according to level of risk and individual risk factor profiles.

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