Cognitive Impairment in Fall-Related Studies in Parkinson’s Disease

Josefa M. Domingos\textsuperscript{a,b}, Catarina Godinho\textsuperscript{b,5}, John Dean\textsuperscript{c}, Miguel Coelho MD\textsuperscript{d}, Anabela Pinto\textsuperscript{d}, Bastiaan R. Bloem\textsuperscript{e} and Joaquim J. Ferreira\textsuperscript{a,b,*}

\textsuperscript{a}CNS – Campus Neurológico Sénior, Torres Vedras, Portugal
\textsuperscript{b}Clinical Pharmacology Unit, Instituto de Medicina Molecular, Lisbon, Portugal
\textsuperscript{c}Life Care Centers of America, Cleveland, Tennessee, USA
\textsuperscript{d}Department of Rehabilitation, Hospital Santa Maria, Lisbon, Portugal
\textsuperscript{e}Department of Neurology, University Medical Centre St Radboud, Nijmegen, The Netherlands
\textsuperscript{f}Laboratory of Clinical Pharmacology and Therapeutics, Faculty of Medicine, University of Lisbon, Portugal
\textsuperscript{g}Center for Interdisciplinary Research Egas Moniz (CiiEM), Instituto Superior de Ciências da Saúde Egas Moniz, Monte de Caparica, Portugal

Abstract
Background: There is increasing evidence to suggest a tight relationship between cognitive impairment and falls in Parkinson’s disease (PD). Here, we draw attention to a potentially significant flaw in the existent falls-related research, namely the apparent exclusion of patients with cognitive impairment or dementia.

Objective: Our objective was to review all published, on-going or scheduled fall-related intervention studies, in order to investigate the extent to which cognitively impaired individuals with PD were included in these studies.

Methods: We analyzed published controlled trials regarding falls and PD in commonly used databases, as well as relevant ongoing clinical trials registered within the World Health Organization database, clinicaltrials.gov and the European Clinical Trials Database.

Results: Fourteen of the fifteen published studies included had explicit cognitive exclusion criteria as part of their study protocol. Most of the 54 on-going PD fall-related studies excluded patients with cognitive impairment.

Conclusions: This suggests that individuals with cognitive impairment or dementia are excluded from fall-related research studies. We strongly recommend that future work in this area should include a representative sample of patients with PD, including subjects with cognitive decline.

Keywords: Falls, Parkinson disease, rehabilitation, cognition, clinical trials

INTRODUCTION
Parkinson’s disease (PD) is a complex heterogeneous neurodegenerative disorder. In order to capture the overall picture of PD, it is important to consider not only the typical motor problems such as tremor, bradykinesia, postural instability, and levodopa-induced motor complications, but also non-motor symptoms, such as pain, depression and cognitive impairment. Mild cognitive impairment (MCI) and PD dementia (PDD) are frequent and incidence increases with age, disease duration, and disease severity [1]. Even though there is still some debate regarding the definition, MCI is considered a cognitive decline that is not normal for age but with basically normal functional activities, and that appears to place patients at risk of progressing to dementia [1–3].
A growing body of class II evidence suggests that there is an increased risk of falls in the presence of cognitive impairment [4–7] as well as in dementia [8, 9] and this trend is present in both community-dwelling and institutionalized older populations. An evidenced based review from the American Academy of Neurology (ANN) pooled data from five studies and indicated an absolute risk of falling of 47% among individuals with dementia during study follow-up [6, 10–13]. Similar findings were reported in populations with PD [14–17]. A randomized, placebo-controlled, crossover, double-blind study demonstrated that one acetylcholinesterase inhibitor, donepezil, may have some symptomatic effect on cognitive deficits with a concomitant significant reduction in the number of falls in non-demented individuals with PD [18].

A more restrictive protocol that reduces or eliminates cognitively impaired individuals from fall intervention studies may have a substantive impact on the representativeness of the study sample. Consequently, current findings with respect to pharmacological [18] and non-pharmacological interventions [19–22] may fall short in providing the best possible evidence for appropriate management in individuals with cognitive impairment and may not be able to be extrapolated to this population. This methodological flaw was recently also highlighted in the study by Amar (2015) that defended that individuals with PD with moderate cognitive impairment face complex problems and warrant inclusion in falls research [23].

Ultimately, if individuals with MCI or dementia are at greater risk for falls, they should be included in specific fall-related research studies in order for the results of these studies to be relevant and applicable to the types of patients seen in actual clinical practice.

The primary goal of this review was to assess the extent of inclusion of individuals with PD and with MCI or dementia in published, on-going or in planning clinical controlled trials which had falls and/or fall-related outcomes.

MATERIALS AND METHODS

Study design: Systematic review

Literature search for published studies

We conducted a systematic search for all controlled trials regarding pharmacologic and non-pharmacological interventions for falls in PD that were published as full text papers up to May 2015. We used the electronic databases Medline, EMBASE, Cochrane Library Central Database and PEDro using the MeSH terms “PD”, or “Parkinson disease” AND “falls” AND “intervention” AND “prevention” to complete the literature search. Full text copies of potentially relevant trials were retrieved and their reference lists were systematically checked.

Literature search for ongoing studies

We also analyzed the major characteristics of ongoing clinical trials from the online open-access World Health Organization (WHO-ICTRP), the Clinical trial.gov database and the European Clinical Trials database (EudraCT) that proposed to evaluate the efficacy and/or safety of therapeutic interventions for the prevention or management of falls in PD. Within these databases, a search was performed for ongoing controlled trials regarding PD and falls using the following keywords: “Parkinson disease” AND “falls”. The studies were hand sorted to exclude duplicate entries and studies that were not related to therapeutic interventions for falls in PD. Data regarding study variables, particularly exclusion on the grounds of cognitive scores were extracted from each study.

Selection criteria for studies

We included published controlled trials regarding therapeutic interventions or prevention of falls for individuals with PD with fall or fall-related outcomes. The type of participants in these interventions included: individuals with a diagnosis of PD; any duration and stage of PD; all ages; any drug, surgical or rehabilitation interventions; and any duration of intervention.

Data extraction

From the published and the on-going trials reviewed we searched the following information for source of support:

a) General characteristics of the trials (scientific study name or main identification number, year of publication, authors, publication status, study design, exclusion criteria related to cognition status, control group, gait and falls related inclusion criteria, drop-outs and adverse effects);

b) Characteristics of participants (number of participants in each group, age, gender, diagnostic criteria, disease severity measures);

c) Characteristics of interventions (type of intervention - pharmacological, surgical, physiotherapy/occupational/speech, dose, mode of administration, duration of follow up);
d) Characteristics of outcome measures (primary outcome measure, secondary or other outcomes and assessment method used for fall recording).

We determined the number of trials that excluded participants due to cognitive impairment regardless of the definition of cognitive impairment used. Extraction of all data was conducted by two independent reviewers (JMD and CG), with disagreements resolved by a third rater (JD).

RESULTS

Characteristics of included studies

Regarding the published intervention-related studies, the search in the databases identified 722 records, of which 15 trials met the inclusion criteria for this review, in which a total of 1380 individuals participated (Fig. 1). There were 14 trials evaluating a non-pharmacological intervention and 1 trial for pharmacological intervention. Thirteen of the trials [19, 20, 22, 24–32, 45] had a parallel group design and two cross-over trials [18, 21]. Chung et al. [18] was a randomized, placebo-controlled, crossover design and double-blind trial. All trials were published in a full paper format. The trial characteristics of the 15 controlled trials that met our pre-defined inclusion criteria are summarized in Table 1.

Regarding the ongoing clinical trials, as of May, 2015, there were 19 registered trials regarding falls in PD in the WHO-ICTRP that met the inclusion criteria. From the European Clinical Trials database 2 additional clinical pharmacological trials were included. The main characteristics of all on-going trials are described in Table 2.

Participant characteristics

Participant characteristics of published trials were variable (Table 1). A clear diagnosis of PD was predominant with the exception of one published trial [26] which instead included participants with a diagnosis of Parkinsonism and no delineation of the characteristics of that terminology. The majority of the studies included individuals in stage II-III on the Hoehn and Yahr scale although six studies also included individuals in stage I [26]. The mean age of participants across trials ranged from 63 (±8.0) and 74.5 (±9.7) years. Fall history was a common inclusion criteria ranging from 2 or more falls in the previous 12 months to 2 or more near falls per week.

Participant characteristics of the on-going trials were also widely variable and are described in Table 2.

Exclusion criteria related to cognitive status

Fourteen of the fifteen published intervention-related studies (n = 14) had explicit cognition exclusion criteria included as part of the study protocol. One study did not mention cognition aspects in the exclusion or inclusion criteria [24]. Forty-two of the fifty-four of the on-going studies registered in the WHO, EudraCT and Clinical Trials.gov database also had explicit cognition exclusion criteria. Exclusion based on cognitive scores indicative of dementia was common. Eleven published and thirty-one on-going studies included in this review excluded participants based on a low Mini Mental Status Examination (MMSE) score (with the cutoff scores ranging from “less than 23” to “25 or lower”) (N = 42). Harro (2014) excluded participants if they had impaired cognitive functioning evidenced by a score of 20 or less on the Saint Louis Mental Status Examination (SLUMS) [27]. None of the studies specifically considered mild cognitive impairment as part of the exclusion criteria.

Due to the consistent nature of the exclusion of individuals with MCI or dementia, we were unable to analyze possible variables or characteristics that could be related to the rate of exclusion by MCI or dementia.

Intervention characteristics

The interventions being investigated were widely varied and predominately studies of non-pharma...
| Study, 2005 [26] | 19 participants | Significant dementia or other disorders of comprehension | Able to walk with firm, continuous support of one person to help carry weight or assist with balance. | Physiotherapy: treadmill walking for 20 minutes per day for 3 days | 6 weeks with 4 weeks follow-up | PRIMARY OUTCOMES: Fall register during Parkinson's disorders. | Randomised, Parallel, Stage 1–4 HY. Person to help carry weight or assist with balance. | RCT, Parallel. Stage 1–4 HY. Person to help carry weight or assist with balance. | Physiotherapy: treadmill walking for 20 minutes per day for 3 days | 6 weeks with 4 weeks follow-up | PRIMARY OUTCOMES: Number of falls during dynamic posturography. Posturography assessment. |
| Nieuwboer, 2007 [21] | 153 participants | Cognitive impairment (MMSE Scores <24) | Mild to severe gait disturbance with score 3–6 | Physiotherapy: 6 weeks with 6 weeks follow-up | SECONDARY OUTCOMES: Falling as a measure of possible adverse effects. Falls diary to measure possible adverse effects. | Randomised, Single-blind, Stage 3–4 HY. | Exercise group age: Parkinson's Disease Rating Scale (UPDRS; item 29). 3 weeks without training. | Exercise group age: Parkinson's Disease Rating Scale (UPDRS; item 29). 3 weeks without training. | 6 weeks with 6 weeks follow-up | SECONDARY OUTCOMES: Falling as a measure of possible adverse effects. Falls diary to measure possible adverse effects. |
| Study | Design | Participants | Inclusion Criteria | Interventions | Outcomes |
|-------|--------|--------------|-------------------|---------------|----------|
| Allen, 2010 | RCT with blinded assessment | 48 participants with PD | Significant cognitive impairment (MMSE <24), able to walk independently (with or without an aid), falls in the last year, or exercise at home 3 times per week | Physiotherapy: a monthly exercise class and 6-months | Number of Falls, Falls risk factors, fall prevention advice in the form of a booklet |
| Smania, 2010 | RCT | 64 participants with idiopathic PD | MMSE score <23 | Intervention group: balance training consisting of feedforward and feedback motor control training. Control group: active joint mobilization, muscle stretching, and motor coordination exercises. | Number of falls, Falls diary |
| Chung, 2010 | Randomized, placebo-controlled, double-blind, crossover | 23 participants with probable idiopathic PD | MMSE score <25, baseline frequency of falling or nearly falling 2 or more times per wall, or falling with a score of 25 cm or less on the Functional Reach test or if they failed to reach criterion on one of the balance tests in the QuickScreen Clinical Falls Risk Assessments. | Physiological: 6 weeks of donepezil or placebo with a 3-week washout between phases | Weekly postcards, Number of daily falls and near falls. |
| Reference | Participants | Cognitive status or exclusion criteria | History of previous falls | Physiotherapy | Intervention group | PRIMARY OUTCOMES | Secondary outcomes | Weekly diaries to |
|-----------|--------------|--------------------------------------|---------------------------|---------------|-------------------|----------------|------------------|------------------|
| Goodwin, 2011 | 130 participants | History of two or more falls in the previous year and who were able to mobilize independently. | | Physiotherapy | Intervention group strength and balance training | 10 week group | Number of falls | Register Falls and fall-related injuries |
| Li, 2012 | 195 participants | MMSE score <24 | Ability to stand unaided and walk with or without an assistive device. | | | 6 months with 3 | | Monthly fall calendars |
| Harro, 2014 | 20 participants with | Saint Louis Mental Status Examination (SLUMS) <20 or less. | Ability to walk continuously without physical assistance for 5 minutes with or without an assistive device. | | | 6 weeks training | | Monthly self-report |
| Volpe, 2014 | 34 participants with | MMSE score <25 | Ability to walk without any assistance | | | 2 months | | Falls diary or telephonic interview |

(Continued)
Table 1 (Continued)

| Study | Design                  | Stage | Fall History | Intervention | Control Group | Outcome Measures                                                                 |
|-------|-------------------------|-------|--------------|--------------|---------------|----------------------------------------------------------------------------------|
| Cannings, 2015 [20] | RCT, Parallel | Stage 2-4 HY | balance and lower limb fallers | 231 participants | PD-WEVB | Monthly falls diaries                                                               |
|        |                          |       |              | 60 minutes of treatment, five days a week for two months |                        |                                                                                  |
|        |                          |       |              |              |               | PRIMARY OUTCOMES: Falls rates and proportion of falls during the intervention period. |
|        |                          |       |              |              |               | Monthly falls diaries                                                               |
|        |                          |       |              |              |               | PRIMARY OUTCOMES: Falls rates and proportion of falls during the intervention period. |
|        |                          |       |              |              |               | Monthly falls diaries                                                               |
| Shen, 2015 [31] | RCT, Parallel | Stage 3-3 HY | technology assisted balance and gait training | 49 participants | MMSE score <23 | Ability to walk independently for 10 meters                                          |
|        |                          |       |              | 12-week intervention period |               | PRIMARY OUTCOMES: Number of fallers, fall rate, and the time to first fall.          |
|        |                          |       |              |              |               | Monthly phone calls                                                                |

(Continued)
Table 1 (Continued)

| Study, Year | Participants | MMSE Score | Fall Interventions | Route of Intervention | Primary Outcomes | Interventions | Control Group | Abbreviations |
|-------------|--------------|------------|--------------------|----------------------|------------------|---------------|---------------|---------------|
| Morris, 2015 [45] | 210 participants with PD, Stage 1-4 | MMSE score < 24 | Medically able and safe to perform the interventions. | Group 1: progressive resistance strength training coupled with falls prevention education. Group 2: movement strategy training combined with falls prevention education. Control group: life-skills information not related to falls. | 14 months, with an initial 8 weeks of intervention, followed by 12 months of ongoing falls measurement. | Monthly falls calendars. | 8 weeks of outpatient therapy once per week and a structured home program. | MMSE = Mini-Mental State examination; RCT = Randomized controlled trial; HY = Hoehn & Yahr; PDQ39 = Parkinson’s Disease Questionnaire. |
### Table 2
Ongoing Clinical trials characteristics with individuals with Parkinson’s disease regarding falls interventions from the WHO, EudraCT and Clinical trial.gov databases

| Source              | WHO | EudraCT | Clinical trial.gov |
|---------------------|-----|---------|--------------------|
| Number of studies   | 19  | 2       | 33                 |
| Study design        |     |         |                    |
| Randomized control  | 16  | 2       | 27                 |
| Controlled trial    | 3   | 0       | 6                  |
| Exclusion by cognition status | | | |
| Excluded based on mini mental score | 12  | 0       | 19                 |
| Excluded based on other cognitive parameter | 4   | 1       | 6                  |
| Missing data        | 3   | 1       | 8                  |
| Type of Intervention|     |         |                    |
| Pharmacological     | 2   | 2       | 8                  |
| Surgical            | 0   | 0       | 1                  |
| Physiotherapy/occupational | 17  | 0       | 24                 |
| Sample size         |     |         |                    |
| Inferior 50         | 8   | 0       | 19                 |
| Between 50-100      | 3   | 0       | 3                  |
| Superior 100        | 8   | 2       | 11                 |
| Disease Stage       |     |         |                    |
| Stage I-II          | 0   | 1       | 4                  |
| Stage II-III        | 3   | 1       | 4                  |
| Stage III-IV        | 7   | 0       | 14                 |
| Stage V             | 0   | 0       | 0                  |
| Missing data        | 9   | 0       | 11                 |
| Method of falls data collecting | | | |
| Diaries             | 6   | 0       | 7                  |
| Calendars           | 1   | 0       | 1                  |
| Post cards          | 0   | 0       | 0                  |
| Phone calls         | 1   | 0       | 2                  |
| Questionnaires      | 11  | 0       | 7                  |
| Missing data        | 0   | 2       | 16                 |
| Fall outcome measure|     |         |                    |
| Primary outcome     | 8   | 1       | 5                  |
| Secondary outcome   | 4   | 1       | 12                 |
| Study duration      |     |         |                    |
| Inferior 8 weeks    | 4   | 0       | 5                  |
| Between 8-24 weeks  | 4   | 0       | 17                 |
| Superior to 24 weeks| 8   | 2       | 9                  |
| Missing data        | 3   | 0       | 2                  |
| Recruiting Status   |     |         |                    |
| Recruiting          | 5   | 0       | 12                 |
| Non recruiting      | 2   | 0       | 2                  |
| Completed           | 12  | 0       | 13                 |
| Other               | 0   | 2       | 6                  |

WHO - www.who.int/trialsearch/AdvSearch.aspx. EudraCT – www.clinicaltrialsregister.eu/ctr-search. Clinical trial.gov - www.clinicaltrialsregister.eu/ctr-search.

(c)ological (i.e. rehabilitation based) interventions with only one pharmacological intervention [18] of a total of 15 published intervention-related studies used in this review.

In the on-going studies, 41 were non-pharmacological while only 12 were pharmacologically based. Physiotherapy was the primary component of the non-pharmacological interventions and included treadmill training alone or with turning exercises [15, 19, 27], cueing gait program [14, 27], strength and balance programs [12, 13, 16, 28, 29], home-based programs [16, 30], teaching strategies for falls prevention [13], tai chi and exercise programs [17], muscle power training [30, 45], technology-assisted balance and gait training [31], and hydrotherapy perturbation-based balance training [32]. The duration of the interventions varied from minimum 6 weeks to 6 months. The only pharmacological intervention consisted of 6 weeks of donepezil or placebo with a 3 week washout between phases.
Common outcome measures used for falls assessment

Outcome measures related to falls included: rates of falling, frequency of falls, frequency of near falls, fear of falling, number of fallers, and number of injurious falls. This was repeatedly measured by using falls diaries, calendars, postcards, and telephone reminders or interviews.

Drop-outs and adverse effects

There were limited reporting regarding adherence, adverse events and drop-outs. The study by Nieuwboer et al. [21] reported that one participant dropped out 3 weeks after randomization due to a necessary change of drug. Ashburn et al. [20] reported that drop-outs occurred in the intervention group (1 partner unwell, 1 disliked exercises, 1 died, 1 withdrew for no reason, 1 withdrew due to falls) and control group (4 unwell, 2 died, and 1 moved away). Allen et al. [19] described that the exercise group had no major adverse events but had 3 drops outs, 1 due to no longer wished to participate and 2 developed health problems unrelated to the intervention. Chung et al. [18] reported that 4 participants dropped out before the second phase (2 on active drug, 1 each during placebo phase and washout) and were excluded from the data analysis. Additionally, before the second crossover period, 2 more participants withdrew but were included in the analysis. Goodwin et al. [24] reported one pelvic fracture by a control group participant.

DISCUSSION

There is a lack of inclusion of individuals with PD with mild cognitive impairment and/or dementia in fall-related intervention studies and this continues to be prevalent in currently ongoing and scheduled trials. This may represent a serious methodological flaw with implications regarding the interpretation and clinical application of current and future fall interventions. This ultimately may lead to – at least partly – inadequate treatment recommendations for those who “really” fall (i.e. the cognitively impaired patients), and may really be useful only for a minority of the target population.

Cognitive status factors have long been recognized as having an important impact on management in PD but are frequently not addressed in the context of physiotherapy. In particular, impaired attention and executive function may exacerbate the difficulties with multitasking and contribute to falls. Cognitive impaired individuals often lose the capacity to prioritize tasks and when performing a dual task activity, they tend to reduce priority and/or attention to the gait or balance task, and focus more upon the completion of the secondary task [33]. This places these individuals at an increased risk for falling under complex multitask circumstances testing [34]. In a study by Alcock et al. [35], it was shown that the association of attentional deficits with postural instability translates into increased fall frequency measured prospectively over a 1 year study period. Another 12-month longitudinal cohort study of 102 older people without dementia (52 subjects with PD and 50 age and sex-matched controls) concluded that mild cognitive impairment might contribute to falls risk beyond conventional risk factors in older people with and without PD [14]. These findings raise a fundamental question. Should individuals with MCI and/or dementia be more widely considered or even recruited for specific fall intervention studies? Cognitively impaired individuals may be less able to comply with certain treatment and assessment components of trials and may also have higher adverse events and drop-out rates. Additionally, the design of clinical trials typically attempts to minimize confounding variables. Certain forms of cognitive impairment may independently contribute to falls (e.g., impulsive movements related to frontal lobe dysfunction). Hence, excluding cognitive impairment is defensible on these bases and so doing interventions to reduce falls should initially be shown as efficacious among non-demented PD patients. Subsequently, the strategy could be applied to those with cognitive impairment. Burton et al., (2015) [36] recently did a systematic review and meta-analysis to evaluate the effectiveness of exercise programs to reduce falls in older people with dementia who are living in the community. Three RCTs [37–39], with high quality and one single-group pre- and post-test pilot study [40] were included. Participants were included if they had a diagnosis by a doctor/specialist, or a validated test, such as the Mini Mental State Examination (MMSE), Saint Louis Mental Status Examination (SLUMS), the Clinical Dementia Rating Scale, or the National Institute of Neurological and Communicative Disorders and Stroke, Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA) Alzheimer’s criteria. Results from this review suggested that an exercise program may potentially assist in preventing falls of older people with dementia living in the community. If such inclusion is possible in people without PD but with dementia, it is plausible to think it can and should also be applied to PD patients with cognitive impairment.
A better understanding of the reasons that underlie the exclusion of individuals with cognitive impaired may allow clinicians and researchers to better identify possible solutions to overcome barriers associated to this exclusion. Due to the consistent nature of the exclusion of individuals with MCI or dementia in our review, we were unable to objectively analyze or identify any potential variables/characteristics (i.e. study type, number of participants, study duration, etc.) that could be related to the rate of exclusion by MCI or dementia. Additionally, the information provided by the WHO-ICTRP and in published trials was limited and insufficient to allow for a profound analysis of possible justifications for exclusion due to cognitive impairments. However, an important factor has to be noted. From our review, the reason for exclusion is dementia, as screened by tests of global cognitive dysfunction (i.e. Mini-Mental State Examination <24 and UPDRS part 1). Different data collection methods for cognition are an important future line of research in this area because instruments such as the MMSE may not identify specific cognitive deficits, such as executive and attentional deficits which are the type of frontal lobe deficits that are more impaired in fallers [41]. Alternative options could include the Montreal Cognitive Assessment (MoCA), which is sensitive to frontal lobe dysfunction and has been shown to be effective as a bedside test for evaluating the risk of falls [42].

Future studies should attempt to design assessment and intervention procedures that include individuals with cognitive limitations by considering several strategies. Screening for cognitive deficits should routinely be included in the work-up of individuals with falls so clinicians can become aware of the testing with regards to the individuals profile and cross reference this data with physical capacity. Actively involving carers in monitoring and encouraging participation between therapist visits for the assigned exercise program was identified as a facilitating factor for inclusions of individuals with dementia [38, 39]. Participants and families may be more likely to enter a clinical trial if they properly understand the potential health benefits (e.g. improved quality of life) that could be realized via free high-quality treatment and follow-up by expert clinicians as part of the study. Difficulties associated with traveling to a facility may be minimized if performing the follow-up evaluations in the participant’s home is considered. Incorporating telemedicine and/or remote monitoring may also enhance the ability of this population to participate in many studies. Targeted cognitive training may offer a novel treatment option for falls that is worthy of an increased research and clinical focus. If the degree of cognitive impairment can affect the success of interventions for falls prevention [43], cognitive training interventions may also be considered of particular interest to reduce this limitation as it may be able to improve cognitive processes thus reducing falls. Additionally, a study by Allan (2009) suggested that to prevent falls in mild-moderate dementia, possible management strategies could also include management of the potentially modifiable factors such as symptomatic orthostatic hypotension, autonomic symptoms and depression instead of prioritising strength and balance exercises that are more difficult for those with cognitive impairment to adhere [44]. Finally, appropriate resource support including financial support for such trials that recognizes the potential extra workload involved might better facilitate this recruitment. The existence of specific guidelines for recruiting cognitive impaired people may also increase the likelihood of researchers to recruit these individuals.

CONCLUSION

In conclusion, our findings suggests that due to the historical and ongoing exclusion of individuals with cognitive impairments, it is unclear if some intervention approaches for falls are effective and safe for this population. We highlight the substantial impact of restrictive protocol exclusion criteria on cognitive impaired PD patients. Even though participation of individuals with cognitive impairment in clinical trials may not always be desirable or feasible, it is still important to determine if they are disproportionately disqualified from participation and as a result, under-represented in these trials, particularly in relationship to their respective motor problems. Increasing participation of this population in clinical trials is critical in order to increase the external validity of the studies.

CONFLICT OF INTERESTS

Bastiaan R. Bloem has served as an editorial board member of Movement Disorders, currently serves as an editorial board member of Physiotherapy Canada, is Associate Editor for the Journal of Parkinson’s disease, received honoraria from serving on the scientific advisory board for Danone, Glaxo-Smith-Kline, UCB and received research support from the Netherlands Organization for Scientific Research, the Michael J. Fox Foundation, the Prinses Beatrix Foundation, the
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FINANCIAL DISCLOSURE/CONFLICT OF INTEREST RELATED TO RESEARCH COVERED IN THIS ARTICLE

All relevant disclosures and conflict of interests are detailed/described/listed at the end of this article.

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APPENDIX

List of Ongoing Clinical trials identification name and registry number from the WHO, EudraCT and Clinical trial.gov databases.

WHO

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WHO

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EudraCT

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Clinical trial.gov

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Clinical trial.gov

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