Exercise- and strategy-based physiotherapy-delivered intervention for preventing repeat falls in people with Parkinson's: the PDSAFE RCT

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NHS

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This report

Abstract

Exercise- and strategy-based physiotherapy-delivered intervention for preventing repeat falls in people with Parkinson's: the PDSAFE RCT

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Background: People with Parkinson's disease are twice as likely to experience a fall as a healthy older person, often leading to debilitating effects on confidence, activity levels and quality of life.

Objective: To estimate the effect of a physiotherapy programme for fall prevention among people with Parkinson's disease.

Design: A multicentre, pragmatic, investigator-masked, individually randomised controlled trial (RCT) with prespecified subgroup analyses.

Setting: Recruitment from NHS hospitals and clinics and community and social services in eight English regions with home-based interventions.

Participants: A total of 474 people with Parkinson's disease (i.e. Hoehn and Yahr scale stages 1–4) were recruited: 238 were assigned to a physiotherapy programme and 236 were assigned to usual care. Random allocation was 50 : 50.

Interventions: All participants received routine care; the usual-care group received an information digital versatile disc (DVD) and a single advice session at trial completion. The intervention group had an individually tailored, progressive, home-based fall avoidance strategy training programme with balance and strengthening exercises: PDSAFE.

Main outcome measures: The primary outcome was the risk of repeat falling, collected by self-report monthly diaries between 0 and 6 months after randomisation. Secondary outcomes included near-falls, falls efficacy, freezing of gait (FoG), health-related quality of life, and measurements taken using the Mini-Balance Evaluation Systems Test (Mini-BESTest), the Chair Stand Test (CST), the Geriatric Depression Scale, the Physical Activity Scale for the Elderly and the Parkinson's Disease Questionnaire.

Results: PDSAFE is the largest RCT of falls management among people with Parkinson's disease: 541 patients were screened for eligibility. The average age was 72 years, and 266 out of 474 (56%) participants were men. Of the 474 randomised participants, 238 were randomised to the intervention group and 236 were randomised to the control group. No difference in repeat falling within 6 months of randomisation was found [PDSAFE group to control group odds ratio (OR) 1.21, 95% confidence interval (CI) 0.74 to 1.98; $p = 0.447$]. An analysis of secondary outcomes demonstrated better balance (Mini-BESTest: mean difference 0.95, 95% CI 0.24 to 1.67; $p = 0.009$), functional strength (CST: $p = 0.041$) and falls efficacy (Falls Efficacy Scale – International: mean difference 1.6, 95% CI –3.0 to –0.19; $p = 0.026$) with near-falling significantly reduced with PDSAFE (OR 0.67, 95% CI 0.53 to 0.86; $p = 0.001$) at 6 months. Prespecified subgroup analysis (i.e. disease severity and FoG) revealed a PDSAFE differing effect; the intervention may be of benefit for people with moderate disease but may increase falling for those in the more severe category, especially those with FoG.

Limitations: All participants were assessed at primary outcome; only 73% were assessed at 12 months owing to restricted funding.

Conclusions: PDSAFE was not effective in reducing repeat falling across the range of people with Parkinson's disease in the trial. Secondary analysis demonstrated that other functional tasks and self-efficacy improved and demonstrated differential patterns of intervention impact in accordance with disease severity and FoG, which supports previous secondary research findings and merits further primary evaluation.

Future work: Further trials of falls prevention on targeted groups of people with Parkinson's disease are recommended.

Trial registration: Current Controlled Trials ISRCTN48152791.

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Glossary

Catechol-*O*-methyltransferase inhibitor A drug that inhibits the action of catechol-*O*-methyltransferase.

List of abbreviations

A&E	accident and emergency	Mini-BESTest	Mini-Balance Evaluation Systems Test
CEA	cost-effectiveness analysis	MMSE	Mini-Mental State Examination
CEAC	cost-effectiveness acceptability curve	MoCA	Montreal Cognitive Assessment
CI	confidence interval	NICE	National Institute for Health and Care Excellence
CONSORT	Consolidated Standards of Reporting Trials	OR	odds ratio
CST	Chair Stand Test	PASE	Physical Activity Scale for the Elderly
DVD	digital versatile disc	PDQ-39	39-item Parkinson's Disease Questionnaire
EQ-5D-3L	EuroQol-5 Dimensions, three-level version		
FES-I	Falls Efficacy Scale – International	PPI	patient and public involvement
FoG	freezing of gait	PSS	Personal Social Services
FRR	falls rate ratio	PSSRU	Personal Social Services Research Unit
GDS	Geriatric Depression Scale		
GLM	generalised linear model	QALY	quality-adjusted life-year
GP	general practitioner	QoL	quality of life
HRQoL	health-related quality of life	RCT	randomised controlled trial
H&Y	Hoehn and Yahr	SAE	serious adverse event
ICER	incremental cost-effectiveness ratio	SD	standard deviation
		T	time
ICF	*International Classification of Functioning, Disability and Health*	T1	time 1, prior to commencement of PDSAFE
IQR	interquartile range	T2	time 2, 6 months later
ITT	intention to treat	TIDieR	Template for Intervention Description and Replication
MDS-UPDRS	International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale		

Plain English summary

People with Parkinson's disease fall often. Falls are scary and make moving about harder. The PDSAFE trial tested a new 'home physiotherapy' programme for reducing falls. People with Parkinson's disease were allocated to one of two groups by chance: they either received the PDSAFE exercises or just normal care. The costs were looked at and people were asked for their views of the PDSAFE exercises.

To take part, people had to have Parkinson's disease, live in their own home, be able to walk, have had at least one fall in the previous year and pass a memory test. PDSAFE was taught by physiotherapists and included exercises and fall avoidance strategies. Everyone had to record falls on a monthly calendar, and balance, strength and walking were tested.

To our knowledge, this was the largest falls trial looking at people with Parkinson's disease in the world: 541 people took part. The number of falls an individual reported differed a lot between people. When all people with Parkinson's disease in the trial were considered, the physiotherapy programme did not reduce falls in the first 6 months. However, it was found that some people had fewer falls after taking part in the exercises, whereas others did not. Those with more severe Parkinson's disease (i.e. problems with movement, memory and freezing of gait) fell more often after the PDSAFE intervention, even though their balance and confidence improved. Those with good memory, moderate disease and two or three falls in the previous year reacted well to PDSAFE and had fewer falls. It was found that PDSAFE reduced near-falls (about to fall but managed to save themselves) and improved balance and confidence. The physiotherapists and those who took part liked the programme and felt that it helped, but it was expensive to run.

In conclusion, a falls prevention programme should be based on each person's needs and a different treatment should be used for those with more severe Parkinson's disease.

Scientific summary

Background

People with Parkinson's disease are twice as likely to fall as the healthy older population. In those with Parkinson's disease, falling is associated with a host of risk factors, including disease severity, duration of disease, self-reported disability and impaired mobility. The strongest predictor of falling, identified from meta-analysis, is having had a previous fall. Evidence suggests that an exercise-based intervention might reduce fall risk, although published research findings are inconclusive.

Objective

The primary aim was to examine the clinical effectiveness and cost-effectiveness of an exercise- and strategy-based intervention (known as PDSAFE) for fall reduction.

Method

This two-group multicentre, single-blinded, randomised (50 : 50) controlled clinical trial of people with Parkinson's disease at risk of falls also comprised a 3-month pre-randomisation monitoring of falls, an economic evaluation and a nested qualitative study of the views of participants.

Participants

Eligibility criteria were as follows: a consultant's diagnosis of Parkinson's disease; living in their own home; independently mobile; experienced at least one fall in the previous 12 months; scored ≥ 24 on the Mini-Mental State Examination (MMSE); had the cognitive ability to give informed consent; able to understand and follow commands; and able to complete a guided personalised exercise and strategy programme.

Outcomes

The primary outcome was risk of repeat falling between 0 and 6 months post randomisation with the fall rate ratio during the same period as a secondary analysis. Data on falls were collected via monthly self-completed diaries. A fall was defined as an event that resulted in a person coming to rest unintentionally on the ground or lower level; a near-fall was an event in which the person would have landed on the ground or lower level if saving reactions, such as stepping or reaching, had not taken place.

Secondary outcomes were balance [measured by the Mini-Balance Evaluation Systems Test (Mini-BESTest)]; functional strength (measured by the Chair Stand Test); falls efficacy [measured by the Falls Efficacy Scale – International (FES-I)]; near-falls, an event in which the person would have landed on the ground or lower level if saving reactions, such as stepping or reaching, had not taken place; freezing of gait (FoG) (measured by the new freezing of gait questionnaire); and the results of the Geriatric Depression Scale (GDS) (15-question version); the 39-item Parkinson's Disease Questionnaire (PDQ-39), a quality-of-life measure designed specifically for people with Parkinson's disease; the EuroQol-5 Dimensions (EQ-5D), a measure of health-related quality of life; and the Physical Activity Scale for the Elderly (PASE). Disease severity was recorded using the International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and cognitive ability was measured using the Montreal

Cognitive Assessment (MoCA). Outcomes were assessed before randomisation and at 6 and 12 months after randomisation. Owing to restricted funding, the last 132 participants recruited were followed to 6 months (primary outcome only).

Pre-stated analysis

The primary outcome was risk of repeat falling between 0 and 6 months post randomisation using self-completed monthly falls diaries with falls rate ratio (incidence rate of falls in time period) and prespecified subgroups as secondary analysis plus secondary outcomes. Outcomes were assessed before randomisation and at 6 and 12 months post randomisation.

Results

A total of 541 people with Parkinson's disease were screened for eligibility and pre-randomisation fall monitoring by a trial assessor in their own home. Of these, 67 were excluded at this time [reasons for not being randomised included being medically unfit ($n = 24$), inadequate completion of falls diaries ($n = 6$), no longer met eligibility criteria ($n = 12$), or changed their mind or did not like the sound of intervention ($n = 18$)]. The remaining 474 participants completed a baseline assessment and were randomised into one of two groups: control ($n = 236$) or PDSAFE intervention ($n = 238$). Males constituted 56% of the trial participants, the mean age was 72 years and the Hoehn and Yahr scale ranges were 1–4 stage.

Loss to follow-up

Sixty-six participants did not engage with the intervention for a number of reasons, such as admission to a care home, deteriorating health, a change of mind about participation, reluctance to commit to the therapy or assessment procedures, and death. Some participants did not provide a reason for non-engagement. A further 20 participants withdrew from the control group.

Therapy content

The PDSAFE intervention, delivered by a physiotherapist, was individually tailored and structured around fall avoidance strategies and balance and strengthening exercises, selected from a menu with six levels of progression. The median number of therapy sessions was 12 (interquartile range 11–12 sessions) and the mean was 11 sessions (standard deviation 2.4 sessions).

Effectiveness

No difference in repeat falling within 6 months of randomisation was found [PDSAFE to control odds ratio (OR) 1.21, 95% confidence interval (CI) 0.74 to 1.98; $p = 0.447$]. Analysis of secondary outcomes demonstrated better balance (Mini-BESTest: mean difference 0.95, 95% CI 0.24 to 1.67; $p = 0.009$) and falls efficacy (FES-I: mean difference –1.6, 95% CI –3.0 to –0.19; $p = 0.026$), with near-falling significantly reduced with PDSAFE (OR 0.67, 95% CI 0.53 to 0.86; $p = 0.001$) at 6 months. Prespecified subgroup analysis (disease severity and FoG) revealed a PDSAFE differing effect. A decrease in falling among those in the moderate group classified by disease (interaction $p = 0.009$) and retrospective falling at entry to the trial (interaction $p = 0.050$). Increased repeat falling following PDSAFE between 0 and 6 months was found among those at the severe end of the disease spectrum and FoG (interaction $p = 0.025$) with a trend of increasing falls among those with cognitive impairment (interaction $p = 0.088$).

Participant views

Most people enjoyed participating in the therapy and reported benefits, although they had mixed views about equipment. The biggest barriers were time and motivation, whereas social support facilitated participation. In order to optimise the benefits of the therapy, people with Parkinson's disease need help for them to mobilise sustained support and encouragement from social support networks.

Economic evaluation

The results showed that the PDSAFE intervention was not likely to be cost-effective for the overall Parkinson's disease population for the NHS perspective over the 6-month time horizon. Compared with the control group, the PDSAFE intervention group had an incremental cost of £925 (95% CI £428 to £1422) and an incremental quality-adjusted life-year (QALY) gain of 0.008 (95% CI 0.006 to 0.021), generating an incremental cost-effectiveness ratio (ICER) of £120,659 per QALY. Although this ICER would not be deemed to be within the realms of what is considered cost-effective, sensitivity analyses reveal cost-effective scenarios.

Conclusions

The physiotherapy programme PDSAFE was not effective in reducing repeat falling across a heterogeneous sample of people with Parkinson's disease. However, fall risk, balance, functional strength, self-efficacy and near-falls improved. Secondary analysis also showed diverse responses to PDSAFE falls management according to FoG and disease severity. A negative effect was found among those participants at the worse end of the spectrum and a positive effect was found among those participants with moderate disease.

Trial registration

This trial is registered as ISRCTN48152791.

Funding

Chapter 1 Background

Introduction

Parkinson's disease

Parkinson's disease (hereafter referred to as Parkinson's) is a progressive neurological condition characterised by impairments of movement and postural control (balance) and non-motor deficits.[1] There are estimated to be around 127,000 people with Parkinson's in the UK.[2] The prevalence of Parkinson's increases steadily with age.[2]

Falls in Parkinson's

Falls among people with Parkinson's are both common and disabling.[3,4] Approximately 40–70% of people with Parkinson's fall each year, and one-third fall repeatedly.[5] Overall, people with Parkinson's are twice as likely to experience falls as a healthy elderly population.[6] There is evidence to show that falls have a major impact on the lives of people with Parkinson's, including debilitating effects on confidence,[7] decreased activities levels[8,9] and reduced quality of life.[10] Such falls are financially costly for individuals and health-care systems. Repeat falls are a risk factor for further falls and carry devastating consequences, such as fractures, immobility and fear of falling leading to dependency and social isolation.[4] Although the incidence of falling increases with disease severity, falls are common even in the early stages of the condition.[11]

Falling among those with Parkinson's is associated with a host of risk factors, including disease severity, duration of disease,[12,13] self-reported disability[12] and impaired mobility,[11] as confirmed by Canning *et al.*[6] The strongest predictor of falling, identified from meta-analysis, is having had a previous fall.[4,6] Loss of motor control [e.g. anticipatory and reactive postural control, reduced leg muscle strength, proprioception and gait speed, increased gait variability and freezing of gait (FoG)] have also been shown to be associated with, and predictors of, falls.[14,15] In addition to the motor symptoms, impaired cognition and orientation,[14] as well as misjudgement and distraction,[16] have also shown significant association with falling.

Falls prevention

Drugs are the main treatment used to manage the symptoms of Parkinson's, while research into finding a cure continues. However, reduced postural control and falls do not respond to medication.[3] It has long been accepted that exercise is a fundamental component of treatment for people with Parkinson's, alongside medical and surgical management, and its positive effects on symptoms are well supported in the literature. There is substantial evidence showing that regular exercise can be particularly beneficial for people with Parkinson's to maintain postural control, mobility, daily living activities and general symptom management.[17,18] At the conception of this trial, there was no definitive evidence that an exercise programme would be as effective in the population of people with Parkinson's as it is in the general population. Research has also shown that selecting and targeting each of the symptoms independently may not be enough to influence the falls rate. Instead, a multidimensional model that combines functional exercises with behavioural strategies is likely to provide a greater influence on reducing falls.[19]

PDSAFE is an example of a multidimensional programme.[19] It is an individualised, home-based, physiotherapist-delivered, personalised treatment programme of exercises and strategies to help prevent falls in Parkinson's. The novelty lies in both the content (i.e. disease-specific exercises and strategies for instability, use of motor relearning and cognitive awareness) and delivery [i.e. personalised feedback using a digital versatile disc (DVD) for adherence and self-management]. The programme comprises (1) exercises for postural control, gait and muscle weakness; (2) strategies for reducing freezing and encouraging stability and gait efficacy; and (3) a feedback model to promote learning and adherence. Frequency of intervention sessions is faded over time, 1 hour twice a week for 1 month, then once a week for a further 2 months, then once a month for another 3 months.

Primary aim of the PDSAFE trial

The primary aim of this trial was to determine the clinical effectiveness and cost-effectiveness of a novel personalised exercise and strategy intervention (PDSAFE) as a supplement to usual health-care management in people with Parkinson's.

Research questions

- Do fallers with Parkinson's who undertake PDSAFE with usual care have fewer falls than those who do not undertake the treatment programme during months 0–6 after randomisation?
- Do fallers with Parkinson's who undertake PDSAFE with usual care have fewer falls than those who do not undertake the treatment programme during months 6–12 after randomisation?
- Do fallers with Parkinson's who undertake PDSAFE have better balance, mobility and quality of life than those who do not undertake the treatment programme?
- Is the PDSAFE intervention cost-effective, compared with usual care for people with Parkinson's, from an NHS perspective?
- What are the personal insights of those who participate in the intervention?

Pilot study

Aims and objectives
Prior to the main trial, a small pilot study was conducted as part of the protocol development work. The aims of the PDSAFE pilot study were to confirm the:

- content and delivery of the novel intervention
- implementation of procedures for recording and checking treatment fidelity
- battery of assessments to be administered at the baseline and follow-up visits.

The objectives of the PDSAFE pilot study were to:

- recruit a sample of up to 20 people with Parkinson's: up to 10 in Southampton and up to 10 in Newcastle
- take informed consent from up to 20 people with Parkinson's
- complete screening measures on up to 20 people with Parkinson's
- test the collection of falls data through the use of diaries with up to 20 people with Parkinson's
- complete baseline assessments with up to 20 people with Parkinson's
- assess the time taken to complete assessments
- determine the feasibility of assessments
- determine the acceptability to participants of assessments
- deliver the PDSAFE intervention to up to 20 people with Parkinson's.

Procedure
Ethics approval was given by the South Central – Hampshire B National Research Ethics Service (reference number 13/SC/0538). Sixteen participants were recruited [six from Newcastle and 10 from Southampton, including one patient and public involvement (PPI) representative]. All participants completed all screening measures [i.e. Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Hoehn and Yahr (H&Y) scale and falls characteristics]. Six participants from each site completed baseline assessments, participated in the intervention for 1 month and completed the battery of assessments post intervention. The remaining four participants in Southampton provided falls diaries only, to test the diary completion required prior to randomisation in the main trial.

Two patterns of treatment delivery were tested to establish the most appropriate way of providing the intensity of treatment in the early stages. In Newcastle, participants had the intervention for two sessions a week for 3 weeks, then once a week for 1 week. In Southampton, participants had treatment for two sessions a week for 2 weeks and then once a week for 2 weeks.

Outcome

Overall, the participants enjoyed the treatment. Participants' comments included 'very pleased he participated – he has found it very beneficial and continues to use several strategies', 'Doing all home exercises and feels his balance is getting better' and 'have enjoyed the exercises and have learned a lot about keeping active'.

The therapists were enthusiastic about the programme and recognised the importance of mapping the house for problem mobility areas and integrating the exercises with video strategies appropriate for each individual. They commented that there was a lot to do in the initial stages around planning the strategies and fitting the weighted vests, so the pattern of treatment of two sessions a week for 3 weeks may be more valuable than two sessions a week for 2 weeks. However, it was agreed that this may not be appropriate for each person and that some flexibility in the way the sessions are delivered should remain. Training was recognised as very important. Some people found the weighted vests difficult to put on and required help from their partner; most people could tolerate only a small percentage of body weight in the vests, yet most people viewed them positively.

The outcomes of the pilot study were discussed at a face-to-face meeting of the grant holders, which was also attended by three PPI members; adjustments to the protocol were suggested and implemented. The pilot study confirmed the content and delivery of the novel intervention for the main trial (including printed versions of the exercises and strategies, video vignettes for play on a tablet or DVD and the use of weighted vests for strengthening exercises). Procedures for recording and checking treatment fidelity were also established, including weekly telephone and Skype™ (Microsoft Corporation, Redmond, WA, USA) consultations with the physiotherapists. As a result of the pilot, the assessment time was shortened and procedures tightened. For example, the handgrip strength measurement test[20] was dropped from the main study, but retained as a substudy in the Portsmouth area; and the shorter (15- instead of 30-question) version of Geriatric Depression Scale (GDS) was used.

Chapter 2 Methods

Material in this chapter has been adapted from the trial protocol by Goodwin *et al.*[21] © Goodwin *et al.*;[21] licensee BioMed Central. 2015. This article is published under license to BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.

Trial design

The PDSAFE trial was a UK, multicentre, community-based, single-blind, randomised controlled trial (RCT) with a 12-month follow-up, with nested economic evaluation and qualitative studies. Ethics approval was given by the South Central – Hampshire B National Research Ethics Service (reference number 14/SC/0039). Local research and development approval was obtained at each participating centre. *Figure 1* shows how people with Parkinson's progressed through the trial.

Initially, four recruitment centres were identified: Southampton, Portsmouth, Bournemouth and Poole, and Exeter. The aim was for each of these to recruit 150 people with Parkinson's to the trial over a 16-month period. Unfortunately, there were several delays in site set-up, and several sites found that they did not have as many people with Parkinson's as anticipated. Four additional sites were opened: Newcastle, Winchester and Basingstoke, Plymouth and Truro. These centres represent a range of socioeconomic environments. Unfortunately, it was not possible to secure additional funding to follow up participants recruited in these new centres beyond the primary outcome measure at 6 months. Therefore, only participants randomised before 1 May 2016 had a final 12-month assessment.

Participants

Inclusion criteria were broad to allow inclusion of a wide spectrum of Parkinson's patients in order to provide a generalisable result. Participants were eligible to be included to the trial if they met the following criteria:

- had a confirmed consultant's diagnosis of Parkinson's
- lived at home
- had experienced at least one fall in the previous 12 months
- were able to give informed consent
- were able to understand and follow commands
- were able to complete a programme of exercises
- scored ≥ 24 on the MMSE
- were willing to participate.

Participants were not eligible to be included in the trial if they:

- lived in a care home with or without nursing
- required assistance from another person to walk indoors
- were wheelchair bound or bedridden unless aided, as defined by H&Y scale stage 5.
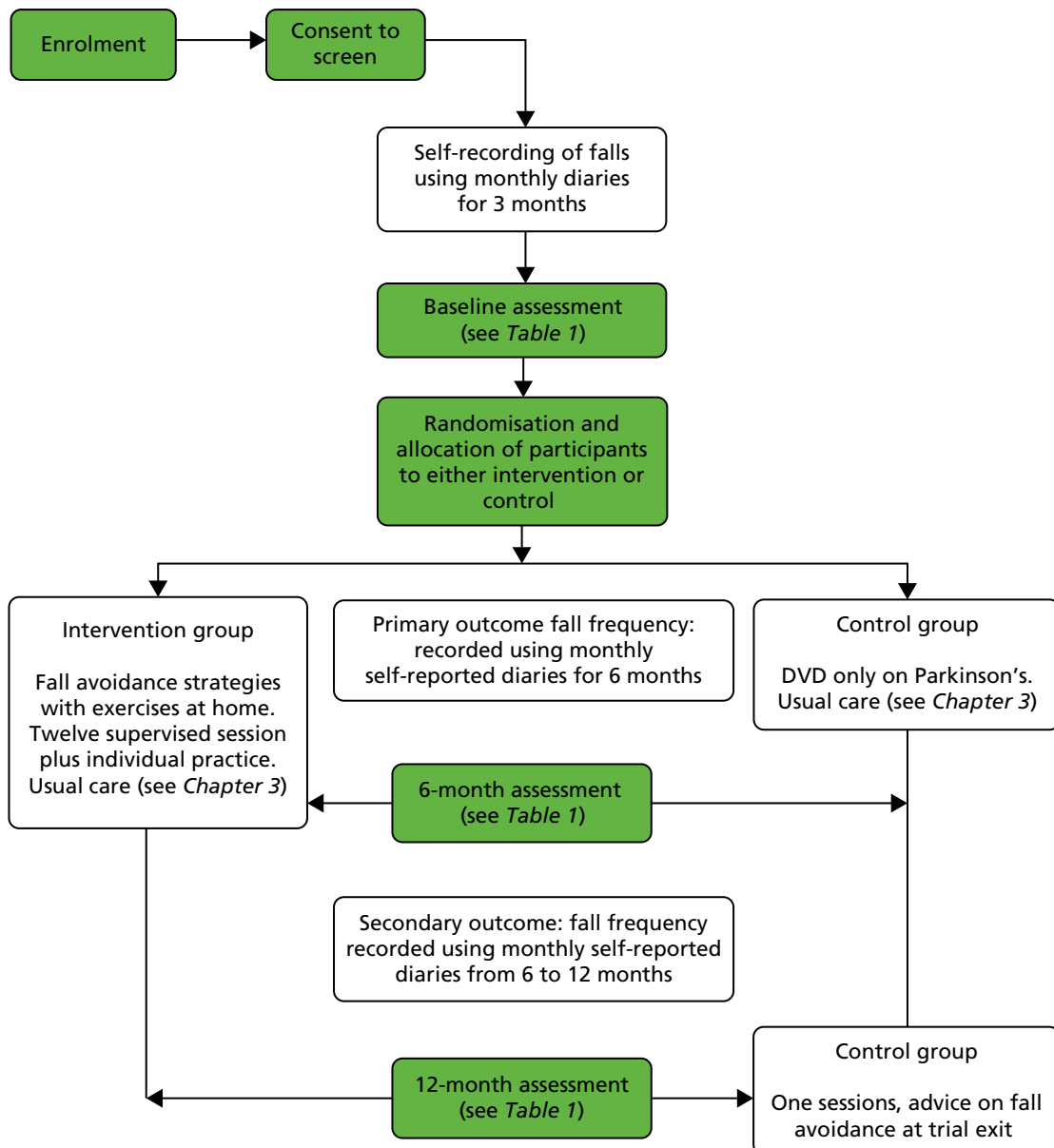
FIGURE 1 Diagram showing trial plan.

Recruitment and selection

Recruitment ran from July 2014 to August 2016. Trial participants were recruited through hospital clinics and Parkinson's services, through local Parkinson's UK groups and websites and through word of mouth/the trial website. Research packs comprising an invitation (see *Appendix 1*), the participant information sheet (see *Appendix 2*), a response slip (see *Appendix 3*) and a Freepost pre-addressed envelope were distributed. Once response slips were received by the trial office, trained trial assessors visited potential participants in their own homes to complete consent and screening assessments. The screening assessments included MoCA,[22] the MMSE, [23] the H&Y scale,[24] demographic information and medical history. Participants were asked to retrospectively recall the number of falls that they had experienced in the previous 12 months. The screening visit was followed by a prospective falls monitoring period of at least 13 weeks.

Three months after a screening visit, the assessor returned to carry out the baseline assessment (October 2014 to November 2016). The assessor checked that the participant was willing to participate in the trial and that they met the criteria to enable them to proceed to the next stage of the trial; the assessor then

conducted the baseline assessments with people with Parkinson's and initiated the randomisation procedure but was blinded to the group allocation. Blinded assessments were repeated 3, 6 and 12 months following randomisation (up to November 2016). Participants recruited during the extension period (those randomised after 1 May 2016) were followed to the primary outcome (6 months) only because of restricted funding.

Randomisation and therapy allocation

Patients were randomised (50 : 50) to receive PDSAFE (intervention group) or usual care plus provision of a Parkinson's information DVD (control group), using an online randomisation service at the Oxford Clinical Trials Research Unit, University of Oxford. Random allocations were computer-generated, stratified by centre and allocated in blocks with a random size of two, four, six or eight participants. This ensured that the allocated groups within centres were as evenly distributed as possible, while maintaining a system in which allocations were unlikely to be deduced by those needing to remain blinded. The randomisation outcome was e-mailed to the trial co-ordinating centre via the PDSAFE e-mail address and forwarded to the therapy team. The assigned therapist contacted participants within 2 days to inform them of the randomisation outcome and arrange the first visit with them (within 2 weeks for those in the intervention group and within 4 weeks for those in the control group). The same therapist at each site saw control and intervention participants.

Participants in the control group continued to receive their usual care. In addition, they were given a DVD, produced by Parkinson's UK, containing information about living with Parkinson's (this was not falls-specific information). A physiotherapist visited the control group participants after randomisation to explain their allocation and the importance of the control group; at the end of the trial, once their final follow-up assessments had been completed, control group participants received guidance on physical activities and strategies for postural control and safety in accordance with their profile of fall events.

For a full description of the PDSAFE intervention refer to *Chapter 3*.

Outcome measures

The outcome measures are summarised in *Table 1*. The primary outcome was risk of repeat falling in the first 6 months after randomisation. A fall was defined as an event that resulted in a person coming to rest on the ground or other lower level not as a result of a major intrinsic event or overwhelming hazard.[25] A near-fall was deemed to have occurred when an individual felt that they were going to fall but managed to prevent themselves from doing so.[26] Fall events (falls and near-falls) were recorded using monthly self-completed diaries, which have been used successfully in other studies.[16] Diaries were given to participants by assessors during the visits to conduct screening, baseline and follow-up assessments. The assessors explained to participants how the diaries should be completed and left writing instructions. Participants were asked to return diaries by post each month in a Freepost envelope provided. See *Appendix 4* for copies of falls diaries and instructions.

Secondary analysis of the primary outcome measure included rates of falling between 0 and 6 months. Secondary outcomes included risk of repeat falling between 6 and 12 months; rates of falling between 6 and 12 months post randomisation; the Mini-Balance Evaluation Systems Test (Mini-BESTest), a test of balance control;[27] the Chair Stand Test (CST); the new freezing of gait test, a questionnaire on FoG;[28] the 39-item Parkinson's Disease Questionnaire (PDQ-39), a quality-of-life measure designed specifically for people with Parkinson's;[29] the short, generic quality-of-life measure known as EuroQol-5 Dimensions (EQ-5D) for economic evaluation;[30] the Geriatric Depression Scale (GDS), 15-question version;[31] the Falls Efficacy Scale – International (FES-I);[32] and the Physical Activity Scale for the Elderly (PASE).[33] The International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS-UPDRS) – motor section,[34] MoCA,[22] data on medications, use of professionals and exercise activity

TABLE 1 Summary table of screening instruments and outcome measures

Screening measure	Source	Time point
MoCA	Assessor	Screening visit
Retrospective recall of falls over the previous 12 months		
MMSE		
H&Y scale		
Demographic information and medical history		
Primary measure		
Fall events 0–6 months (falls)	Monthly self-report diaries	Completed from screening visit to end of participation in trial (maximum of 15 months)
Measures		
Fall events 0–6 months (near-falls and fractures)	Monthly self-report diaries	Completed from screening visit to end of participation in trial (maximum of 15 months)
Fall events 6–12 months (falls, near-falls and fractures)	Monthly self-report diaries	
Mini-BESTest (a test of postural control/balance control)	Assessor	Completed at baseline and at each follow-up assessment (at 3, 6 and 12 months)
Timed CST		
Handgrip strength test (substudy in one area only)		
PASE		
PDQ-39 (a quality-of-life measure designed specifically for people with Parkinson's)		
GDS – 15-question version	Self-report	
FES-I		
NFoG test [a questionnaire on FoG (freezing is closely linked to falling)]		
Medication use		
MDS-UPDRS – motor section		
Health professionals and exercise		
Economic measures (people with Parkinson's)		
Health and social care resource use sheet	Assessor	Completed at baseline and at each follow-up assessment (at 3, 6 and 12 months)
EQ-5D	Self-report	
Economic Measures (carer)		
Carer demographic information and caring role	Self-report	Completed at baseline and at each follow-up assessment (at 3, 6 and 12 months)
CES	Self-report	
CSI	Self-report	

CES, Carer Experience Scale; CSI, Caregiver Strain Index; CST, Chair Stand Test; EQ-5D, EuroQol-5 Dimensions; FES-I, Falls Efficacy Scale – International; MDS-UPDRS, International Parkinson and Movement Disorder Society – Unified Parkinson's Disease Rating Scale; Mini-BESTest, Mini-Balance Evaluation Systems Test; NFoG, new freezing of gait; PASE, Physical Activity Scale for the Elderly; PDQ-39, 39-item Parkinson's Disease Questionnaire.

outside the trial were not regarded as outcome measures, but were measured at all time points for characterisation of the population. The Carer Experience Scale[35] and the Caregiver Strain Index[36] were administered to carers at baseline and follow-up time points to capture some broader effects of the intervention.

Power and sample size

Primary outcome: risk of repeat falling between 0 and 6 months

The power and sample size calculations were based on the findings of a previous trial by Ashburn *et al.*[37] This was a rehabilitation trial similar to PDSAFE in design. In the EXSART trial,[37] the risk of repeat falling in a 6-month period was 68% in the control group and 56% in the exercise group. However, falls risk was anticipated to be lower in PDSAFE because EXSART was restricted to people who had fallen twice or more often in the previous year. Therefore, it was assumed that the risk of repeat falling between 0 and 6 months would be 63% for the control group and 50% for the intervention group. This required 228 participants per group, with data for analysis of 456 participants in total. Allowing for a 5% drop-out rate between randomisation and 6 months meant that 480 participants needed to be randomised. Furthermore, allowing for a 10% drop-out rate between agreeing to the 3 months pre-randomisation falls collection and randomisation meant that 534 participants needed to be recruited to the pre-randomisation falls collection period. In total, 541 participants were recruited to the pre-randomisation falls collection period. Power calculation scenarios are summarised in *Appendix 6*, *Tables 26* and *27*.

Power calculations (see *Appendix 6*) for rates of falling were based on Tango[38] and related to the number of falls during a fixed follow-up period, analysed using negative binomial regression conditioned on baseline counts: specifically, formula 23 in the paper[38] was used, assuming equal rates in the baseline and follow-up periods in the control group and a follow-up period of twice the length of the baseline. Anticipating a falls rate ratio (FRR) of 0.8 between 0 and 6 months post randomisation, that is a 20% reduction in the rate of falling in the intervention group compared with the control group, and based on a rate of 2.5 falls in the 3-month baseline period, 197 participants per group were required at analysis, which led to 488 participants being recruited to the pre-randomisation falls collection period.

Other scenarios were considered for the differences in risk of repeat falling or for the FRR (see *Appendix 6*, *Tables 26* and *27*) and generally led to recruiting fewer than 600 participants to the pre-randomisation falls collection period. All the calculations aimed for 80% power in 5% two-sided tests between the intervention and control groups.

Embedded substudies

Once people with Parkinson's were consented to take part in the main trial, participants were asked if they would be willing to take part in the qualitative substudy that ran alongside the main trial. The qualitative researcher contacted suitable participants on the basis of a theoretical sampling strategy (see *Chapter 5*). Forty–two selected participants from the intervention group agreed to partake in qualitative interviews, before and after receiving treatment (see *Chapter 5*).

At the point of recruitment, participants were asked if they had a carer. An information sheet was provided for the carer, along with an invitation letter, response slip and pre-paid Freepost envelope; the substudy explored carers' quality of life. If a carer expressed a wish to take part, they were invited to attend the participant's (people with Parkinson's) baseline visit and informed consent was taken from them at that time. There were 463 participants with a carer; 189 carers agreed to take part.

Statistical analysis

A statistical analysis plan was finalised before the data set was unblinded. An intention-to-treat (ITT) approach was used for the main analyses with data analysed on the basis of group allocation. When there were incomplete diaries, a participant was coded as a repeat faller if they reported two or more falls in their incomplete diaries or if there was a report of two or more falls from a retrospective recall at the end of the trial; otherwise, they were included as a non-repeat faller if they had completed $\geq 50\%$ diary days for the period in question. Participants not reporting two or more falls, completing $< 50\%$ of diary days and with no other indication of repeat falling during a follow-up period were excluded.

Repeat faller status during 0–6 months (primary outcome) and 6–12 months post randomisation was analysed in logistic regression controlling for site, age, gender, H&Y scale stage as a regressor, the logarithm of retrospectively collected number of falls in the year prior to screening, repeat fall status prior to screening and the logarithm of the prospectively collected rate of falling during the 3-month period prior to randomisation. A small quantity, 0.5, was added to numerators of the rates of falling so that participants with zero falls during the period were included; the results are not sensitive to the quantity added.[39] These controlling variables were finalised in a blind analysis without access to the group indicator, as specified in the analysis plan, and were included in all regression models. Rates of falling during the periods 0–6 months and 6–12 months post randomisation were examined in negative binomial models fitted with command nbreg in Stata® version 11 (StataCorp LP, College Station, TX, USA). The logarithm of a participant's days of diary follow-up was included in nbreg modelling as an offset.

Odds ratios (ORs) and FRRs are presented with 95% confidence intervals (CIs). The geometric means of individual participant rates (with 0.5 added to the numerator, as before) of falling during 6-month follow-up periods are presented as rates per 6 months to accommodate the skewed distribution across participants. Prespecified subgroup analyses for falling between 0 and 6 months post randomisation were undertaken to identify the differential impact of the intervention according to MoCA status (≤ 25 and ≥ 26) and freezing status, and removing participants with most severe disease by virtue of the MDS-UPDRS (≥ 58) and H&Y scale stage (1–3). Differential effects were further explored on the basis of MoCA, MDS-UPDRS and number of falls in the year prior to screening by creating subgroups defined by tertiles at baseline. All the subgroup analyses involving tertiles were exploratory, that is they were not pre-stated. Both MoCA and MDS-UPDRS had been pre-stated but with different cut-off points and had shown some indication of differential effects.

Retrospective falls recall was examined by Canning et al.[40] as pre-stated subgroups but with different cut-off points; we wished to check the statistically significant interactions that they reported. Therefore, the decision was taken to examine subgroups defined by tertiles, not selected cut-off points. Subgroup analysis started with likelihood ratio tests for interaction in logistic models and Wald tests for interaction in the negative binomial models. Within-subgroup intervention effects are presented with 95% CIs. A secondary per-protocol analysis was carried out, as prespecified, by excluding participants from the PDSAFE group who received fewer than seven of the planned 12 sessions. A similar approach to analysis was followed for continuous secondary outcomes, additionally controlling for the outcome assessed at baseline. Analysis was conducted in SPSS version 24 [(Statistical Product and Service Solutions) SPSS Inc., Chicago, IL, USA] and Stata.

Safety reporting

Following a full risk assessment, PDSAFE was classified as a low-risk trial and, as such, in agreement with the ethics committee and sponsors, proportional safety reporting was implemented. Incidents of hospitalisation and disability, falls or incapacity are expected among this patient population. Therefore, only death, life-threatening events or new disability leading to prolonged hospitalisation attributed to the trial intervention were considered to be serious adverse events (SAEs). Similarly, any hospitalisation that was planned prior to randomisation or that could not be attributed to the PDSAFE intervention or assessments was not recorded

as a SAE. Adverse events, such as hospitalisations, changes in health status and falls, were collected routinely as part of follow-up assessments and were monitored for potential SAEs. Falls diaries were also reviewed: if a fall resulting in hospitalisation had happened while someone was participating in the PDSAFE intervention and trial assessments, it would have been recorded as a SAE, but no one had such an event. All suspected SAEs were reviewed by Professor Helen Roberts, a medical physician, who adjudicated whether or not they were related to the trial activity.

An independent Data Monitoring Committee was established. The group met regularly throughout the trial to undertake interim reviews of the trial's progress, including the review of updated figures on recruitment, data quality, adherence to protocol and follow-up, and main outcomes and safety data. Falls rates in particular were monitored.

Patient and public involvement

Patient and carer involvement was incorporated at all levels of the PDSAFE trial. Several PPI representatives were involved in the design of the study, including the development of participant information sheets, consent forms and intervention resources. Mr John Wood acted as PPI representative on the Trial Steering Committee. The trial was presented to several local Parkinson's support groups; representatives were invited to the results launch event in September 2017 and contributed to discussion on the interpretation of results and key messages. PPI representatives will also be involved with the dissemination of the findings through existing patient networks, mainly through Parkinson's UK and its newsletter service.

Chapter 3 The PDSAFE intervention and its delivery

This chapter details the PDSAFE intervention and its delivery. Background information is provided to support the conceptual development of the intervention, the protocol is presented using the TIDieR (Template for Intervention Description and Replication)[41] and descriptive statistics demonstrate the content of the intervention delivered over the intervention period.

Background for intervention design

A role for exercise in the treatment of both the physical and cognitive/behavioural symptoms of Parkinson's has been advocated and is supported by the European Physiotherapy Guidelines for Parkinson's Disease.[42] In reviewing 70 clinical trials, the guidelines suggest that there is strong evidence that specific physiotherapy interventions help to improve transfers, balance, gait, physical capacity and movement functions,[42] all isolated falls risk factors. A recent Cochrane review[43] stated that the overall aim of physiotherapy intervention is to optimise independence, safety and well-being, thereby enhancing quality of life; however, the intervention that is most effective at achieving this remains unclear.

Evidence suggests that a multidimensional intervention to reduce falls, incorporating balance, functional strength and strategy training, and thus appreciating the need for motor, cognitive and behavioural training, may be more effective than interventions focusing on independent risk factors such as postural control and/or functional strength alone.[19]

The PDSAFE intervention is delivered in the home, tailored to an individual's specific falls mechanism and functional presentation and personalised to rehabilitate the primary strategy or strategies that contributed to the fall(s) (*Figure 2*). Not only does this allow the protocol to align with all components of the *International Classification of Functioning, Disability and Health* (ICF)[44] as a person-centred approach, it also follows the consensus-based clinical practice recommendations for falls management in Parkinson's.[45] From this, personalised exercise prescription, within a menu of exercises, allows an individualised programme to be designed specific to the falls-related risk factors (impairments) that contribute to the primary 'problematic' strategy (as recommended by the *European Physiotherapy Guidelines for Parkinson's Disease*[42]). The specific 'impairment' training enables physiological improvements in Parkinson's symptoms and deficits, which allow functional training and strategy task practice in everyday life (see *Figure 2*). In this way, the rehabilitation of the falls-related strategy and its contributing falls risk factors not only works towards reducing the risk of similar falls again, but also embeds the training in everyday function and, therefore, is more likely to have a greater overall effect across all components of a participant's life (and, thus, full ICF model).

Intensity is maintained across all aspects of the frequency, intensity, time and type (FITT) principle (as published in the American College of Sports Medicine guidelines)[46] to drive physiological adaptation. 'Frequency' is regulated to a minimum of three times per week, 'intensity' must be perceived as 'moderately hard/hard' for all activities of the programme, 'time' is set to a maximum of 60 minutes and 'type' of exercise is tailored and specific to each individual's falls mechanism. With the consideration of all factors, it is therefore possible to design a multidimensional programme that does not lose intensity as a result of its many components. In addition, the high intensity, continuous progression and titrated support from intensive to independent practice maintains focus and adherence and encourages personal commitment and investment, as well as fostering an understanding and empowerment of the rehabilitation process for the individual. The addition of visual feedback both in therapy time and as a review through personalised DVDs also aids accurate independent practice and continuation of therapy. Thus, continuous progress and adaption to the neurodegenerative properties of the condition can be made to maintain safety.
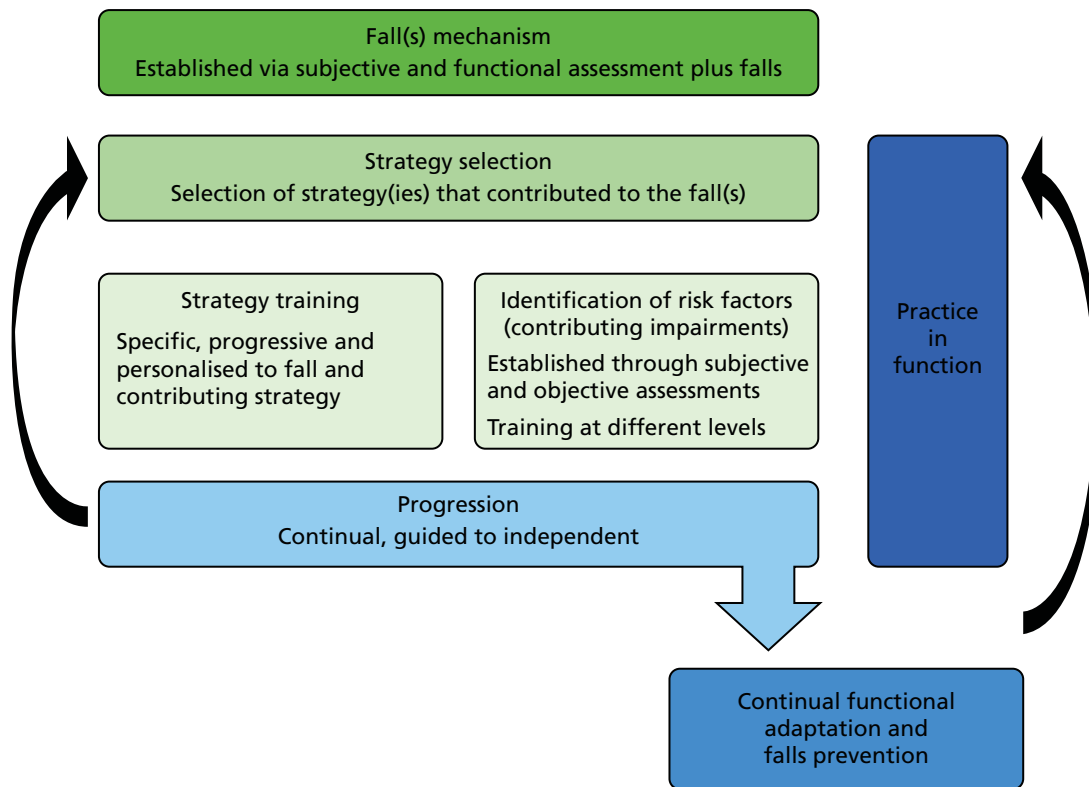
FIGURE 2 Conceptual model of the PDSAFE falls prevention protocol intervention.

In appreciation of the mechanisms of neurorehabilitation and exercise prescription, the PDSAFE intervention protocol is structured in a way that enables intensive, repetitive practice that is salient to an individual and their specific falls profile, thus meeting their needs for effective neuroplastic change. In addition, the embedding of the training in strategy task-related practice across all functional activities enables rehabilitation to take place across all levels of life participation and not just in relation to a specific task, goal or previous fall behaviour.

As a result of its unique structure and delivery, the PDSAFE intervention (see *Figure 2*) reflects the evidence base for falls prevention in Parkinson's, meets the holistic recommendations of the ICF framework for practice and facilitates onward progression and independent self-management of the condition by the individual. The novelty lies in both the content (disease-specific exercises and strategies for instability, use of motor relearning and cognitive awareness) and delivery (personalised feedback using a DVD for adherence and self-management).

Intervention protocol

In line with the recommended methods of reporting intervention design, TIDieR[41] is detailed in *Table 2*. The 12 items detailed in the checklist are an extension of the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement – item 5[47] and the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 statement – item 11[48] and are intended to improve the reporting of interventions.

For a visual representation of the intervention, please refer to the film available at: www.youtube.com/watch?v=emNr0REIm4A&list=PLT3AipgP4l_x7OVNryanVgtcvPZXVJyX1 (accessed 21 February 2019).

TABLE 2 The PDSAFE protocol description, as per TIDieR guidelines

TIDieR	Checklist requirement	Protocol description
1	Protocol name	PDSAFE: a personalised falls prevention programme of home exercises for postural control training, muscle strengthening and task-orientated movement strategy training
2	Protocol rationale and theory of main elements	• Personalised: the individual programme for each participant is derived from falls mechanism and underlying disease specific impairments • Postural control, functional strength and strategy: the programme must include elements of all exercise prescription from a standardised menu of options • Intensive, repetitive, progressive: elements of exercise prescription and neurorehabilitation followed
3	Protocol materials	For the participant: • participant exercise folder (including safety guidelines, daily checklist, personalised postural control and functional strength exercises, progression guidelines and intensity guidelines) • personalised DVD of falls prevention strategy training and exercises or the Parkinson's UK DVD, *Keeping Active* • Weighted vest (up to 10 kg, if required) • Foam balance pad (if required) For the physiotherapist: • the PDSAFE protocol documentation, including intervention paperwork • standardised strategy menu and postural control and functional strength exercise menu • a tablet to record strategy training and give 'in-time' visual feedback • pre-recorded library of strategy training vignettes • laptop for burning personalised DVDs and uploading study documentation
4	Procedures of protocol delivery	• Randomisation to intervention or comparison arm (50 : 50) • All participants contacted within 48 hours by telephone to inform them of group allocation • Intervention participants seen first by week 2 and regularly until month 6 • Comparison participants seen first up to week 6 and second at month 12
5	Protocol providers	• All sessions for both groups are delivered by a physiotherapist: advanced clinical reasoning required to align postural control, functional strength and strategy components with falls mechanisms • All therapists complete compulsory 2-day initial training, monthly continuing professional development, weekly peer-led case discussion and fidelity checks with lead therapist (once a month for the first 3 months and then 3-monthly for duration of involvement in trial)
6	Mode of protocol delivery	• All sessions for both groups are face to face and individualised • Participants are also left with an individualised exercise folder and DVD for independent strategy training practice
7	Location of protocol delivery	• All sessions for both groups are home/community based. This may include regular visits or previous falls locations, if feasible • Therapist training sessions take place at trial sites and are available virtually or by telephone
8	Protocol duration, intensity and dose	Intervention Supervised sessions comprise: • 12 1-hour, physiotherapy sessions progressing from intensive supervision to independent practice; sessions are twice weekly to begin with (sessions 1–4), then weekly (sessions 5–7), then monthly (sessions 8–12), followed by 6 months' independent practice • From assessment, selection of 1–3 falls mechanism strategies alongside a postural control, functional strength and strategy exercise programme selected from standardised menu

continued

TABLE 2 The PDSAFE protocol description, as per TIDieR guidelines (*continued*)

TIDieR	Checklist requirement	Protocol description
		• Once the programme is selected, every session includes fall history review, warm-up, exercise practice and progression, functional task practice with strategy training and use of video for 'in-time' visual feedback and making personalised DVDs
		Independent practice:
		• Daily (or a minimum of three times weekly) independent practice of the exercise programme (approximately 30 minutes), including safety review, warm-up, exercise practice, progression review, functional practice of strategy training (may include watching the DVD) and compliance monitoring • Participants are expected to rate their 'perception of work', or intensity, as 'moderate to hard' or 6 to 10. Therapists' progress and teach participants how to independently progress their programme to maintain this level
		Comparison group
		Supervised sessions comprise:
		• Initial visit to participant to provide Parkinson's UK DVD and reassure them of their importance in the trial • Comparison treatment visit (following final trial assessment): a 1-hour session to advise on personal strategy training and risk factor modification based on fall mechanisms
9	Protocol personalisation	• Detailed neurological physiotherapy assessment, focusing on falls mechanism and potential underlying impairment, guides individual selection of falls-related strategy • Strategy training and contributing falls risk impairments inform the selection of individualised postural control and functional strength exercise programme from a standardised menu • All training is progressed at a participant-specific rate to maintain the required intensity • Daily exercise practice is promoted but a minimum of three times a week is accepted as necessary to accommodate participants' requirements

Delivery outcomes

Delivery of the PDSAFE intervention was over 2 years and 4 months. The intervention was delivered in a total of eight clinical sites across nine NHS trusts.

Therapists

Physiotherapists were recruited by each site. Trial requirements stated that each therapist should have experience in Parkinson's or falls rehabilitation. It was initially designed that each site would have one treating therapist and a trained cover for periods of absence. However, owing to clinical workload and logistical delivery, a total of 18 therapists were trained over the study period. One lead therapist co-ordinated the team, delivered the training and development activities, and monitored the fidelity of intervention delivery.

Training, facilitated by the lead therapist, included attendance at one of the compulsory 2-day training events held on three separate occasions. In addition, therapists were asked to attend a virtual weekly meeting by telephone to discuss clinical cases and problem-solve within the boundaries of the intervention protocol. These sessions were chaired by the lead therapist, with a total of 122 telephone contacts made available over the intervention period. To maintain a high standard of clinical reasoning throughout the intervention period, therapists were also asked to attend (either physically or virtually) monthly 'masterclasses' on key clinical topics such as cognition and dual tasking, turning, FoG and balance. Alternating with masterclasses, therapists were asked to present case studies on key topics for team discussion. Twelve 'masterclass' topics (some were repeated for new therapists) and seven case study reviews were held over the intervention period.

Fidelity of the intervention was a priority to encourage uniformity of practice. The lead therapist observed each therapist in a treatment session with a participant, once a month for the first 3 months of delivery and then once every 3 months for the delivery period. Following the observation, a clinical reasoning discussion was completed and a report written. Therapists could also request additional joint sessions with the lead therapist if they had concerns or queries regarding a particular participant. This ensured that the PDSAFE intervention was uniformly delivered across all sites and by all therapists. A total of 75 fidelity sessions were held over the intervention period, with all therapists being assessed.

Intervention sessions

A total of 2587 sessions were delivered to the 291 intervention participants, with the majority of participants receiving the anticipated 12 sessions (mode = 12).

Figure 3 presents the total number of sessions received by participants allocated to the intervention arm of the trial. The majority of participants, 236 out of 238, received the exercise assessment and at least one supervised session. Two participants did not start because they had changed their mind and 19 received fewer than seven sessions; reasons for not fully engaging included admission to a nursing home, deteriorating health, commitment was too much and caring for others; in some cases, no reason was given.

All interventions sessions included a brief review of falls; warm-up exercises; review, practice and progression of a participant's individual exercise programme; and strategy training in functional scenarios as a basic structure. Each therapist tailored the strategies treated, exercises prescribed and functional tasks practised from a menu for each participant.

Selection of strategies

Evidence from the literature and from previous studies of falls among patients with Parkinson's, as well as expert opinion, were used to determine the most frequent falls mechanisms in Parkinson's.[19] Eight strategies were defined: avoiding tripping, dual tasking, freezing cues, moving in tight spaces, picking up an object, reaching, stepping backwards and turning. As described above, through the process of taking a detailed falls history, clinical assessment and advanced clinical reasoning, therapists determined the most likely 'fall mechanism' for each participant (levels 1 and 2 in *Figure 2*). For example, in the case of a participant who repeatedly reported catching their foot and falling, regardless of the task being undertaken or location, would be most likely to have a falls mechanism of tripping; thus, the strategy 'avoiding tripping' would be selected by the therapist.
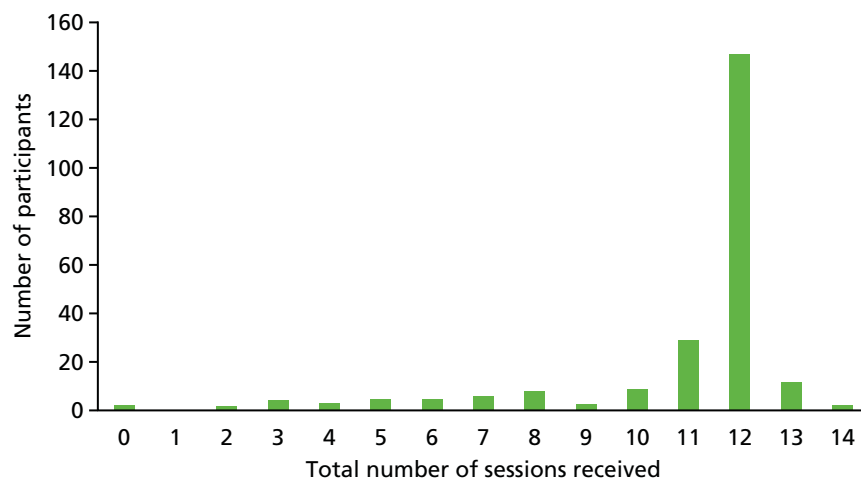
FIGURE 3 Total number of intervention sessions received by participants.

Over the 291 participants who received the PDSAFE intervention, strategies were selected a total of 440 times, with a strategy being used in treatment a total of 3447 times over the period. This provides a large sample to consider the clinical reasoning process of the therapists selecting the strategies. *Figure 4* demonstrates the number of times each strategy was selected as a potential falls mechanism corresponding to the number of times that strategy was used in a treatment session.

Importantly, this allows description of the strategies selected as primary falls mechanisms and thus treated for the majority of the intervention period versus strategies that may have been selected as a secondary or subsequent strategy and thus treated less frequently or for a shorter period of time.

It is apparent that 'avoiding tripping' was the most widely used strategy. It was selected following assessment a total of 116 times, used 1110 times during treatment sessions and accounted for 26% of all strategies selected. The figures for 'turning' are similar [selected 107 times and used 938 times during treatment (26% of the total)]. 'Freezing cues' was also frequently selected as a strategy [selected 79 times and used 365 times (24% of the total)]. It is clear from *Figure 4* that all other strategies were selected and used in treatment with similar frequencies to each other.

Selection of exercise prescription

Once the strategy or strategies most appropriate for addressing a participant's falls mechanism had been selected, therapists used advanced clinical reasoning and assessment skills to determine the physical impairments and deficits in physical falls risk factors that were most likely to contribute to the fall mechanism (see *Figure 2*). For example, the participant described above, who frequently caught their foot and subsequently fell, was allocated the 'avoiding tripping' strategy. The therapist must consider a number of reasons why the participant has a tendency to catch their foot, such as weakness of the muscles used to lift the toes, failure to transfer weight onto the supporting leg appropriately because of hip weakness or reduced limits of postural control stability, or failure to achieve enough clearance from the ground because of weakness in the hip flexors. Through assessment, the therapist determines the most likely impairment and designs a functional strength and postural control exercise programme from the available menu that treats this impairment.

Evidence from the literature and from previous studies of falls among patients with Parkinson's, as well as expert opinion, were used to determine what exercises were available on the menu for therapists to select from.[19]
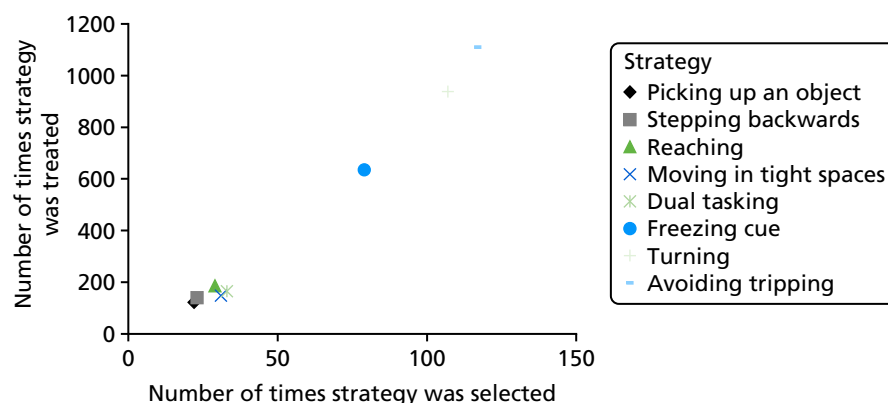
FIGURE 4 Stratification of strategies used in delivery of PDSAFE intervention.

Table 3 shows the menu of exercises available for the therapist to select from when putting together an individual participant's PDSAFE intervention.

Exercises were available on six levels; working through the levels enabled progression (level 4 in *Figure 2*) and maintenance of intensity for each exercise. All programmes had to include at least one balance and one strengthening exercise. A total of 1693 exercises were selected by all therapists over the intervention period with an average of six (range one to eight) exercises prescribed per participant across the period. *Figure 5* shows a spread of all exercises being used over the intervention period.

Figure 5 demonstrates the predominance of the more dynamic postural control (compensatory step and lunge and heel/toe walking) and strengthening exercises over other exercises from the menu. The complex nature of the compensatory step and lunge exercise makes it suitable for the treatment of many of the falls risk factors associated with Parkinson's; for example, high dynamic stepping actions help with motor control, compensatory stepping helps with the regain of an appropriate base of support from a loss of postural control or a trip by increasing stepping amplitude for those who freeze and expanding limits of stability for those who fall when reaching. The practice of stepping backwards with appropriate postural control and weight distribution will assist those who fall stepping backwards. A common symptom of the Parkinsonian gait is loss of foot clearance, heel strike and step length[45] (hence the predominance of tripping as a falls mechanism); thus, the high frequency of the use of heel/toe walking to improve these impairments is also unsurprising. As each exercise programme had to include both strengthening and postural control exercises, the high frequency of selection of strengthening exercises can be attributed to the fact that the postural control menu contained fewer exercises that could be selected. This is less of a clinical reasoning observation and more related to the ratio of exercises in the menu.

TABLE 3 Exercise menu for the PDSAFE intervention

Function		Exercise
Balance/postural control		
	Standing	Standing balance
		Tandem stand
		Reaching
		Compensatory step and lunge
	Walking	Heel/toe walking
		Toe/heel walking backwards
		Tandem walking
		'Figure of 8' walking
		Picking up an object
		Stepping over an object
Strengthening		Sit to stand
		Standing toe and heel raises
		Forward stepping up and down
		Side stepping up and down
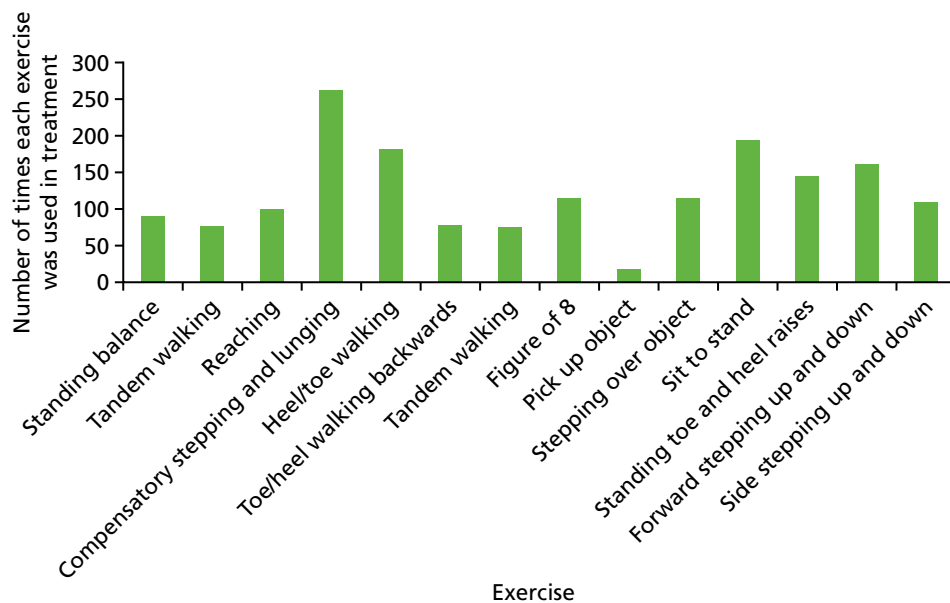
FIGURE 5 Exercise use frequency across all of the intervention, in all participants.

Summary

The PDSAFE intervention was deeply rooted in evidence from both rehabilitation after falls and exercise prescription literature. The protocol was a holistic model encompassing all aspects of the ICF and its design allowed a personalised, sophisticated, complex intervention to be prescribed for each participant. 'Personalised', 'intensive' and 'progressive' were key parameters of the intervention, demanding a high level of commitment and collaboration between the therapist and the participant. The intervention was delivered to a high standard. All requirements of fidelity were met and the intervention was comparable across all sites. Delivery was significantly enhanced by the level of training and support provided to the delivery team and a high standard of clinical reasoning and protocol delivery was maintained. The majority of participants received the planned number of sessions. There was a slight rise in the number of participants receiving only seven or eight sessions as this is the point at which the therapists visited less frequently and participants were required to complete longer periods of independent practice. It is likely that this led to some participants withdrawing at this point because of the reduced support/motivation from the therapist. There was a clear predominance of some strategies, which is likely to reflect the demographic of the intervention group (i.e. more frequent fallers and people with Parkinson's who freeze, plus those who have more advanced disease and thus are more likely to have difficulty turning: with axial rigidity, poor stepping and impaired cognition). The predominance of 'avoiding tripping', 'turning' and 'freezing cues' is in line with the reasons for falling provided by participants most frequently in the previous literature.[26] The design of strategy selection leading to supported exercises to treat falls risk factors provided a protocol design that was deliverable, with all participants receiving both strategies and exercises as planned. Owing to the complexity of the exercises, some exercises are better able to be adapted for multiple impairments and thus are used more frequently. Previous studies[19] have provided the same intervention for all participants, regardless of fall mechanism. The use of all the strategies and exercises demonstrates the need for a complex intervention and variability as 'one size, clearly does not fit all'.

Chapter 4 Statistical trial results

Participants

Recruitment of participants ran from July 2014 to August 2016 (see *Appendix 5*, *Figure 14*).

Figure 6 provides the CONSORT flow diagram of participants' assessments. A total of 640 people with Parkinson's were invited to participate, but 99 either did not respond or did not meet the eligibility criteria, which left 541 people for consent and completion of a screening visit with a trial assessor in their own home. Of these 541 people, seven did not score the minimum score on the MMSE and were excluded. The remainder went on to complete prospective falls diaries for 3 months (i.e. a minimum of 13 weeks). A further 60 people were excluded during this time [reasons for not being randomised were as follows: medically unfit (*n* = 21), dislike of completing falls diaries (*n* = 6), no longer met eligibility criteria (*n* = 12), reported cognitive issues (*n* = 2), died (*n* = 1) or decided not to participate in the trial (*n* = 18)]. The remaining 474 (88%) people completed a baseline assessment and were randomised into one of two groups: control (*n* = 236) or the PDSAFE intervention (*n* = 238). Recruitment and randomisation graphs can be found in the appendices. The groups allocated to PDSAFE and control were similar at baseline (*Table 4*) in terms of age, gender, disease severity, disease duration, cognitive ability, freezing, medication and coexisting conditions and living status. Retrospective recall of falls was also similar between the groups, but the rate of falling in the 3 months prior to randomisation was greater in those subsequently randomised to the intervention group.

Delivery of intervention

In the PDSAFE group, 66 participants did not engage with the intervention for a number of reasons, including admission to a care home, deteriorating health, changing their mind about participation, feeling the commitment to be too great, or death; in some cases, no reason was given. The therapy aim was to provide 12 supervised sessions for each participant and, on average, participants had a median of 12 sessions [interquartile range (IQR) 11–12 sessions] or a mean of 11 sessions [standard deviation (SD) 2.4 sessions]. A total of 21 participants received fewer than seven sessions and, along with a further four participants for whom the number of sessions was not available, were excluded from per-protocol analyses.

Falling outcomes

In *Table 5*, the prospective completion of diaries is described during the period of baseline diary completion prior to randomisation, and in the 12-month period of post-randomisation follow-up. The percentage who returned no diaries was generally low (2–4%) during the period 0 to 6 months; during the final 6 months the percentage who returned no diaries was higher (1–12%). These percentages exclude the number who withdrew or died during the respective periods. Among those returning any diaries for the period in question, the IQR of the numbers of days completed was 90–92 (within target). The target number of days varied between 89 and 92 days across participants, depending on the calendar months covered by their 3-month baseline period.

There was a trend towards increased repeat falling during the 6 months following randomisation in the PDSAFE group compared with the control group (OR 1.21, 95% CI 0.74 to 1.98; *p* = 0.447). During the final 6 months of follow-up, there was a trend towards decreased repeat falling (OR 0.86, 95% CI 0.45 to 1.65; *p* = 0.657). No statistically significant differences between the groups were found (*Table 6*).
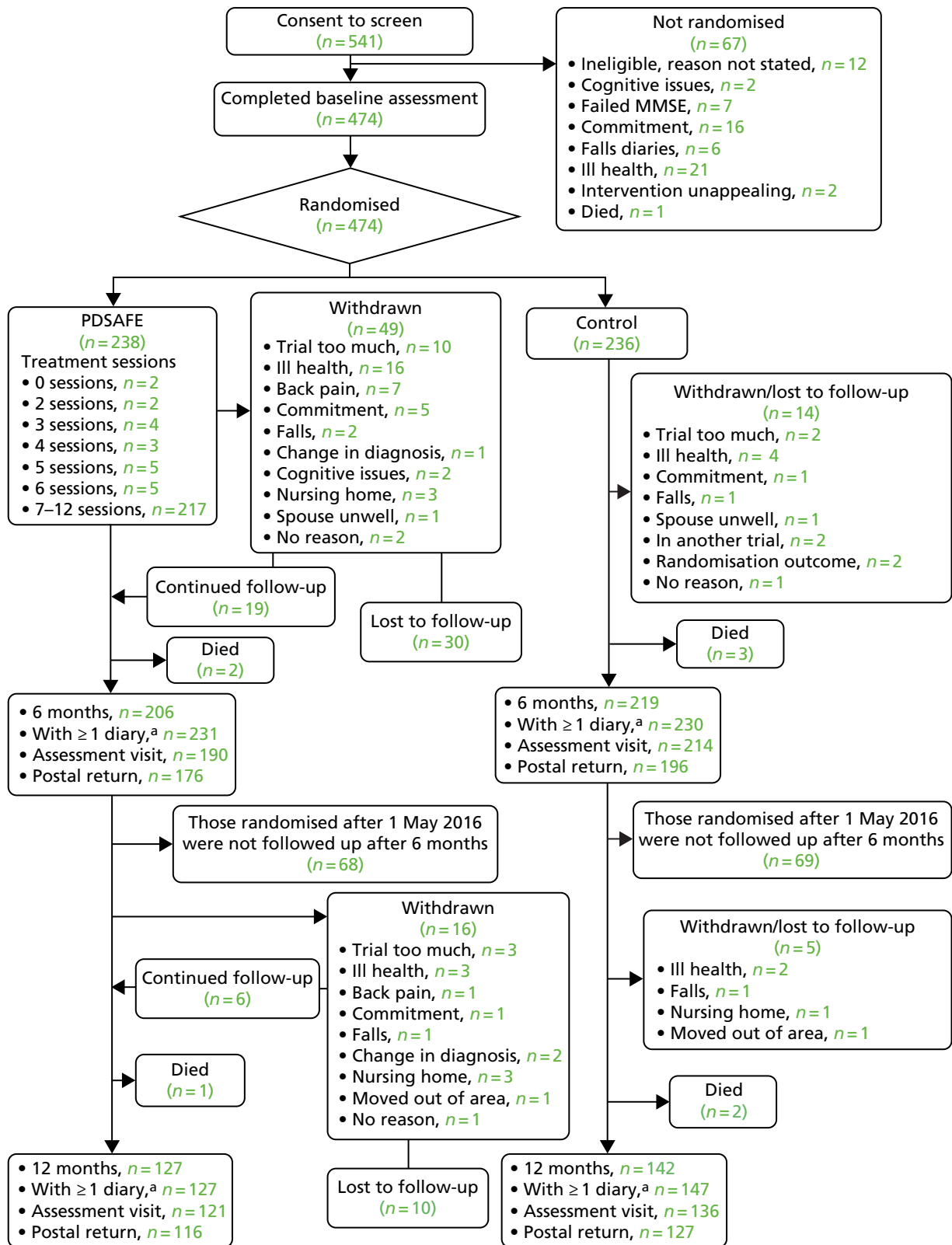
FIGURE 6 Flow diagram of participants' progression through the trial. a, Number with any diaries during the preceding 6 months. Adapted from Chivers Seymour et al.[49] © Author(s) [or their employer(s)] 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by the BMJ Publishing Group Ltd. This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

TABLE 4 Baseline characteristics in the intervention and control groups

	Trial group	
Characteristic	**PDSAFE (*n* = 238)[a]**	**Control (*n* = 236)[b]**
Gender, *n* (%)		
Male	147 (62)	119 (50)
Female	91 (38)	117 (50)
Age (years)		
Mean (SD)	71 (7.7)	73 (7.7)
Minimum, maximum	51, 91	46, 88
Disease duration (years)		
Mean (SD)	8 (6.6)	8 (5.8)
Minimum, maximum	0, 36	0, 29
MMSE score		
Mean (SD)	28 (1.7)	29 (1.6)
Minimum, maximum	24, 30	24, 30
MoCA score		
Mean (SD)	26 (2.9)	26 (3.2)
Minimum, maximum	15, 30	9, 30
≤ 25 (cognitively impaired), *n* (%)	91 (38)	93 (39)
Living status, *n* (%)		
Lived alone	48 (20)	59 (25)
With a spouse/partner	174 (73)	166 (70)
With a friend/family	15 (6)	10 (4)
H&Y scale stage, *n* (%)		
1	26 (11)	30 (13)
2	78 (33)	56 (24)
3	102 (43)	112 (48)
4	32 (13)	38 (16)
MDS-UPDRS		
Mean (SD)	32 (15.2)	33 (17.3)
Minimum, maximum	2, 77	4, 92
Phenotype		
TD, *n* (%)	21 (9)	19 (8)
PIGD, *n* (%)	194 (83)	206 (88)
Indeterminate, *n* (%)	20 (8)	10 (4)

continued

TABLE 4 Baseline characteristics in the intervention and control groups (*continued*)

Characteristic	Trial group	
	PDSAFE (*n* = 238)[a]	Control (*n* = 236)[b]
FoG in the past month, *n* (%)	152 (64)	139 (59)
Number of falls in the 12 months prior to screening		
Median (minimum, maximum)	3 (1, 1460)	3 (1, 1095)
Mean (SD)	26 (132.7)	19 (105.4)
Repeat falling in 12 months prior to screening, *n* (%)	186 (78)	189 (80)
Rate of falls/person/3 months prior to randomisation		
Median (minimum, maximum)	1.98 (0, 319)	0.99 (0, 73)
Mean (SD)	5.9 (22.8)	3.0 (7.3)
Rate of near-falls/person/3 months prior to randomisation		
Median (minimum, maximum)	4.4 (0 to 440)	4.3 (0 to 601)
Mean (SD)	13.8 (35.8)	15.6 (51.4)
Medications, *n* (%)		
Levodopa	208 (88)	216 (92)
Dopamine agonist	108 (46)	106 (45)
Monoamine oxidase inhibitor	52 (22)	46 (20)
Catechol-*O*-methyltransferase inhibitors	59 (25)	41 (17)
Other Parkinson's medication	19 (8)	23 (10)
GDS score at baseline, *n* (%)		
> 5 (suggestive of depression)	147/235 (63)	164/236 (70)
≥ 10 (indicative of depression)	50/235 (21)	49/236 (21)
Coexisting conditions, *n* (%)		
Orthopaedic	109 (46)	129 (54)
Cardiovascular/respiratory	85 (36)	96 (41)

PIGD, Parkinson's-induced gait deficit; SD, standard deviation; TD, tremor dominant.
a Missing values in the intervention group: living status (*n* = 1), MDS-UPDRS (*n* = 1), disease duration (*n* = 1), FoG (*n* = 1), rate of falling in the 3 months prior to randomisation (*n* = 1), tremor dominant/Parkinson's-induced gait deficit/ indeterminate phenotype (*n* = 3).
b Missing values in the control group: living status (*n* = 1), MDS-UPDRS (*n* = 1), tremor dominant/Parkinson's-induced gait deficit/indeterminate phenotype (*n* = 1).

TABLE 5 Diary completion during pre randomisation: 0–6 months and 6–12 months post randomisation

Characteristic	Trial group	
	PDSAFE	Control
Randomisation, *n*	238	236
Baseline		
Number with no diaries	1/238	0/236
Number of diary days among those with diaries	(*n* = 237)	(*n* = 236)
Median	92	92
IQR	90–92	90–92
Minimum, maximum	12, 92	26, 92
n/N with complete diaries (%)	196/238 (82)	198/236 (84)
n/N with ≥ 50% diary days (%)	229/238 (96)	226/236 (96)
0–6 months post randomisation		
Number entering 0–6 months period	238	236
n/N with no diaries (%)	7/238 (3)	6/236 (3)
n/N in falls rate ratio analysis (%)	231/238 (97)	230/236 (98)
n/N exiting (died or withdrawn from follow-up during 0–6 months) (%)	32/238 (13)	17/236 (7)
n/N exiting with no diaries	2/206 (1)	3/219 (1)
Number of diary days among those not exiting with diary days	(*n* = 204)	(*n* = 216)
Median	182	182
IQR	153–183	174–183
Minimum, maximum	3184	29,184
n/N with complete diaries (%)	130/238 (55)	158/236 (67)
n/N with ≥ 50% diary days (%)	203/238 (85)	211/236 (89)
Number in follow-up at 6 months	206	219
Number in trial follow-up randomised after 1 May 2016		
Southampton	5	4
Portsmouth	7	6
Bournemouth	2	2
Newcastle	15	13
Hampshire	13	18
Plymouth	10	11
Cornwall	16	15
Total	68	69
6–12 months post randomisation		
Number entering 6–12 months period	138	150
n/N with no diaries (%)	11/138 (8)	3/150 (2)
n/N in falls rate ratio analysis (%)	127/138 (92)	147/150 (98)
n/N exiting (died or withdrawn from follow-up during 6–12 months) (%)	11/138 (8)	7/150 (5)
n/N exiting with no diaries (%)	5/127 (4)	2/143 (1)

TABLE 5 Diary completion during pre randomisation: 0–6 months and 6–12 months post randomisation (*continued*)

	Trial group	
Characteristic	**PDSAFE**	**Control**
Number of diary days among those not exiting with diary days	(*n* = 122)	(*n* = 141)
Median	180	180
IQR	151–183	153–183
Minimum, maximum	4184	30,184
n/N with complete diaries (%)	94/138 (68)	112/150 (75)
n/N with ≥ 50% diary days (%)	114/138 (83)	132/150 (8)

TABLE 6 The ITT analysis of falling outcomes: 0–6 and 6–12 months

	Trial group			
Period	**PDSAFE**	**Control**	**OR (95% CI)**[a]	***p*-value**[a]
Repeat falling restricted to ≥ 50% diaries, n (%)				
Baseline	127/231 (55)	92/230 (40)		
Baseline[b]	112/203 (55)	80/211 (38)		
0–6 months	125/203 (62)	116/211 (55)	1.21 (0.74 to 1.98)	0.447
Baseline[b]	55/114 (48)	47/132 (36)		
6–12 months	57/114 (50)	71/132 (54)	0.86 (0.45 to 1.65)	0.657
Fall rates	***Falls/person/6 months*[c]**		***FRR (95% CI)***	
Baseline	4.5	3.3		
0–6 months	3.4	2.7	0.98 (0.80 to 1.19)	0.824
6–12 months	2.7	2.8	0.83 (0.62 to 1.11)	0.200
Near-fall rates	***Near-falls/person/6 months*[c]**		***NFRR (95% CI)***	
Baseline	8.0	8.1		
0–6 months	4.7	5.6	0.67 (0.53 to 0.86)	0.001
6–12 months	3.9	3.7	1.01 (0.67 to 1.52)	0.968

NFRR, near-falls rate ratio.
a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period and H&Y scale stage (NFRR additionally controlled for log rate of near-falling in the pre-randomisation falls collection period).
b Baseline repeat falling restricted to participants included in the analyses for 0–6 and 6–12 months.
c Geometric mean of individual fall rates with 0.5 added to all numerators.

These analyses followed the planned treatment for participants with incomplete diaries during a follow-up period, that is participants were classified as a repeat faller if they reported two or more falls in their incomplete diaries or if a check of all PDSAFE records indicated two or more falls in that period. They were classified as a non-repeat faller if fewer than two falls were reported in the incomplete diaries, there was no indication of repeat falling in the period in the PDSAFE records and ≥ 50% of diary days for the period had been completed. Otherwise they were excluded. Two sensitivity analyses are shown in *Appendix 7*, *Table 28*, where analysis of repeat falling is also reported, restricted to participants with complete diaries and including all participants with any diaries during the follow-up period in question. Although there were no changes in the statistical significance or otherwise depending on these treatments of missing diaries, there were changes in the magnitude of ORs.

Participants typically reported rates of falling, expressed per 6 months, of between three and five falls (see *Table 6*). There was little difference in the rate of falling between the two groups in the first 6 months of follow-up, indicated by the FRR, and a slightly greater difference, with FRR of 0.83 (95% CI 0.62 to 1.11; $p = 0.200$), during the following 6 months. The analysis of rates of falling is based on participants with any amount of diary completion for the follow-up period in question, with only participants returning no diaries excluded.

Rates of near-falling are also shown in *Table 6*, expressed per 6-month period. Near-falling was greater in the period prior to randomisation than subsequently. During the 6 months post randomisation, the ratio of near-falling rates between the PDSAFE and control groups was significantly reduced ($p = 0.001$), with a rate of near-falling in the PDSAFE group of 0.67 (95% CI 0.53 to 0.86) that of the control group. This reduction in near-falling was not maintained during the following 6 months. Like the analysis of falling rates, the analysis of near-falling rates also includes participants irrespective of the amount of diary completion for the period of follow-up in question (as long as any diaries were returned for the period).

In *Table 7* a comparison is made between the overall falling (and near-falling) results following the ITT analysis and a per-protocol analysis (excluding participants in the PDSAFE groups receiving fewer than seven sessions). This shows the findings to be similar, there being no suggestion of reduced falling in the PDSAFE group when the analysis is restricted to those receiving seven or more sessions.

TABLE 7 Comparison of ITT and per-protocol analyses of falling and near-falling outcomes: 0–6 and 6–12 months – whole group

| | Analysis | | | |
| | ITT | | Per protocol | |
Period	**OR (95% CI)[a]**	***p*-value[a]**	**OR (95% CI)[a]**	***p*-value[a]**
Repeat falling restricted to ≥ 50% diaries				
0–6 months	1.21 (0.74 to 1.98)	0.447	1.16 (0.71 to 1.92)	0.538
6–12 months	0.86 (0.45 to 1.65)	0.657	0.92 (0.47 to 1.77)	0.793
Fall rates	*FRR (95% CI)*	**p-value[a]**	*FRR (95% CI)*	**p-value[a]**
0–6 months	0.98 (0.80 to 1.19)	0.824	0.99 (0.81 to 1.22)	0.982
6–12 months	0.83 (0.62 to 1.11)	0.200	0.84 (0.63 to 1.13)	0.268
Near-fall rates	*NFRR (95% CI)*	**p-value[a]**	*NFRR (95% CI)*	**p-value[a]**
0–6 months	0.67 (0.53 to 0.86)	0.001	0.67 (0.53 to 0.86)	0.001
6–12 months	1.01 (0.67 to 1.52)	0.968	1.01 (0.67 to 1.52)	0.963

NFRR, near-falls rate ratio.
a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period and H&Y scale stage (NFRR additionally controlled for log rate of near-falling in the pre-randomisation falls collection period).

Secondary outcomes

Analysis of the secondary outcomes collected by the assessing therapist during home visits (Mini-BESTest, FES-I, FoG and MDS-UPDRS) is reported in *Table 8*, with CST results reported in *Tables 9* and *10*. At the 6-month visit, the PDSAFE group had improved mean Mini-BESTest score of 0.95 points (95% CI 0.24 to 1.67 points; $p = 0.009$), controlled for baseline Mini-BESTest score and other covariates (see *Table 7*); better falls confidence as assessed by a lower mean FES-I score of 1.60 points (95% CI 3.00 to 0.19 points; $p = 0.026$), controlled for similar covariates; and improved balance as assessed by the CST ($p = 0.041$). There were no significant differences at 12 months.

TABLE 8 Secondary outcomes at 6 and 12 months

| Outcome measure | Visit | Trial group, mean (SD), *n* | | Mean difference (95% CI)[a] | *p*-value |
		PDSAFE (*N* = 238)	Control (*N* = 236)		
Mini-BESTest (0–28, lower values worse)	Baseline[b]	18.3 (5.7), 183	17.3 (6.1), 211		
	6 months	19.4 (5.9), 183	17.5 (6.4), 211		
	6 months – baseline	1.1 (3.8), 183	0.2 (3.8), 211	0.95 (0.24 to 1.67)	0.009
	Baseline[b]	18.5 (5.8), 115	17.5 (6.1), 126		
	12 months	17.9 (6.5), 115	17.4 (6.7), 126		
	12 months – baseline	–0.7 (4.5), 115	–0.2 (3.8), 126	–0.41 (–1.48 to 0.66)	0.449
FES-I (16–64, higher values worse)	Baseline[b]	34.1 (11.0), 189	35.1 (11.5), 211		
	6 months	33.4 (10.6), 189	36.2 (11.4), 211		
	6 months – baseline	–0.7 (7.9), 189	1.1 (7.2), 211	–1.6 (–3.0 to –0.19)	0.026
	Baseline[b]	33.4 (10.7), 119	33.7 (11.3), 135		
	12 months	34.8 (11.2), 119	37.2 (11.6), 135		
	12 months – baseline	1.3 (8.2), 119	3.5 (9.3), 135	–1.4 (–3.41 to 0.66)	0.184
PASE (0–4, lower values worse)	Baseline[b]	107.8 (73.5), 153	100.1 (67.1), 177		
	6 months	110.2 (70.4), 153	100.6 (68.0), 177		
	6 months – baseline	2.4 (50.8), 153	0.5 (49.5), 177	–1.05 (–11.3 to 9.21)	0.841
	Baseline[b]	108.1 (71.9), 98	98.6 (61.1), 115		
	12 months	99.4 (72.8), 98	87.6 (62.3), 115		
	12 months – baseline	–8.7 (53.0), 98	–11.0 (48.5), 115	–0.55 (–13.9 to 12.8)	0.935
PDQ-39 (0–100, higher values worse)	Baseline[b]	27.4 (14.3), 126	28.7 (15.9), 153		
	6 months	28.3 (15.0), 126	29.5 (16.5), 153		
	6 months – baseline	0.8 (8.3), 126	0.9 (9.0), 153	0.12 (–2.0 to 2.28)	0.911
	Baseline[b]	27.2 (13.6), 77	28.9 (15.9), 100		
	12 months	29.1 (15.4), 77	31.7 (15.5), 100		
	12 months – baseline	1.9 (8.6), 77	2.8 (11.2), 100	0.48 (–2.53 to 3.49)	0.754

TABLE 8 Secondary outcomes at 6 and 12 months (*continued*)

Outcome measure	Visit	Trial group, mean (SD), *n*		Mean difference (95% CI)[a]	*p*-value
		PDSAFE (*N* = 238)	Control (*N* = 236)		
GDS (0–15, higher values worse)	Baseline[b]	7.7 (2.3), 154	7.7 (2.1), 183		
	6 months	7.8 (2.5), 154	8.0 (2.5), 183		
	6 months – baseline	0.3 (1.8), 154	0.2 (1.9), 183	–0.02 (–0.42 to 0.39)	0.942
	Baseline[b]	7.7 (2.1), 96	8.0 (2.2), 118		
	12 months	7.8 (2.5), 96	8.5 (2.4), 118		
	12 months – baseline	0.2 (2.0), 96	0.4 (1.7), 118	–0.21 (–0.72 to 0.31)	0.421

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage and the outcome in question assessed at baseline.
b Baseline results restricted to existing participant assessment at 6 months.

TABLE 9 Inability to perform the CST at the 6- and 12-month visits

Period	Trial group, *n/N* (%)		PDSAFE/control OR (95% CI)	*p*-value[a]
	PDSAFE	Control		
Baseline	45/236 (19)	45/235 (19)		
Baseline among participants with a 6-month assessment	29/188 (15)	35/213 (16)		
6 months	27/188 (14)	47/213 (22)	0.61 (0.37 to 1.02)	0.076
Baseline among participants with a 12-month assessment	15/119 (13)	21/134 (16)		
12 months	23/119 (19)	38/134 (28)	0.66 (0.37 to 1.17)	0.208

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage and CST ability at baseline.

Analysis is shown in *Table 11* of the secondary outcomes self-reported by participants after the 6- and 12-month home visits and returned by post. No statistically significant differences between the groups overall were found for these outcomes.

Subgroup analysis

In the statistical analysis plan, a subgroup analysis excluding participants with severe disease by virtue of a MDS-UPDRS score of ≥ 59 or H&Y stage 4 was prespecified. These analyses yielded very similar results to those shown in *Table 6* for the group as a whole.

TABLE 10 Change from baseline in CST assessed at the 6- and 12-month visits

| Period | Trial group, median (IQR); n | | p-value[a] |
	PDSAFE	Control	
Baseline among participants with 6-month assessment	14 (11–18); 159	14 (11–18); 178	
6-month assessment	12 (10–15); 161	13 (10–16); 166	0.041 (n = 401)
Baseline among participants with 12-month assessment	14 (11–17); 104	14 (12–18); 113	
12-month assessment	12 (9–14); 96	13 (11–15); 96	0.163 (n = 253)

a Mann–Whitney U-test incorporating participants unable to perform CST and times from participants able to perform CST.

In addition, subgroup analyses were prespecified among those with reported freezing of gait or not and among the cognitively impaired (i.e. MoCA score of ≤ 25) and not impaired (i.e. MoCA score of ≥ 26) at baseline. The results of these analyses, relating to the period 0–6-months following randomisation in the case of the falling outcomes, and to the 6-month home visit in the case of the MINI-BESTest and FES-I, are shown in Figure 7. There was a significant interaction between the PDSAFE intervention effect and freezing status ($p = 0.025$). Among those with Parkinson's who experienced freezing, the OR of repeat falling was doubled in the PDSAFE group (2.04, 95% CI 1.03 to 2.70; $p = 0.042$) compared with the control group. With a p-value for interaction of 0.088, there was a trend of differential PDSAFE effect in relation to the rate of falling according to the prespecified MoCA subgroups, with a FRR of 1.19 (95% CI 0.88 to 1.61; $p = 0.255$) in the cognitively impaired subgroup (i.e. MoCA score of ≤ 25). Subgroup-specific effect sizes and p-values are given in Appendix 8 (Table 29) and Appendix 9 (Table 30) for the analyses of repeat falling and fall rates, respectively.

The results of further subgroup analyses exploring the differential effects of PDSAFE on the basis of tertiles of MDS-UPDRS, MoCA and the retrospective falls question asked at screening are shown in Figure 7. A further prespecified subgroup analysis excluding the most severe participants according to MDS-UPDRS ($\approx 10\%$ were excluded) did not show statistically significant PDSAFE-to-control effects for falling outcomes. In an exploratory subgroup analysis, only the middle tertile showed a PDSAFE reduction in falls, whereas the most severe tertile showed an increase in falls rate. A similar pattern was found across the tertiles according to the retrospectively reported number of falls in the year prior to screening, with p-value for interaction of 0.050 and only the middle tertile showing a PDSAFE reduction in falls. The analysis of subgroups defined by tertiles of MoCA, MDS-UPDRS and the number of falls, retrospectively, reported in the year prior to screening were not specified in the protocol, but were carried out to explore further the prespecified subgroups in relation to MoCA, and, because Canning et al.[40] report prespecifying subgroup analysis in relation to falls history, the MDS-UPDRS and cognition.

The same subgroup analyses were also explored with respect to near-falls and other secondary outcomes, and results for near-falling, Mini-BESTest and the FES-I are also shown in Figure 7. The effect of PDSAFE did not differ significantly across subgroups for any of these three outcomes, with interaction p-values > 0.05; in general, the PDSAFE effect can be seen to be more consistent across the various parts of the participant group. Details of these analyses are shown in Appendices 8–12 (Tables 29–33).

TABLE 11 Change from baseline in secondary outcomes, returned postally following the 6- and 12-month visits: PASE, PDQ-39 and GDS – whole group

Assessment and visit	Trial group, mean (SD)		Mean difference (PDSAFE – control) (95% CI)[a]	p-value[a]
	PDSAFE (N = 238)	Control (N = 236)		
PASE (0–400, lower values worse)				
Baseline[b]	107.8 (73.5); n = 153	100.1 (67.1); n = 177		
6 months	110.2 (70.4); n = 153	100.6 (68.0); n = 177		
6 months – baseline	2.4 (50.8); n = 153	0.5 (49.5); n = 177	−1.05 (−11.3 to 9.21)	0.841
Baseline[c]	108.1 (71.9); n = 98	98.6 (61.1); n = 115		
12 months	99.4 (72.8); n = 98	87.6 (62.3); n = 115		
12 months – baseline	−8.7 (53.0); n = 98	−11.0 (48.5); n = 115	−0.55 (−13.9 to 12.8)	0.935
PDQ-39 (0–100, higher values worse)				
Baseline[b]	27.4 (14.3); n = 126	28.7 (15.9); n = 153		
6 months	28.3 (15.0); n = 126	29.5 (16.5); n = 153		
6 months – baseline	0.8 (8.3); n = 126	0.9 (9.0); n = 153	0.12 (−2.0 to 2.28)	0.911
Baseline[c]	27.2 (13.6); n = 77	28.9 (15.9); n = 100		
12 months	29.1 (15.4); n = 77	31.7 (15.5); n = 100		
12 months – baseline	1.9 (8.6); n = 77	2.8 (11.2); n = 100	0.48 (−2.53 to 3.49)	0.754
GDS (0–15, higher values worse)				
Baseline[b]	7.7 (2.3); n = 154	7.7 (2.1); n = 183		
6 months	7.8 (2.5); n = 154	8.0 (2.5); n = 183		
6 months – baseline	0.3 (1.8); n = 154	0.2 (1.9); n = 183	−0.02 (−0.42 to 0.39)	0.942
Baseline[c]	7.7 (2.1); n = 96	8.0 (2.2); n = 118		
12 months	7.8 (2.5); n = 96	8.5 (2.4); n = 118		
12 months – baseline	0.2 (2.0); n = 96	0.4 (1.7); n = 118	−0.21 (−0.72 to 0.31)	0.421

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage and the covariate value at baseline.
b Restricted to participants with a 6-month assessment.
c Restricted to participants with a 12-month assessment.

Appendices 13 and *14* (*Tables 34* and *35*) repeat the subgroups analyses for the repeat falling and falls rate outcomes shown in *Tables 6* and *7*, but include corresponding analyses carried on a per-protocol basis. Although there are some differences (including changes in *p*-values around the cut-off point of 0.05), the overall picture remains similar to that of *Figure 7*. *Appendices 15–17* (*Tables 36–39*) detail subgroup analyses for the MDS-UPDRS, PASE, PDQ-39 and GDS and these are displayed graphically in *Appendix 18* (*Figure 13*).

Serious adverse events

As described in *Chapter 2*, *Safety reporting*, for this trial a SAE was defined as a death, a life-threatening event or a new disability leading to prolonged hospitalisation, attributed to the trial intervention. No SAEs were reported in this trial. From the CONSORT flow diagram (see *Figure 6*), it can be seen that, in total, three participants died in the PDSAFE group and five in the control group, from causes unrelated to the trial protocol.
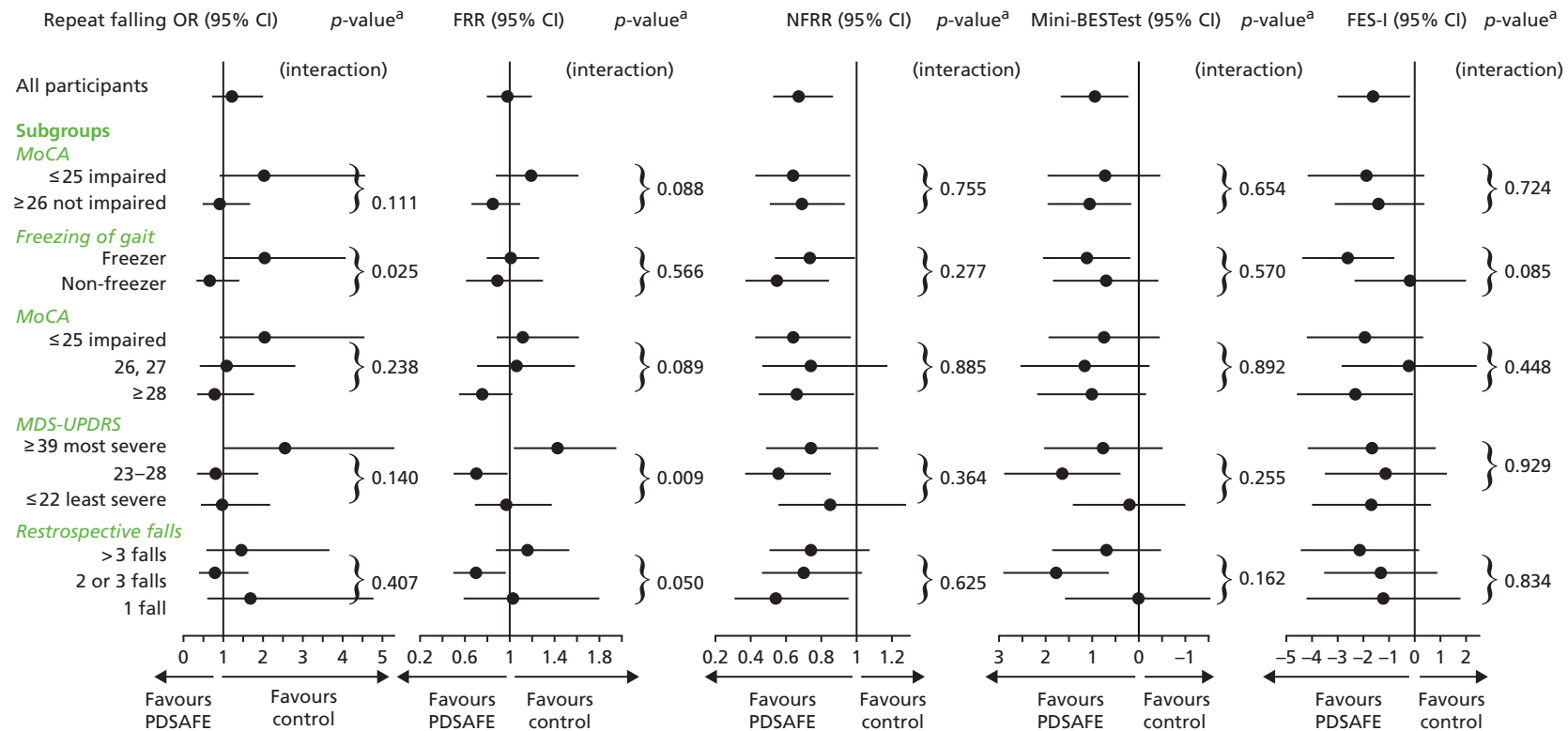
FIGURE 7 Overall and subgroup analyses of falling and near-falling outcomes during 0–6 months and secondary outcomes at 6 months. a, Test for interaction of PDSAFE contrast differing across subgroups, controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage and the outcome in question assessed at baseline. Adapted from Chivers Seymour *et al.*[49] © Author(s) [or their employer(s)] 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by the BMJ Publishing Group Ltd. This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/. NFRR = near-falls rate ratio.

Information on hospitalisations was self-reported by participants during the baseline, 3-month, 6-month and 12-month home visits. At each visit, participants were asked about any hospitalisation that occurred since the previous visit and its duration. In the first 6 months following randomisation, nine PDSAFE and 20 control group participants reported hospitalisations; of these, one PDSAFE participant reported two stays. During the 6- to 12-month follow-up period, 18 PDSAFE and 21 control group participants reported hospitalisations; of these, two PDSAFE and four control group participants reported two stays.

Information on fractures was obtained from a variety of sources, including fall-specific information associated with the falls diaries and from self-reported hospitalisations. In the first 6 months following randomisation, five fractures were reported by PDSAFE participants and nine by control group participants; during the period 6–12 months post randomisation, PDSAFE participants reported seven fractures and control group participants reported three fractures.

Chapter 5 Qualitative process evaluation: part 1

The next two chapters describe the two-stage qualitative process evaluation. This chapter explores the expectations and experiences of participants in the PDSAFE intervention in a longitudinal qualitative study.

Aims

- To explore the expectations of people with Parkinson's about the intervention.
- To explore the experiences of people with Parkinson's about participation in the intervention, including its perceived impact.
- To gain insight into the barriers to and facilitators of participating in the intervention.

Qualitative methods

Design

A longitudinal qualitative study was conducted alongside the main PDSAFE RCT. The qualitative study drew on the principles of grounded theory[50] as follows:

- gathering rich, in-depth data through 'intensive interviewing'
- conducting detailed analyses, which become increasingly theoretical
- using line-by-line coding to ensure a high level of familiarity with the data
- writing reflective memoranda to assist with data interpretation
- employing theoretical sampling.

Theoretical sampling refers to a strategy that 'allows the researcher to generate theoretical insights by drawing on comparisons among samples of data'.[51] As per the theoretical sampling strategy, participants with a range of different characteristics were included, to confirm that the qualitative findings were broadly applicable to the variety of people with Parkinson's included in the larger sample. Previous research has suggested that these key characteristics might affect participants' experiences of the PDSAFE intervention.

Longitudinal qualitative studies are comparatively rare in health research, although they have been identified as particularly useful when exploring conditions of change such as might occur in those with long-term and progressive illnesses, as in this study.[52]

Methods and data collection tools

Qualitative semistructured interviews were conducted to explore the experiences of participants in the intervention arm of the PDSAFE trial; they were chosen for their capacity to generate rich, in-depth data about the social realities of participants, in context.[53]

Two qualitative interviews were carried out with people from a subset of those who participated in the PDSAFE intervention arm of the trial (see the following section). The initial interview took place after randomisation [time 1 (T1)], but prior to commencement of the intervention. It focused on the impact of Parkinson's and the participants' expectations of the intervention. The second interview was carried out 6 months later (T2), and elicited information about participation in the intervention arm of the trial (*Table 12*). Because the focus was on exploring participants' experiences of the intervention, the control group were not included in the qualitative substudy.

TABLE 12 Content of interview guides

Content of interview guide	
T1 (after randomisation but prior to start of intervention)	**T2 (6 months after initial interview)**
• Introduction and impact of Parkinson's • Typical day • Managing movement and stability • Experiences of previous therapy and expectations about treatment • Perceived benefits and challenges of treatment • Looking forward to/not looking forward to treatment • Anything else	• Introduction and changes • Experience of the intervention • Facilitators of and barriers to participation • Perception of falls and mobility since T1 • Expectations vs. experiences • Anything else

Initial interview schedules were informed by scoping the relevant literature, which was carried out by referring to study protocols for primary questions of interest. Interview schedules were developed iteratively, in collaboration with the main trial team and stakeholders (including trained physiotherapists, rehabilitation experts and qualitative researchers), other clinical and academic experts (i.e. two qualitative researchers, two social networks experts) and two expert patients. Both interview guides were piloted with expert patients, to ensure that the questions made sense, and revised as necessary. The qualitative Research Fellow employed on the PDSAFE trial completed all the interviews at T1 and T2.

Sample and recruitment

Recruitment for the qualitative study took place from only the first four trial sites (Southampton, Portsmouth, Bournemouth and Poole, and Exeter), so that the qualitative Research Fellow had sufficient time to carry out both sets of interviews and complete analysis.

Participants who were eligible for the PDSAFE trial (see *Chapter 2*) were invited to 'opt in' to qualitative interviews at the time of recruitment to the main trial. Only those participants randomised to the intervention arm were approached to participate.

Theoretical sampling was used to represent the views of participants with a range of characteristics, and included:

- location (at least 10 people from each site)
- age (at least two people aged < 80 years and two aged > 80 years in each site)
- gender (a minimum of two men and two women per site)
- severity of disease (at least one participant per site with disease severity of H&Y scale stages 1, 2 or 3/4)
- number of falls [at least one person experiencing a single fall in the previous 12 months, one who had repeat falls (more than one fall and fewer than 10 falls in the last 12 months) and one who had multiple falls (more than 10 falls in the previous 12 months) per site]
- time since diagnosis [at least one person per site who had been diagnosed for (1) ≤ 5 years, (2) 6–10 years, (3) 11–15 years and (4) ≥ 16 years]
- living status (at least one person who lived alone per site).

Procedure

During the screening visit for the PDSAFE main trial, assessors asked participants if they would be interested in participating in the qualitative substudy, and left a qualitative study patient information sheet if participants expressed an interest. If a participant was randomised to the intervention arm, the qualitative Research Fellow telephoned them to answer any questions they had and to explore if they were still interested in participating in the qualitative substudy. Once their participation was confirmed, a convenient time for the first qualitative interview (before the treatment with the therapist commenced) was identified.

The Research Fellow then scheduled a second follow-up interview 6 months later. Just prior to the scheduled second interview, the researcher checked with the trial manager and administrator that the participant had not withdrawn from the trial for any reason and then telephoned the patient to confirm that the second scheduled interview was still convenient.

Ethics

Ethics approval and relevant NHS trust governance approvals to carry out this qualitative study were covered within the main trial approvals processes. All data were anonymised, and information about participants was kept separate from the data in locked filing cabinets. The qualitative Research Fellow did not contact potential participants until they had expressed an interest in taking part, and participants also had the opportunity to clarify any queries before confirming participation. Written informed consent was taken immediately before each interview.

Qualitative analysis

Interviews were transcribed verbatim and then checked for accuracy by a member of the research team who had carried out the data collection. Analysis of interview transcripts was carried out using inductive thematic analysis, in which dominant themes were identified through close examination of the data.[54,55] Interview transcripts were read and re-read to ensure a high level of familiarity with the data before line-by-line coding. A coding manual was then created to define emerging codes and themes for initial interviews at T1 and T2, and these codes were then applied to the remaining transcripts. The coding manual was developed iteratively and revised throughout the coding process to ensure that the codes adequately reflected the data. The coding manual was discussed and agreed by core members of the research team at various stages of the coding process.

All interviews were transcribed and analysed by the qualitative Research Fellow. In addition, two T1 and three T2 interview transcripts were independently coded by the senior investigator with qualitative expertise, and discussed with the Research Fellow to promote thorough, careful and reflexive practice in the development of the coding framework.[53]

Findings

Participant characteristics

Forty-two participants were recruited at T1. Of these, 37 were interviewed at T2, although two of these participants had withdrawn from the main RCT. Consequently, 35 participants remained in the trial, and completed interviews at T1 and T2. Their demographic characteristics are shown in *Table 13*.

Participant characteristics in the qualitative sample were comparable to the overall trial sample, with the exception of time since diagnosis (the mean was slightly higher in the qualitative sample), number of falls in the previous 12 months (again, the mean was slightly higher in the qualitative sample) and living status (with slightly more participants in the qualitative sample living alone). The higher numbers of people within the last two categories reflect the theoretical sampling, in which we deliberately sampled for these characteristics. All transcripts were included in the thematic analysis.

Findings from the thematic analysis

The transcripts were analysed in two tranches: first, those from the first set of interviews at T1, followed by the second set of interviews at T2.

TABLE 13 Characteristics of participants in the qualitative substudy

Characteristic	Interview at T1 only (n = 42)	Interviewed at T1 and T2 and remained in trial and qualitative study (n = 35)	Interviewed at T1 and T2, but withdrawn from trial (n = 2)	Interviewed at T1 and T2 (n = 37)
Gender, n (%)				
Male	24 (57)	18 (51)	2 (100)	20 (54)
Female	18 (43)	17 (49)	0 (0)	17 (46)
Age range (years)	57–84	57–84	68–79	57–84
Age group (years), n (%)				
≤ 59	2 (5)	2 (6)	0 (0)	2 (5)
60–69	15 (36)	11 (31)	1 (50)	12 (32)
70–79	20 (47)	17 (49)	1 (50)	18 (49)
≥ 80	5 (12)	5 (14)	0 (0)	5 (14)
Mean age (years)	71	71	70	71
H&Y scale stage, n (%)				
1	4 (10)	4 (11)	0 (0)	4 (11)
2	12 (28)	10 (29)	1 (50)	10 (27)
3	23 (55)	20 (50)	1 (50)	21 (57)
4	3 (7)	1 (3)	0 (0)	2 (5)
Time since diagnosis (years), n (%)				
< 5	15 (36)	15 (36)	0 (0)	14 (38)
6–10	7 (17)	7 (17)	0 (0)	5 (14)
11–15	13 (31)	13 (31)	1 (50)	12 (32)
≥ 16	8 (19)	8 (19)	1 (50)	6 (16)
Time since diagnosis (years) (range)	1–35	1.5–21	13–35	1.5–25
Mean time since diagnosis (years)	10	9.2	24	10.4
Falls in previous 12 months, n (%)				
1	11 (26)	10 (29)	1 (50)	11 (31)
2–10	24 (57)	19 (54)	1 (50)	20 (57)
> 10	3 (7)	2 (6)	0 (0)	2 (6)
> 100	4 (10)	4 (11)	0 (0)	4 (11)
Range of falls in the previous 12 months by groups	1 to ≥ 200	1 to ≥ 200	1 to 4	1 to ≥ 200
Mean number of falls in the previous 12 months	32.5	37.5	2.5	35.7
Living status, n (%)				
Lives alone	13 (32)	10 (29)	2 (100)	12 (33)
Living with partner	27 (64)	23 (66)	0 (0)	23 (62)
Living with relative	1 (2)	1 (2.5)	0 (0)	1 (2.5)
Living with carer	1 (2)	1 (2.5)	0 (0)	1 (2.5)

For the first set of interviews, 13 main themes were generated, including 40 subthemes and 104 codes. The 13 main themes were:

1. Parkinson's diagnosis
2. Parkinson's symptoms and experience of Parkinson's
3. reflections on the forthcoming PDSAFE intervention/therapy
4. previous experience of rehabilitation therapies
5. effect of Parkinson's on day-to-day routines and life
6. effect of Parkinson's on mobility
7. losses attributed to Parkinson's
8. adaptation
9. falls and risk
10. well-being and Parkinson's
11. other health and social issues
12. trial and study participation
13. importance of social networks.

The second interviews at T2 generated 17 main themes, which included 33 subthemes and 75 codes. The 17 main themes comprised:

1. activities
2. after the sessions ended
3. experience of the assessor sessions
4. barriers to the PDSAFE intervention
5. deteriorating mobility
6. equipment and technology
7. experience of physiotherapy and other exercise outside of PDSAFE
8. facilitators of continuing with the PDSAFE intervention
9. falls
10. impact and treatment of Parkinson's condition
11. impact of health condition
12. impact of condition
13. impact of PDSAFE intervention
14. PDSAFE physiotherapy sessions
15. strategies
16. therapist input
17. other.

These themes and supporting data have been organised in the rest of this chapter to reflect the three main research aims for the qualitative study. The following four main themes will be discussed below:

1. expectations of participants about the PDSAFE intervention
2. experiences and perceived impact of the PDSAFE intervention for participants
3. barriers to participating in the PDSAFE intervention
4. facilitators of continuing with the PDSAFE intervention.

The following sections include verbatim extracts from interview transcripts. The interviewer was the qualitative Research Fellow.

Expectations of participants about the PDSAFE intervention
The first interview guide included a question enquiring about previous therapies, rehabilitation and experiences of exercise, in order to better understand participants' expectations about the intervention. Almost all of the participants had experienced some form of physiotherapy in the past, although not necessarily in relation to

their Parkinson's. This previous experience of rehabilitation and exercises appeared to influence participants' expectations about the intervention, with many anticipating that this would involve a programme of exercises:

> *Well, as I said, hopefully they will come up with a series of exercises that I can do, hopefully every day, or most days, which will keep me a bit mobile and stop me getting stiff. I dread the thought of being really really stiff and not being able to move and get around; I don't want that to happen.*
>
> *Participant with Parkinson's (21/057)*

(Throughout the report, the numbers at the end of the quotation sources indicate anonymised participant identifier/anonymised site identifier.) Some participants described in some detail what they expected, which included tailored exercises, stretching, freezing exercises and exercises for postural control, co-ordination, stiffness and muscle tone:

> *I'm hoping that they will give me some useful exercises that will deal with, well, the balance; now the question in my mind is whether they will go on from that and talk about also posture, which is something I desperately need and general muscle tone I suppose, so I'm sort of hoping that they will cover all three things.*
>
> *Participant with Parkinson's (43/017)*

> *I anticipate that she will do things like check my balance and um, my mobility and coordination and give me exercises to help improve my balance.*
>
> *Participant with Parkinson's (54/040)*

> *A few participants highlighted everyday tasks that they anticipated the programme might help with, such as getting dressed, and also wider benefits, such as improvement in confidence and helping to sustain social contacts:*

> *Yes, so, that's really why I put my name down [for participating in the trial], because I thought, well anything that can help me keep going as long as possible, because I have got one daughter in Dubai and one daughter in Germany, so, and no daughters in England [laughter] and they are not likely to be coming back, so ah, I want to keep going.*
>
> *Participant with Parkinson's (43/058)*

Participants appeared to value the fact that the intervention was to be delivered at home, citing reasons such as convenience, problems travelling because of poor mobility and relief at not having to visit hospital or clinic sites, or park a car. One person highlighted that, although they were happy for the PDSAFE intervention to take place at home, they felt that appointments outside the home were important to fulfil the need to 'broaden outlook' on life.

Most participants talked about anticipated benefits of the PDSAFE intervention. These included general improved mobility, as well as enhanced functional and physical improvements, for example better postural control, stability, posture, co-ordination, muscle tone and pain control, help with FoG, maintenance or improvement of mobility and walking with more confidence:

> *Well, as I said, hopefully they will come up with a series of exercises that I can do, hopefully every day, or most days which will keep me a bit mobile and stop me getting stiff. I dread the thought of being really really stiff and not being able to move and get around; I don't want that to happen.*
>
> *Participant with Parkinson's (21/057)*

> *Interviewer: Is there anything that you are hoping that you might achieve from the therapy sessions?*

> *Participant with Parkinson's (21/053): Well, maybe that I can walk without, walk with more confidence possibly, and also I have tried using a stick before and I don't like using a stick because I don't think it helps your posture. My posture at the moment is pretty good and I've seen so many people with sticks, really bent over and I'd like to be taught how to use, if need be, a stick properly.*

40

A few participants highlighted more general, functional tasks and a desire that partaking in the intervention would maintain or improve their general independence. The wish to help others by taking part in a trial was also another major motivator for participation in the study:

Interviewer: *Anything that you are hoping it might help with?*

Participant with Parkinson's (32/061): *Mainly co-ordination and manipulation of such things as my buttons. If I can remain independent so much the better.*

Interviewer: *OK, so is there anything you think it might help you achieve?*

Participant with Parkinson's: *Helping others with Parkinson's, if they can learn something about physio[therapy] and how it can help people, so that it helps others in the future.*

Interviewer: *OK, that's important, anything you would like to achieve personally?*

Spouse: *Cure Parkinson's! I'm joking.*

Participant with Parkinson's (32/023): *But it can't do that, can it?! I hope it will help give me my independence back a bit, or some independence, some mobility, I miss my independence. Parkinson's is so frustrating.*

A small minority of people expressed feelings of anxiety or nervousness about the initial therapy sessions; some of this was related to perceived expectations about what it might involve and the intensity of the sessions. Others voiced that they had not previously had success with physiotherapy and so wondered how beneficial it might be:

I will be a bit nervous until I know quite the intensity of it, everybody's a little bit aware you know that, I mean, what does intense mean?

Participant with Parkinson's (21/049)

Perceived challenges or barriers to participation included concern about having a 'bad day' or an 'off day', including anxieties about medication:

I suppose one thing that might be worrying is if the physio[therapist] comes round to do some exercises and I am having an off spell 'cause I have, you know, sometimes I've got a day that's like that and it makes a difference; sometimes the drugs haven't kicked in properly for whatever reason and it might be a down spell, an off spell, and I might sort of have to, you know, that might have to be taken into account.

Participant with Parkinson's (21/039)

Some also had concerns about the time commitment, and expressed ambivalence about or dislike of physical activity:

I mean the thought of doing it every day for 6 months is a bit daunting and I said at the time, I am not absolutely sure I can promise that every day.

Participant with Parkinson's (21/057)

Interviewer: *And anything you're not looking forward to at all?*

Participant with Parkinson's (21/026): *Well, the, the further drain on my time and, you know, doing physical exercise is not my favourite thing.*

At the time of the second interview, participants were asked if their expectations about the intervention had been fulfilled. The majority were not surprised by what they had been asked to do, and were pleased with the content of the PDSAFE intervention. Those few with unrealistic or inappropriate expectations acknowledged this at the second interview:

Interviewer: *Did the physiotherapy meet your expectations, was it what you thought it would be?*

Participant with Parkinson's (43/034): *Yes, I suppose generally there was not much else she could do really to make sure that everything I did was done correctly and that I understand what it was doing and why it helped.*

I knew it would be personal to me but I didn't expect it to be so personal, I know that sounds a bit ambiguous but she almost assessed how I was doing each time and geared it specifically to what I could and couldn't do.

Participant with Parkinson's (54/040)

A number of participants suggested that they had not fully appreciated the time and commitment the intervention programme would take, sometimes suggesting that the programme was onerous or a 'bind'. This reflected anxieties and concerns from the first interviews about being able to find time in already busy schedules to complete the programme daily:

Interviewer: *So it was not quite what you thought it was going to be . . .*

Participant with Parkinson's (32/008): *No. It was alright in the winter when you, when I have got nothing to do, but when the vegetables started to come, it became a bit of a bind trying to find time to do it, and I wanted to pack it in.*

The experiences and perceived impact of the PDSAFE intervention for participants

During follow-up interviews, participants were asked to describe the content of the PDSAFE intervention. All of the participants spoke about the exercises and strategies that they were encouraged to use. Most participants were able to describe these in detail, and described a range of exercises.

Most people found the level of the programme acceptable and usually recognised the progressive nature of the exercises over time:

They got harder [laughs] . . . The expectations were greater, um, for example I could just about put one foot in front of the other and walk the line, like you do if you are drunk, if I did it quickly; so then the next stage was to do it slowly and it is much more difficult and so it was graded.

Participant with Parkinson's (43/058)

Participants also described a variety of strategies that they had been taught as part of the intervention, including swaying from side to side to promote motion, not cutting corners, walking with one foot in front of the other, using wider steps so as not to shuffle, having feet further apart to prevent falling and picking up feet.

Interviewer: *Did the physio[therapist] give you any sort of strategies to use or hints?*

Participant with Parkinson's (54/069): *Well, if I ground to a halt, because I have been freezing a little bit, just to psych meself up and to count from one to four and then I could go [i.e. move] on the four.*

Most participants commented on the expectation that they would engage with the programme daily, or as close to this as possible, and tried to conform to this, although this appeared to be challenging for some, particularly if they had other commitments on the same day:

> *The idea is to do the exercises every day, she said, if you could do them three or four times a week that would be sufficient, not ideal, but it would be sufficient, so I did try.*
>
> *Participant with Parkinson's (21/057)*

The PDSAFE intervention involved the use of a range of equipment, including a weighted vest or jacket, the step, the exercise folder and log, a metronome and/or a DVD. Some recognised that the intensity of the exercises increased with the use of equipment:

> *I would do the exercise, I'd be out the garden doing it out there during the summer and using the step for the legs . . . there in the sunshine, and then I got a weighted jacket, which was harder, more challenging.*
>
> *Participant with Parkinson's (21/039)*

Experiences of using the equipment were mixed, with many participants commenting particularly on the weighted vest:

> *I was doing stepping on that [i.e. the step] and that was fine, um, and then she put little feet on it to make it harder, but every time she came, she made it a little bit more difficult and the real shock was when she came with the weighted vest. Have you seen the weighted vest? It's a torture chamber, honestly, so I picked it up and I said 'Am I supposed to be wearing this? . . . I can hardly lift it' and it actually weighed 14 pounds and I had to really sort of struggle to get it on and then do it up and I had to do the stepping with this vest on. Well, I couldn't believe it, I said 'Are you sure this is doing me good?' and she said 'Yes, [laughter] it definitely is' and then after I had done that for a few weeks she wanted to put some more weights in it. I said 'Look I am sorry, but this is really as much as I can cope with'.*
>
> *Participant with Parkinson's (21/057)*

Although views about use of the equipment were mixed, a small number of participants were disappointed that the vests, steps and folders had to be returned once the physiotherapy visits ceased.

Several people mentioned that the filming and resulting DVD helped them to understand issues with their gait or posture:

> *There was one of me, my posture, which was, I did not mean to be alarmed because I knew my posture was awful. I did try, as it is one of the things she has helped me with quite a lot actually is the posture and, erm, I suppose it has improved a bit. Well anyway, the DVD was helpful in seeing how awful it was.*
>
> *Participant with Parkinson's (21/026)*

However, more commonly, participants disliked, or experienced problems with the technology. Some felt that the DVD/metronome was unnecessary or did not help them, some did not use it and some preferred to do exercises to counting or using the beat of music. Some participants described technical problems with the DVD or would have preferred to see the programme on a portable device such as a tablet.

Follow-up interviews also explored the perceived impact and benefits of the PDSAFE intervention for those taking part. The majority of participants felt that they had made some progress in terms of mobility (including improved posture, postural control, functional strength, walking better, falling less frequently and/or enhanced control of freezing symptoms). Some also described improvements in functional activities:

> [Laughs] I thought 'what have I let myself in for?' initially, but once you start doing the exercises and you know you can do them, you know, like putting my socks on was very difficult and that's better now, stretching, that helped a lot.
>
> *Participant with Parkinson's (54/074)*

In follow-up interviews, over one-third of participants reflected that either their falls had reduced or they were better able to recognise falls triggers since embarking on the PDSAFE intervention:

> I think they [i.e. falls] are less frequent because I am thinking in my mind all the time, walk sensibly, open this door sensibly, do this sensibly, because otherwise you are going to fall.
>
> *Participant with Parkinson's (32/014)*

Other perceived benefits of the PDSAFE intervention included increased awareness of limitations, for example recognising the need to plan things carefully, increased awareness of safety and recognising poor posture. Linked to this was enhanced recognition of the need to 'slow down' and 'not rush(ing) around':

> I think the most useful thing, probably, is that I have had to learn [pause], to slow down, . . . I mean before I would just dash everywhere, not run I don't mean, but you know just sort of walk and then I would get my feet in a muddle and you know all that sort of stuff and I think that is probably the thing I have learned most, to control that so that, you know, if I am in a hurry I can still function without fear of tripping.
>
> *Participant with Parkinson's (43/050)*

Around half the participants interviewed at T2 also spoke of increased confidence, independence and general well-being:

> It made you feel you could do it independent. It was a good help.
>
> *Participant with Parkinson's (32/054)*

> I feel more confident.
>
> *Participant with Parkinson's (43/027)*

Although most participants interviewed at follow-up perceived some improvements, physically, functionally, in falls reduction or more generally (as described above), a small number felt that they had not experienced any benefit from participation in the PDSAFE intervention. Several of these participants simply questioned whether or not the intervention could make any difference to them in the face of a deteriorating condition, even if they felt that the programme was, in itself, good.

Barriers to participating in the PDSAFE intervention

During the follow-up interviews at T2, participants were asked for their views about the barriers to and facilitators of taking part in the PDSAFE intervention. The time commitment to complete the exercise programme was identified as one of the major barriers to continued participation, particularly towards the end of the programme and beyond. Participants often described the programme as being fairly

time-consuming or requiring a big commitment. Although for some this was not an problem, others found this challenging, particularly if they already led busy lives, which seemed to be a particular issue for those whose Parkinson's was not so advanced:

There was nothing difficult about it; the only difficulty about it was me staying on target with the exercises between the visits. I found, because I lead a fairly active life anyhow, I couldn't always find the time to get to do the regular exercises.

Participant with Parkinson's (43/055)

A lack of motivation was also commonly offered as the reason for giving up the exercise programme, particularly when visits from the treating physiotherapist became less frequent or stopped altogether:

It would be trying to do it every day [is the most difficult part]. But that day, I know that if I do it I would be better and more flexible and more co-ordinated but it is just motivating myself to do it sometimes. It's the hardest, that's . . . it's the hardest thing to do.

Participant with Parkinson's (54/040)

However, not all participants ceased the programme at the end of the visits from the physiotherapists (see the following section). Another common barrier alluded to previously, was use of the programme equipment or technology. The two items most often mentioned as problematic were the weighted vest and the DVD with metronome.

For some people, illness, injury and other life events, such as a family death, prevented them from participating fully or at all in the programme. Illnesses and injuries mentioned during the interviews as barriers included problems with knee and shoulder, heart attack, shingles, pain, cancer and high blood pressure. Difficult life events included bereavements and family illness:

I had one week off in March when I was away for the week and then in the beginning of June my husband died and that threw us all out completely.

Participant with Parkinson's (32/014)

Participants also described their experience of 'off' or 'bad' days as another barrier. These days were characterised by difficulty in engaging with the programme, particularly at times when medication was not optimised, participants felt particularly ill or symptoms were at their worst:

And sometimes, you know, with Parkinson's you have your off periods where your drugs haven't kicked in and there are times when I am having an off evening and I try and do my exercises, but the off spell seemed to be longer than normal, so I might have to miss it then, so it's just choosing the time of day.

Participant with Parkinson's (21/039)

Finally, a couple of barriers mentioned by just a few people included fear and forgetting to engage with the programme.

Facilitators of continuing with the PDSAFE intervention

In the same way that a reduction in and eventual cessation of visits from the treating physiotherapist acted as a barrier to continued participation in the programme, the knowledge that the physiotherapist would be visiting again acted as a facilitator of participation for participants. Interviewees commented that they tried harder when they knew that the physiotherapist would be returning and expressed the view that they did not want to disappoint her. Some mentioned the importance of reinforcement for their efforts provided by

the therapist, and looked forward to her visits. A few suggested that they engaged in the exercises only when the therapist was present. Even the occasional participant who did not feel that they gained a lot from the programme appeared to value the therapist's presence:

Also, having the physiotherapist visiting regularly, that gives you something to aim for, like, when you know that she is coming next week and you want to make sure that everything is up to date and that you are doing the exercises properly, so having that sort of check and balance if you like helps to keep . . . and it ran very smoothly.

Carer (21/056)

Support and encouragement from one's partner, spouse or carer was another important facilitator. This could take several forms, for example the partner or carer completing the exercises alongside the participant, or reminding the participant to complete them:

And it was nice as well because she included me, it was really nice because obviously I would do the exercises with him, but she didn't make me feel that I shouldn't be there and she included me, which I thought was really nice. I thought at first did she just want me to go out of the way and think I was interfering, but no she was really good. Obviously, I like to know what is happening, because when I do them with him I would like to know what she is doing. That is quite good.

Spouse (43/059)

Another facilitator mentioned by participants was the written information about the PDSAFE programme provided in a blue folder to those taking part in the intervention arm of the trial:

Well, on every session, whenever she came, we started straight away with the list of exercises which she gave me, which she showed me . . . I had a list, a chart that she gave me, so I could tick off each one as I did it.

Participant with Parkinson's (43/050)

For some, particularly those with already busy lives, the intervention was easier to engage with if integrated into their daily lives. Participants found novel ways of building the exercises into their daily routines, for example doing them while completing chores, gardening or while in the kitchen. Others would integrate exercises, for example walking or stepping exercises, into leisure activities such as dog walking, playing golf or simply walking into town, or adapted exercises to their environment:

I did them in the morning. I did them while the kettle was boiling. Once you knew what to do it was quite simplistic so I would do my marching you know, and then I would go and put the kettle on and I would do this bit and that and by the time I went out in the morning it had all been done.

Participant with Parkinson's (43/058)

Other facilitators of the PDSAFE intervention included seeing direct improvements or feeling a sense of progress.

Chapter 6 Qualitative process evaluation: part 2

This second qualitative process evaluation chapter reports on the expectations and experiences of the physiotherapists who delivered the PDSAFE intervention, which were explored using a series of individual interviews.

Overview

The second stage of the qualitative process evaluations involved conducting in-depth, semistructured interviews with a group of the treating therapists. Six of the treating therapists (not those trained to provide cover) were interviewed by an independent researcher. Data were managed and analysed using framework analysis[56] and five themes emerged:

1. views on the PDSAFE concept and therapist involvement
2. benefits and limitations of the PDSAFE intervention
3. influences on intervention success
4. perceptions of patients' experiences and engagement
5. PDSAFE intervention usability and transferability.

Theme 1: views on the PDSAFE concept and therapist involvement

This theme describes therapists' thoughts on the concept of PDSAFE, their involvement in delivering the programme and the challenges they faced.

Views on the PDSAFE concept and study involvement

On a conceptual basis, therapists responded positively towards PDSAFE; the intervention was described as being holistic, comprehensive and inherently relevant to an individual's problems and environment. The approach focusing on strategies to enable functional activity was seen as differing from the prevalent approach used in usual practice/the NHS, which was described as being exercise driven:

> I thought it was very good, it takes a slightly different tack than a traditional NHS assessment because it's sort of strategy driven rather than exercise driven so it's potentially looking at a person at a functional level, trying to kind of really drill down when they are falling and why they are falling but at a much more of a global level and trying to really focus in on that, not address that problem through the provision of exercises but more actually looking at practising functional activities that are linking in with the falls.
>
> *Therapist 6*

Having PDSAFE in the individual's environment, 'where the falls happen', was seen by all the therapists as the ideal. Being in the person's home, setting their environment and situation was considered to give much better insight into how to tailor treatment:

> It had relevance to them, [. . .] and their problems, they demonstrated their problems by when you look at them and you map the house and you have a really good look at them. So the relevance for them is excellent, so they know that this is their problem and you start working towards trying to solve that problem or a couple of problems that they do have with stuff that is functional, that they need to do for their everyday lives.
>
> *Therapist 1*

All therapists reported enjoying the experience. One therapist commented that the PDSAFE approach was so different that working with it was initially difficult. Another therapist noted at times feeling constrained/unsupported when patients were unwell and the links back to clinical services seemed less apparent:

> I suppose initially actually not approaching it from a training base but approaching it from a strategy training in a functional side was quite hard to embrace to start with but now I've got the hang of it, I absolutely love it and I think it's a really ingenuitive different way of actually looking at how therapists approach the treatments to their patients. I've really, really enjoyed it.
>
> *Therapist 3*

Intervention challenges

There was a consensus that working with patients who had cognitive issues and/or dyskinesia was the most challenging aspect of the delivery of the PDSAFE intervention. This group were noted as challenging to support in usual practice, and one therapist noted needing to seek support during the intervention from a colleague to help their patient progress. This difficulty was attributed to patients with cognitive issues being unable to retain an understanding of the PDSAFE structure, rationale and content covered. Some therapists felt that this group required different support to PDSAFE. Others consider PDSAFE to be capable of helping this group if they had support from a significant other or carer:

> We had a fair few that did pass the cognitive screens to be part of the trial but then it is very different to pass a screen like that and then actually be able to participate in the trial, [. . .] It was fine if they had a partner or someone that they were living with to support them, but if they didn't, that was really hard and we had to use so many different strategies and took lots of our time to try and get them on board and get them familiar with the programme and sometimes it still wouldn't really work.
>
> *Therapist 5*

Promoting exercises was seen as more challenging among patients who were unused to exercise/deconditioned, were less physically able and were unwilling to change their routines/habits. There was also comment that many patients struggled to grasp how to progress their exercises:

> I think it's very easy to follow the sort of structured exercises and things but that carry-over into function is the biggest, I found the biggest hurdle and was starting to say to patients at the start of my treatment. I said you know there's gonna be exercises which support the use of a strategy and the crux of it for you I felt was to have that transferred into function and you know and that's where the real hard work is for you is to try and change habits, things that you do on a daily basis without really thinking. So I try and sort of prep them, yeah, there was resistance to that I think.
>
> *Therapist 2*

More individually raised challenges included working with patients who had overly protective spouses/partners and fitting the required number of sessions in around seasonable periods/patients' busy schedules:

> With the higher-level people, only that they had busy lives and getting a schedule to fit in. [. . .] and several of them had really active social lives and travelled and went away and went to rugby matches and so fitting in all the appointments at the appropriate times was difficult.
>
> *Therapist 1*

Theme 2: benefits and limitations of the PDSAFE intervention

This theme outlines the benefits and limitations attributed to the PDSAFE intervention by therapists.

Ingredients of intervention success

Most therapists associated having minimal/no cognitive difficulties as a key element for intervention success. Cognitive issues were explained as potentially reducing motivation (owing to reduced understanding of intervention intent) and preventing carryover from treatment:

> *I think the whole thing worked very well as long as they had the cognitive capacity to understand how it all knitted together, which aided their motivation.*
>
> *Therapist 4*

This issue then limited a patient's ability to progress. However, the belief that cognitive acuity was important for intervention effectiveness was not universal; Therapist 1 did not feel that any group benefited more than any other and reported that all of her patients progressed, including those with cognitive issues:

> *Everybody progressed, everybody really enjoyed it, all the people I had, even the ones with cognitive impairment were very compliant [. . .] whoever benefits are the ones that are motivated to exercise and I have to say that every participant I saw, mine and (two other therapists) were all motivated. I can't say that anyone benefited more than anybody else.*
>
> *Therapist 1*

Those described as 'motivated' to exercise and to integrate PDSAFE into their routines were thought more likely to derive benefit. Those with mild to moderate Parkinson's, who were functionally independent, were seen by some as ideal candidates in terms of potential to benefit. Finally, being concerned over one's personal risk of falls was discussed explicitly by one therapist as important for facilitating the required lifestyle changes:

> *I think people who have had a significant enough experience of a fall to see why they would want to work on it, so I think sometimes when patients maybe in the trial had had one fall a very long time ago or whose symptoms were so mild that they couldn't really engage so much with changing their daily habits to prevent them falling, the problem wasn't really significant enough I suppose.*
>
> *Therapist 2*

Factors associated with reducing intervention effectiveness

In line with therapist comments on the limitations of the PDSAFE intervention, cognitive impairment and/or dyskinesia were noted as limiting intervention success:

> *There were issues regarding patients with cognitive impairment which made it that much more difficult. [. . .] Patients with dyskinesia which made it again very difficult for anyone who wasn't really used to cope with some of those issues but I think for the . . . mainly for the person who isn't that severely affected, I think it had a better outcome.*
>
> *Therapist 4*

One therapist commented that PDSAFE could then become a burden to the patients who, on being given a programme to work on, could not obtain sufficient benefit. Support was noted as a key issue, particularly for those with cognitive problems; patients with no support reportedly struggled to complete all exercises and, as a result, could only partially engage in PDSAFE. The time since a patient's last fall/the significance of the last fall to the patient was suggested as influencing intervention effectiveness. As PDSAFE was recognised as requiring changes to routines, some therapists commented that, if falling was not a big concern, patients may be less likely to alter these routines.

The extent to which a patient felt able to cope with new commitments was also identified as influential; those with multiple conditions and accompanying appointments, or busy lives generally, were noted as being more likely to withdraw from the treatment because of an inability to take on the substantial commitment posed by PDSAFE:

> *Where people haven't progressed is where you've got some underlying cognition problems, whether they forget the appointments, where you turn up and they are out and where they just don't get the intensity, you can't build them up to that intensity and they have to commit like 6 days or up to 6 days, 5–6 days they have to be doing this for half an hour, so that is quite a commitment to them and so you need to be motivated, you need to be knowing what you're doing, why you're doing it and what benefit you are going to get from it and if you haven't got that type of person, it's a hard slog.*
>
> *Therapist 6*

> *Those patients that are so severe that they've got so much going on in their life and they've got different appointments to attend, they've got sort of other illnesses, they're so tired, they are falling quite frequently and for want of a better phrase 'in a pickle' basically. The patients who have got so much on, the idea of doing these, you know, looking at this blue folder and using the blue folder to do anything extra on top of everything else that is going on is just too much for them really. It was quite a struggle and you would go and you would feel like it was just one thing too many at that time.*
>
> *Therapist 2*

Other factors reported as reducing intervention effectiveness included the following:

- patient attitude/motivation (patients who embraced illness and inactivity were seen as less likely to engage/benefit from PDSAFE)
- physical ability (e.g. those with walking aids participated at a lower level, which limited the benefit they could achieve)
- medication (side effects in some in cases hindered participation).

Theme 3: influences on intervention success

This theme highlights the factors and patient characteristics perceived to improve or reduce the likely success of PDSAFE at an individual level.

Strengths associated with the PDSAFE intervention

Several strengths were attributed to the PDSAFE intervention. The focus of PDSAFE on an individual's functional problems and issues, in their own environment, was seen as a core strength of the programme. One therapist overtly related this patient-centred focus and approach to building patients' confidence in their functional abilities:

> *It boosts a lot of people's confidence, especially the fact that you can take them anywhere, take them outside, [. . .] I did get someone on the beach [. . .] she said to me that her friends had commented periodically, how much better her gait pattern was and how much more confident she was and she felt more confident.*
>
> *Therapist 1*

A number of therapists commented on how helpful the PDSAFE programme structure was not only for them, but also for their patients. This structure was described as being extremely clear and different from usual practice in that there was no 'wait and see' element:

> *The fact that you had very, very clear guidelines to work towards and I thought it was a clear and easy-to-follow intervention programme, [. . .] you had a clear progression and a clear way to lead but you also had a huge amount as a therapist of decision-making yourself and using your clinical reasoning to come to the decisions of what strategy you chose or exercises you chose, so again, it didn't dumb you down.*
>
> *Therapist 3*

The opportunity afforded by PDSAFE to reinforce functional strategies was reportedly appreciated by therapists. The range of strategies available was also considered to be particularly good; this was seen as giving therapists the ability to respond flexibly and creatively to their patients' individual needs:

> *It was a good variety and, from a strategy point of view, you could really open it up and could treat in many different sorts of ways out and about and in their own home and doing anything that they find particularly difficult. So it was quite open at that stage.*
>
> *Therapist 6*

Limitations associated with the PDSAFE intervention

Therapists described a number of limitations associated with the PDSAFE intervention. The three most commonly discussed related to the following:

1. PDSAFE was seen by a number of therapists as less suited to patients with cognitive issues and/or dyskinesia.
2. Some therapists reported that progressions posed ceiling and/or floor effects on exercises, namely exercises could not be made simpler than the lowest-level exercise (even though in usual practice it could be adapted) and, similarly, exercises could not be made more challenging than the uppermost exercise progression.
3. Therapists also reported that being unable to deviate from the set exercise positions inhibited their freedom to clinically reason and adapt the exercise to suit an individual, for example if a patient had a comorbidity, such as knee arthritis, that prevented them from adopting certain positions:

> *I probably would have treated them in a different position, so somebody for example, if they are, if they've got lots of arthritis or if they've got any other comorbidities, it's difficult to then start loading joints if they are a bit arthritic in order to then strengthen. Previously, I would have then maybe looked at strengthening up in lying or on their tummy so I would have done it slightly differently [. . .] rather than on a protocol. I could only, for example, strengthen people up in, say, standing and obviously if you've got an arthritic knee or hip, it's actually quite difficult. So there were some limitations with it but from an exercise point of view.*
>
> *Therapist 6*

Consequently, therapists reported that some patients remained 'stuck' at a certain point in the programme. Both of these issues led to therapists suggesting ways to improve the PDSAFE intervention for future implementation (see *Theme 5: PDSAFE intervention usability and transferability*). Other limitations concerned (1) exercises becoming repetitive for some patients and (2) some progression (specifically involving the metronome) promoted dual tasking at the expense of movement quality:

> *I definitely think the exercises, I want to be a bit more sort of creative with the patient and I think sometimes they potentially started to find things quite repetitive (Interviewer: yeah, yeah) so I probably would want to involve other exercise ideas, maybe to make them a bit more fun as well. That's not necessarily a PDSAFE criticism, it's a general, a lot of exercises we described are often quite boring.*
>
> *Therapist 2*

Yeah I think the variety of exercises and the fact that there is a lower limit and an upper limit to what you can do so you can't progress further than a certain point. You can't strip the exercise back past a certain point as well, I suppose.

Therapist 2

Theme 4: perceptions of patients' experiences and engagement

This theme describes therapist perceptions of patients' experiences and their engagement with PDSAFE during the programme lifetime and beyond.

Perceptions of patient experience

Most therapists perceived that a majority of patients enjoyed the PDSAFE experience, reporting patients to be engaged and 'on board with it'. However, one therapist noted occasions when patients had not seemed to enjoy the overall experience, for example when coexisting musculoskeletal conditions were exacerbated by PDSAFE activities or when patients were not open to changing their routines:

I think most people were on board with it [. . .] I don't think I had any dropouts at all or not due to not wanting to do it. It was they were withdrawn because their diagnosis changed but most people were on board with the programme and wanted to do it and wanted to be part of the trial so that went well.

Therapist 5

There are a couple of patients who had musculoskeletal problems and had problems with pain who probably didn't enjoy it as much just because they associated movement with discomfort.

Therapist 2

Therapists described a number of particular elements of PDSAFE that they believed patients to have most enjoyed. Three of the most commonly discussed of these were (1) the focus of the programme being on issues most relevant to the individual patient, (2) the clear structure attributed to the programme and (3) the intensity and level of input/contact with therapists to support activity. Other features reported as being positively received by patients related to the novel focus on strategy training, the chance to exercise, the opportunity to use equipment and the confidence regarding managing a fall and the resultant feeling of increased safety developed within the programme:

I think it's having somebody supervise them, I think it's somebody coming in and they are not being left with a piece of paper, doing a list of exercises, they are actually having somebody come in and teach them something that they can relate to and for us it was falling but it might have also been getting up out of a chair, rolling over in bed, getting their food out of the boot of the car from shopping, you know.

Therapist 6

The intensity of the programme, that it was centred around them as an individual and the strategy training practice which was different to what they had received before.

Therapist 3

Aspects of the programme that were least enjoyed included (1) completing paperwork, for example falls diaries (although it is worth noting that these were a product of the research trial rather than the intervention itself), (2) reduced contact in later stages of the programme, 3) changing habits/the home environment and (4) exercise. Regarding falls diaries, some therapists attribute this to the tedium of

completing paperwork whereas others felt that embarrassment was a factor. Regarding exercise, for some this was due to the difficulty of the exercises whereas for others, more physically able, exercises might become a bore:

> *It's always about the documentation, the tick sheets – it's always a recurring issue so we got to the 6 months' point and the majority, the ones that had done well without any cognitive impairment, didn't need the tick sheets, they think 'I do this every day' or 'Monday, Wednesday, Friday is my days', I've got a reference for the exercises and they were glad to see the back of that. Although it's just a tick sheet and doesn't take long, it becomes a bit of a nuisance doing it so that's the thing that I found people moaned about more than anything else.*
>
> *Therapist 4*

> *I think they probably found it difficult when it went down to monthly and they were used to seeing you more regularly than that and I think probably filling in their forms, none of them liked filling in their fall forms [laughter] and I can understand why because you are focusing in on your . . . falling is . . . whenever I fall over, which thank god is not very often, but if I fall over in the street or trip over the dogs fairly frequently, it's embarrassing, isn't it? I really don't want to dwell on that and I cover up my grazes and I kick my dog out of the way and I carry on my way that nobody sees. If you ask somebody constantly to write down their falls and reminisce about them, I think people found that difficult.*
>
> *Therapist 1*

Patient engagement in the PDSAFE intervention

Therapists perceived most patients to be motivated during the most intensely delivered points of PDSAFE. Patient engagement following intervention tapering was described as variable; some therapists perceived patient engagement to reduce when contact changed to monthly visits, others felt that their patients continued to engage through to programme completion. All therapists raised uncertainty and/or concern regarding the likelihood of their patients continuing the exercise programme. There was a feeling that some would continue, many would 'ease off' in terms of intensity/frequency of exercise and some would not continue. Although it was recognised that therapy contact could not continue indefinitely, it was considered that there was a need for some form of follow-on programme/group. Therapist reports of patient feedback support this also:

> *I did find that a few people, quite a few, lost motivation towards the end. So they started off quite motivated and then towards the end they would lose it so when I was seeing them at a less intense level, they definitely lost motivation and a few of them, I would say to them at the end, will you continue they would say – probably not just doing it themselves and be more likely to go to a group, some of them do tai chi and other exercise classes that are Parkinson's related or non-Parkinson's related and they would continue with that.*
>
> *Therapist 5*

> *They all said 'is that it?' so I think my feeling is that with exercise-based programmes you've just got to keep seeing people or move them on to something else.*
>
> *Therapist 1*

Theme 5: PDSAFE intervention usability and transferability

This theme discusses therapists' perceptions of the usability of PDSAFE tools, the training they received, ways to enhance the original programme and its transferability to clinical practice.

Evaluations of therapist training

Training was highly praised, the knowledge of staff was commended and, for the most part, therapists reported feeling supported:

Absolutely fantastic, loved every second of it, comprehensive. I don't think anything could train you for the completely different way, obviously [name] did the training and then we did the case studies to make us try and think strategy based and I think until you are actually out there and actually doing it, the training couldn't have been any better and the early fidelity checks were paramount, I think.

Therapist 3

The one instance in which a therapist felt unsupported initially related to part-time working patterns and difficulty synchronising schedules to arrange a telephone conversation. The monthly group discussions and masterclasses were valued as very supportive, inspirational and good sources of continuing professional development. The peer support/double visits were particularly valued as learning and support opportunities. Some therapists noted that although the training in class was good, much learning occurred when implementing the programme, and peer support/double visits were vital to this. There were few negative comments; one therapist reported experiencing a large gap between receiving training and beginning the intervention, which resulted in the therapist struggling/feeling less confident when initially commencing treatment. Another comment was made regarding time spent working through paperwork (e.g. the treatment protocol, which detailed the treatment structure) during initial training, reducing time for practical learning:

The training was delivered and I then had a very long wait before I got my first participant. I can't remember how long but I can't remember if I'm honest, but it could have been over a month and I couldn't . . . it was then difficult to really feel confident with delivering the protocol because you are new, you can't totally remember, you read the paperwork and you read what's given to you and you've got a reasonable idea but it's all the conversations, it's all the scenarios that was discussed so whether somebody could have come and did one . . . our first visit, a few of our first assessments, then that might have worked.

Therapist 6

Tool utility

Therapists commented on the utility of various tools, equipment and documentation used in the PDSAFE intervention. Some of these resources were praised by all participants as exceedingly useful. The use of one-to-one videos, whereby the therapist recorded a patient's movement and then talked them through an assessment of this, was considered a very useful facility that was, for the most part, appreciated by a majority of patients. There were some therapists who noted some patients struggling to focus on the recorded movement, instead attending to their appearance:

The one thing I did find really useful was when you are doing a strategy with someone and you've got them doing a functional task and you video them and then give them immediate feedback, they can see themselves.

Therapist 1

The weighted jacket and the metronome received a more mixed review. The participants reportedly found it very difficult to put on the weighted jacket themselves; some patients found this a considerable struggle and required assistance. Concern was raised regarding being able to use the jacket if people did not have significant others/carers to help. The weighted jacket was also seen as (1) having potential to aggravate musculoskeletal issues and (2) being intimidating/off-putting, especially for those who were unused to

exercise/weight training. It was not only patients, but sometimes also partners/spouses, who were intimidated by the jacket:

> *I would say there was an element of them trying to protect their partner a little bit and not want them to do too much, so things like the weighted vest, even if the participant themselves were quite keen on using it, their wives were not.*
>
> *Therapist 5*

However, some therapists reported that with practice donning the jacket became easier, and some patients responded well/enjoyed wearing it:

> *I think sometimes with the strengthening part of the programme they may have been quite daunted by the thought of wearing a vest, especially some of the females. The actual, the realisation that they could actually do far more than they ever thought that they were capable of that was really encouraging.*
>
> *Therapist 4*

The metronome was seen as being disliked by many patients because of the associated difficulty of dual tasking, although some therapists reported patients enjoying working with this. There was some suggestion that trying to maintain speed could reduce quality of movement (see *Theme 2: benefits and limitations of the PDSAFE intervention*).

The pre-recorded DVDs were unanimously reported to be used infrequently by patients. A number of therapists noted technical difficulties associated with this, and reasoned that the effort of setting up the DVD was not justified by the benefit patients derived from watching it. Another explanation was that some patients did not feel the need to remind themselves how to perform the exercises. Therapists noted being surprised by this finding.

Suggestions for improving the PDSAFE intervention

Increasing the number of exercises in the exercise library was a common suggestion/request, as was allowing more flexibility in modifying exercise progressions and postural sets to aid clinical reasoning and individual intervention tailoring. Other suggested improvements included the following:

- Increase the choice of functional activities and strategies.
- Allow a more flexible blue folder composition so that it can be simplified for people with cognitive issues. Remove old cards when new ones are issued to reduce confusion.
- Emphasise video feedback one-to-one sessions with patients and therapists over DVD usage.
- For exercises, consider having A4 laminated sheets with pictures and few words that can be put up on a patient's wall.
- Consider spreading the first two sessions over four sessions, as there is a lot to assimilate.
- Make computer versions of paperwork more readily available for patients who struggle to complete forms in hardcopy.
- Add patient demo to PDSAFE training to help therapists understand the flexibility of the programme and how things may be adapted if initial choices fail.
- Potentially encourage more 'double'/fidelity sessions and sooner in the programme as these are valuable learning opportunities.

Feasibility and desirability of integrating the PDSAFE in clinical practice

Therapists felt that PDSAFE could be delivered in the community. Although it was recognised that aspects of the programme would work in a hospital setting (e.g. exercises) and that group exercise particularly could be motivational, devoid of vital context, hospital delivery was still seen as a less desirable setting. The need for context in order for patients to learn strategies and attain carry-over was stressed by all. For some, delivering the programme in a hospital, divorced of this context, was possible but less optimal/ effective, whereas others considered it infeasible.

There was recognition that PDSAFE, as delivered, amounted to double the therapy sessions usually delivered as part of routine care. This led to therapist uncertainty regarding whether or not PDSAFE would be funded adequately in the current climate; as a result, this issue was noted as being decisive when evaluating the feasibility of delivery of PDSAFE in clinical practice:

> *I guess it comes down to funding anyway, if the funding is there to deliver it as it is, then yes I imagine that it would be hard to get, just because of the time involved and it's not just even the intensity of the programme, it's all that extra stuff in terms of the admin[istration] and the [tele]phone calls to arrange the appointments and things and the yeah, whether it was put into a community service for people with Parkinson's as a – you are seeing them anyway but we want you to deliver it like this rather than what you would normally do, then yes, I guess, but you would have to have that funding there.*
>
> <div align="right">*Therapist 5*</div>

There was discussion regarding who should be involved in the delivery of PDSAFE; there was a feeling that a qualified physiotherapist would be needed to assess, develop the treatment programme and progress patients, but that therapy assistants could take on some sessions to check in and support patients when they were implementing their personal programmes.

Chapter 7 Economic evaluation

Overview

The cost-effectiveness analysis (CEA) of the PDSAFE physiotherapy intervention compared with usual care in people with Parkinson's is presented in this chapter. Cost-effectiveness was estimated using a 'within-trial' analysis, based on health-care resource use and health-related quality of life (HRQoL) utility data collected over the 12-month trial period. Results are presented using an incremental cost-effectiveness ratio (ICER), estimated by dividing the difference in mean costs between arms by the difference in mean quality-adjusted life-years (QALYs) between arms. ICER estimates were compared with a £20,000- and £30,000-per-QALY threshold applied by the National Institute for Health and Care Excellence (NICE).[57]

Methods

Resource use

In line with NICE economic evaluation recommendations, this CEA adopted an NHS and Personal Social Services (PSS) perspective.[58] Data for CEA were collected at baseline and at 3, 6 and 12 months. Costs were evaluated in Great British pounds using a 2016 base year. All analyses were undertaken according to the principle of ITT and in Stata/SE version 12.0. Costs included intervention costs (apportioned per participant) and NHS and social care resource use costs. Intervention costs were collected directly from trial records. For resource use costs, unit costs were obtained from national sources: the Personal Social Services Research Unit's (PSSRU's) *Unit Costs of Health and Social Care*[59,60] and NHS Reference Costs 2015 to 2016.[61] Quantities were collected from the trial participants. The resource use questionnaire collected information on (1) primary care services provided in the NHS system [e.g. general practitioner (GP) visits, physiotherapy, occupational therapy], (2) secondary care services provided in the NHS system [e.g. ambulance call outs, accident and emergency (A&E) attendances, hospital stay] and (3) social care services (e.g. home care visits, meals on wheels). Medication use was collected separately. All resource use data were originally collected from participants by interview with an assessor. This was revised after identifying a risk of unblinding of assessors during the interview by the question asking participants how many times they saw a physiotherapist. Therefore, the whole section containing the number of times a physiotherapist was seen was then collected via postal questionnaire, which was completed by participants. Questions on fall-related A&E attendances and hospitalisation admissions were also embedded into the falls diaries for validity checks. Unit costs in the financial year 2015/16 published by the PSSRU[59] and NHS Reference Costs 2015 to 2016,[61] when information was not available from the PSSRU, were attached to each item of resource use. *Table 14* shows the unit costs applied to each resource use item and *Table 15* shows details of assumptions varied in each sensitivity analysis.

Cost of personalised home-based physiotherapy

The cost of implementing the PDSAFE intervention was collected from the trial co-ordinator and lead therapist. The analysis followed an ITT principle; therefore, only the participants allocated to the intervention arm were assumed to incur the cost of treatment and any research-only cost was excluded. This ensures the relevance of the cost estimates if the programme were to be 'rolled out' to larger numbers of people.

Therapy session costs included the personnel costs (i.e. salary) of the therapist, travel costs, equipment costs and consumables. The salary cost of the therapist was calculated based on NHS band 6 full-time equivalent (£41,005.91) taken from the 2016 Health Service pay scale.[66] A 2-day training course was carried out with the involved therapists to train them in delivering the home-based personalised physiotherapy intervention. Cost of training included time spent by the trainer (lead therapist), room hire and training materials. During the delivery of the therapy sessions, all participants were provided with printed materials and compact discs

TABLE 14 Unit costs for health-care resource use

Resource use item (unit used in the source)	Unit cost (£)	Source
NHS resource use		
GP (per contact)	36.00	PSSRU 2015/16.[59] Per-patient contact lasting 9.22 minutes, with qualifications
Practice nurse (per hour)	43.00 (11.11 per contact)	• PSSRU 2015/16[59] Nursing average cost per hour, with qualifications • Duration of contact per patient is 15.5 minutes (PSSRU 2014/15,[62] based on the 2006/7 UK general practice survey[63])
Parkinson's nurse (per hour)	75.00 (19.63 per contact after inflation)[a]	• PSSRU 2014/15.[62] Cost per hour of patient-related work as a nurse specialist (community) with qualifications • Duration of contact per patient is 15.5 minutes (PSSRU 2014/15,[62] based on the 2006/7 UK general practice survey[63])
Health visitor (per contact)	54 (54.72 after inflation)[a]	PSSRU 2014/15.[62] Cost per face-to-face contact in health visiting services
Social worker (per hour)	79.00	PSSRU 2015/16.[59] Cost per hour of client-related work with qualification. Assume average contact is one hour
NHS physiotherapist (per contact)	49.00	*NHS Reference Costs 2015 to 2016*.[61] Allied health professionals, physiotherapist, adult, one to one (A08A1). National average unit cost
Occupational therapist (per contact)	79.00	*NHS Reference Costs 2015 to 2016*.[61] Allied health professionals, occupational therapist, adult, one to one (A06A1). National average unit cost
Speech or language therapist (per contact)	88.00	*NHS Reference Costs 2015 to 2016*.[61] Allied health professionals, speech and language therapist, adult, one to one (A13A1). National average unit cost
A day case at hospital (per case)	733.00	*NHS Reference Costs 2015 to 2016*.[61] *Table 15*: unit costs by point of delivery, 2013–14 to 2015–16. Unit costs per finished consultant episode (time a patient spends in the care of one consultant) for a day case
Hospital outpatient attendance (per attendance)	117.00	*NHS Reference Costs 2015 to 2016*.[61] *Table 15*: unit costs by point of delivery, 2013/14 to 2015/16. Unit cost per outpatient attendance
A&E by ambulance (per incidence)	236.00	*NHS Reference Costs 2015 to 2016*.[61] *Table 15*: costs by currency for ambulance services between 2013/14 and 2015/16. Unit cost per 'see and treat and convey'
Ambulance followed by emergency care only (i.e. paramedics, but not conveyed to hospital) (per incidence)	181.00	*NHS Reference Costs 2015 to 2016*.[61] *Table 15*: costs by currency for ambulance services between 2013/14 and 2015/16. Unit cost per 'see and treat or refer'
A&E by own/public transport (per incidence)	138.00	*NHS Reference Costs 2015 to 2016*.[61] *Table 15*: unit costs by point of delivery, 2013/14 to 2015/16. Unit cost per A&E attendance
Hospital stay for treatment (per day)	373.00	*NHS Reference Costs 2015 to 2016* main schedule.[61] Average of cost per elective and non-elective inpatient excess bed-days across all currency codes. Elective inpatient excess bed-days, average across all currency codes: £395. Non-elective inpatient excess bed-days, average across all currency codes: £351

TABLE 14 Unit costs for health-care resource use (*continued*)

Resource use item (unit used in the source)	Unit cost (£)	Source
Respite care at hospital (per day)	264.75	*NHS Reference Costs 2015 to 2016* main schedule.[61] Estimated from the day cost for respite care with length of stay of 4 days or fewer (£1059/4 = £264.75)
Social care resource use		
Home care/home help (per hour)	30.75 (15.37 per contact)	PSSRU 2015/16.[59] 1.5 Home care for older people. Average standard hourly rate for services provided in-house. Assumed 30 minutes per contact
Meals on wheels (per time)	3.00	South Lanarkshire Council service, social care and health, meals at home (meals on wheels)[64]
Day centre (per attendance)	61.00	PSSRU 2015/16.[59] 1.4 Local authority own-provision day care for older people. Unit cost per client attendance
Lunch club (per time)	3.09	Glasgow City Council, social care and health, adults and older people, a lunch club[65]
Sitting service (per hour)	21.00	PSSRU 2015/16.[59] 6.12 Short-break provision for disabled children and their families. Unit cost per family per hour. Assumed 1 hour per contact
Night care (per hour)	31.83	PSSRU 2015/16.[59] 11.6 Home care worker. Applied price multipliers for unsocial hours: 1.035 for an independent sector home care hour. Assumed 1 hour per contact

a   Hospital and Community Health Service inflation factor 1.013 [2014/15 pay and prices index (PPI) 293.1, 2015/16 PPI 297.0].

TABLE 15 Details of assumptions varied in each sensitivity analysis

Scenario	Element	Position in base-case analysis	Variation for the sensitivity analysis
1	Time horizon	6 months, in line with the primary end point of the trial and the completion of all the therapist sessions	12 months, with non-collected data at 12 months being imputed
2	Cost	12 therapist sessions in total (12 sessions × 1 hour per session). Intervention cost per person = £649	10 actual sessions conducted. Intervention cost per person = £546
3	Cost	12 therapist sessions in total (12 sessions × 1 hour per session). Intervention cost per person = £649	Total therapist sessions reduced to eight sessions (eight sessions × 1 hour per session). Intervention cost per person = £442.80
4	Missing data	Missing data assumed to be missing at random and a mixed strategy of imputation was conducted	Complete-case analysis: missing data assumed to be missing completely at random
5	Routine visits of physiotherapist	NHS routine use of physiotherapists was included in the total NHS costs	Visits of physiotherapist between baseline and 6 months was not included as there might be bias in the collected data

(CDs) of the intervention demonstration. In addition, a proportion of participants used assisted equipment including weighted vests, balance pads and steps. This equipment was kept by the physiotherapists and could be used with different participants. Annuitisation was carried out to spread the costs over the anticipated lifespan of this equipment.

Analysis

A cost–utility analysis of the PDSAFE physiotherapy intervention compared with usual care was conducted after imputation. Differences in costs and QALYs between the two groups were estimated using generalised linear models (GLMs), which take into account the typically skewed nature of cost and QALY data. Histograms revealed that the cost data were right-skewed; therefore, gamma distribution was used. For QALYs, as suggested in a previous National Institute for Health Research Health Technology Assessment report,[67] decrement of QALY was originally predicted in the regression using a gamma distribution. Decrement of QALY was calculated as the difference between the maximum QALYs that could possibly be accrued within the time frame and the actual QALY gained. However, this analysis cannot proceed with the imputed data; therefore, a Gaussian family was used instead given that the distribution of QALYs was close to a normal distribution. Covariates in the GLM were selected based on statistical significance using regressions with complete cases from the full list of demographics, medical history and screening measures. The chosen covariates included in the model were age, gender, H&Y scale stage, MoCA score, MMSE score, presence of diabetes, history of myocardial infarction, history of ischaemic heart disease, history of deep-brain stimulation and whether or not the participant had an informal carer. Baseline utility score and baseline cost were also included to adjust for any imbalance of utility between groups.[68]

Mean costs and QALYs for each group were estimated using the method of recycled predictions. The ICER was estimated from the difference in cost and QALYs from the GLM regression. A 1000-iteration bootstrapping was conducted to investigate the uncertainty surrounding the ICER estimate and the probability that the intervention was cost-effective under a wide range of hypothetical thresholds (£0–200,000). These results were represented in a cost-effectiveness plane and cost-effectiveness acceptability curve (CEAC), respectively.

Utility and quality-adjusted life-year

Effectiveness was expressed as QALYs. QALYs were estimated by the area-under-the-curve approach using the utility index values at each data collection time point, which were generated using the EuroQol-5 Dimensions, three-level version (EQ-5D-3L), questionnaire, with preference weights from the UK general population.[69] EQ-5D-3L questionnaires were completed by participants during an interview conducted by assessors at baseline and at 3, 6 and 12 months. The EQ-5D-3L is a commonly used standardised generic preference-based quality of life (QoL) measure addressing five domains: (1) mobility, (2) self-care, (3) usual activities, (4) pain/discomfort and (5) anxiety/depression.[70] For each dimension, participants indicate the level of problems experienced on a three-level scale: (1) no problem, (2) some problems or (3) extreme problems. These responses were then converted to utility scores using the value set elicited from the UK general population. The EQ-5D-3L is the preferred measure of HRQoL in adults by NICE technology appraisal.[57] Participants who died had their utility score set to zero from the next assessment point after death. The area-under-the-curve method was then used to estimate the QALY score over the 12-month period, following the trapezium rule assuming a linear change in utility between each assessment time point.

Missing data and multiple imputation

Data were missing if participants did not return a questionnaire or returned an incomplete questionnaire. Multiple imputation was conducted at aggregate level for both cost and utility values to avoid convergence issues of the imputation model (the model becomes very statistically demanding when there are too many variables with missing data to predict, which usually leads to model convergence failure, meaning that the model cannot be executed). The EQ-5D-3L scores were imputed as utility values and cost items were imputed as categories, namely NHS cost excluding hospitalisation, hospitalisation cost and social care cost. To maximise the use of the completed data, a single item on resource use in both the interview and postal questionnaire was assumed to indicate that no resource was used for that item during that assessment period.[71] Hospitalisation data in falls diaries were checked and filled up the responses from the resource

usage questionnaire if the response was missing. The aggregate-level missing data were imputed with multiple imputation with chained equations and predictive mean matching method for all imputed variables. The intervention and control groups were imputed separately. The multiple-imputed data sets were then used to estimate the difference in QALYs and costs, and the ICER.

Sensitivity analyses

A number of sensitivity analyses were undertaken to assess the robustness of the base-case results to alternative assumptions. These sensitivity analyses are summarised in *Table 15*.

The time horizon for the base-case analysis was 6 months, as all the participants completed their 6-month data collection and it was the primary end point. Nonetheless, for half of the participants, 12-month data were collected and the effect of intervention may last after the trial period; therefore, the time horizon was varied to 12 months. Sensitivity analyses were carried out on the number of physiotherapy sessions to gain an insight into the most cost-effective level of provision. Complete-case analysis was conducted assuming that data were missing completely at random to assess the impact of imputation strategies on the incremental cost and QALYs. Finally, the participants may have found it difficult to differentiate between the NHS routine physiotherapist and the trial physiotherapist; thus, the reported number of visits may not be accurate. Therefore, the use of an NHS physiotherapist between baseline and 6 months was excluded from the total cost in the sensitivity analysis.

Subgroup analysis

Following on from the statistical analysis plan outlined earlier, three subgroup analyses were undertaken to identify if the intervention was potentially more or less cost-effective than the overall group. The clinical effectiveness analysis found that the PDSAFE intervention reduced the number of falls in the participants who had scored in the middle level of the MDS-UPDRS (i.e. a score of 23–29), were not cognitively impaired (a score of ≥ 26 in the MoCA), did not have freezing symptoms at baseline and had two or three falls during the 12-month monitor period prior to recruitment. Therefore, the ICERs were estimated in the subgroups defined by the above criteria. Interaction variables of the treatment and the group indicator were added into the regression to obtain the incremental effects without splitting the sample. The incremental effects were generated using recycled prediction methods to balance the covariates.

Results

Intervention cost

The PDSAFE intervention costs are detailed in *Table 16*. The cost per patient for each of the breakdown items is shown in *Figure 8*. The cost of the intervention was a main cost driver that made up a large portion of the difference between treatment arms. Within the cost of intervention, the therapist time and travel expenses account for > 95% of the total cost; thus, assumptions were varied around the number of sessions.

Missing data

The number and percentage of missing data for each collected cost item and EQ-5D-3L questions at the four assessment points are shown in *Table 17* for the whole sample, and in *Table 18* for the intervention and control (usual-care) groups, respectively. Baseline for the resource use refers to the 3-month monitor period prior to randomisation. Approximately half of the data were missing (primarily attributed to the termination of data collection) for the 12-month follow-up for both the resource use and the EQ-5D-3L data. For the 6-month follow-up, the proportion of data missing for variables collected via postal questionnaires (i.e. NHS resource use excluding hospitalisation) ($\approx 28\%$) was almost twice that for variables collected through the face-to-face interview ($\approx 15\%$). The proportions of data missing at each assessment were much higher ($\approx 10\%$ higher for all variables) in the PDSAFE intervention group than in the control group (see *Table 18*).

TABLE 16 The PDSAFE intervention costs

Item	Unit cost (£)	Quantity (n)	Sum (£)
Therapists training			
Trainer (lead therapist)	165 per day	1.75 days	288.75
Room hire for 2 days	150 per day	2 days	300.00
Training materials	3.50 per therapist	14 therapists	49.00
Therapy sessions			
Therapist time	43.62 per visit	238 participants × 12	124,578.72
Consumables (clinical notes)	1.20 per visit	238 participants × 12	3427.20
Travel expenses	8.00 per visit	238 participants × 12	22,848.00
Patient equipment during the sessions			
Printed materials	2.00 per patient	238 participants	476.00
CDs	0.08 per patient	238 participants	19.04
Weighted vests	54.16 each	23.8[a]	1289.01
Balance pads	19.41 each	59.5[b]	1154.90
Step	11.99 each (6.31 after annuitisation[c])	15.87[d]	100.14
Total cost (per patient) (£)	649.60		

CD, compact disc.
a Approximately 1 in 5 participants used a vest. Each vest can be used for two participants for all the visits. (238/5)/2 = 23.8.
b Approximately 1 in 2 participants used a balance pad. Each pad can be used for two participants for all the visits. (238/2)/2 = 59.5.
c Estimated life is 2 years. Annuitisation was applied to estimate the cost of 1 year of use of these steps. Formula: $E = K/\{[1 - (1 + r)^{-n}]/r\}$. K = 11.99, r = 3.5%, n = 2; E = 6.31.
d Approximately 1 in 15 participants used a step count.
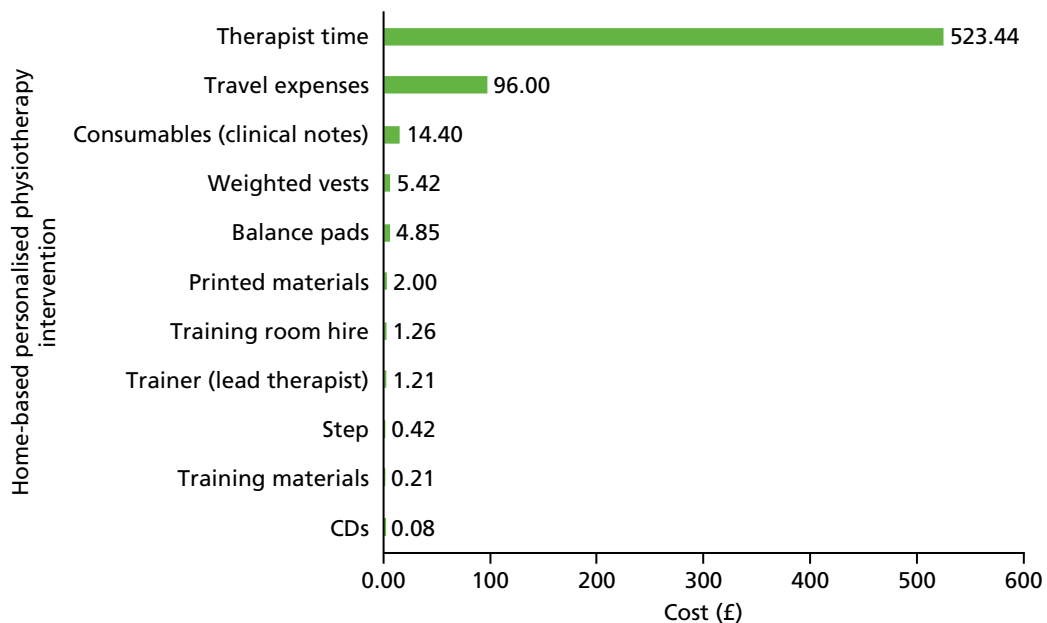
FIGURE 8 Cost of PDSAFE home-based personalised physiotherapy intervention. CD, compact disc.

TABLE 17 Overall missing data for the cost items and EQ-5D-3L

Data items collected from the trial	Time point, *n* (%)			
	Baseline	3 months	6 months	12 months
NHS resource use				
GP	51 (10.76)	95 (20.04)	124 (26.16)	238 (50.21)
Practice nurse	53 (11.18)	102 (21.52)	130 (27.43)	240 (50.63)
Parkinson's nurse	52 (10.97)	98 (20.68)	129 (27.22)	241 (50.84)
Health visitor	52 (10.97)	98 (20.68)	137 (28.90)	245 (51.69)
Social worker	52 (10.97)	100 (21.10)	138 (29.11)	247 (52.11)
NHS physiotherapist	52 (10.97)	99 (20.89)	136 (28.69)	244 (51.48)
Occupational therapist	51 (10.76)	99 (20.89)	140 (29.54)	243 (51.27)
Speech therapist	52 (10.97)	102 (21.52)	139 (29.32)	245 (51.69)
Day hospital	52 (10.97)	96 (20.25)	138 (29.11)	245 (51.69)
Outpatient clinic	51 (10.76)	95 (20.04)	131 (27.64)	241 (50.84)
A&E by ambulance	53 (11.18)	100 (21.10)	138 (29.11)	244 (51.48)
Ambulance with paramedics only	132 (27.85)	124 (26.16)	144 (30.38)	243 (51.27)
A&E by own transport	56 (11.81)	103 (21.73)	142 (29.96)	251 (52.95)
Hospitalisation	1 (0.21)	45 (9.49)	65 (13.71)	209 (44.09)
Social care resource use				
Home care help	13 (2.74)	61 (12.87)	79 (16.67)	230 (48.52)
Meals on wheels	1 (0.21)	46 (9.70)	70 (14.77)	217 (45.78)
Day centre	2 (0.42)	47 (9.92)	71 (14.98)	217 (45.78)
Luncheon club	3 (0.63)	47 (9.92)	73 (15.40)	221 (46.62)
Sitting service	2 (0.42)	48 (10.13)	71 (14.98)	217 (45.78)
Night care	1 (0.21)	48 (10.13)	70 (14.77)	217 (45.78)
EQ-5D-3L				
Mobility	1 (0.21)	45 (9.49)	71 (14.98)	217 (45.78)
Self-care	1 (0.21)	45 (9.49)	71 (14.98)	217 (45.78)
Usual activities	1 (0.21)	47 (9.92)	72 (15.19)	217 (45.78)
Pain and discomfort	1 (0.21)	45 (9.49)	71 (14.98)	217 (45.78)
Anxiety and depression	4 (0.84)	46 (9.70)	70 (14.77)	217 (45.78)
Visual analogue scale	9 (1.90)	47 (9.92)	73 (15.40)	217 (45.78)

Resource use and costs

Table 19 reports the use of each resource item (mean number of visits, SD, median, minimum and maximum) accrued over the 6-month primary follow-up period in the intervention and the control groups. The total costs of NHS service use excluding hospitalisation and of hospitalisation and of social care services are presented in *Table 20* (before and after the imputation) and *Figure 9*. Overall, there was no difference between the intervention and control groups in the cost of NHS and social care service use. The total 6-month cost of service use per patient was £3137 (95% CI £2602 to £3673) in the intervention group and £3069 (95% £2621 to £3518) in the control group. *Figure 9* shows that resource use was

TABLE 18 Missing data for resource use and EQ-5D-3L QoL in the intervention and control groups

Data items collected from the trial	Trial group, *n* (%)							
	PDSAFE (*N* = 238)				Control (*N* = 236)			
	Baseline	3 months	6 months	12 months	Baseline	3 months	6 months	12 months
NHS resource use								
GP	31 (13.03)	59 (24.79)	77 (32.35)	126 (52.94)	20 (8.47)	36 (15.25)	47 (19.92)	112 (47.46)
Practice nurse	31 (13.03)	60 (25.21)	79 (33.19)	126 (52.94)	22 (9.32)	42 (17.80)	51 (21.61)	114 (48.31)
Parkinson's nurse	31 (13.03)	60 (25.21)	80 (33.61)	127 (53.36)	21 (8.90)	38 (16.10)	49 (20.76)	114 (48.31)
Health visitor	32 (13.45)	58 (24.37)	84 (35.29)	130 (54.62)	20 (8.47)	40 (16.95)	53 (22.46)	115 (48.73)
Social worker	32 (13.45)	60 (25.21)	84 (35.29)	131 (55.04)	20 (8.47)	40 (16.95)	54 (22.88)	116 (49.15)
NHS physiotherapist	30 (12.61)	60 (25.21)	82 (34.45)	130 (54.62)	22 (9.32)	39 (16.53)	54 (22.88)	114 (48.31)
Occupational therapist	31 (13.03)	59 (24.79)	85 (35.71)	127 (53.36)	20 (8.47)	40 (16.95)	55 (23.31)	116 (49.15)
Speech therapist	31 (13.03)	61 (25.63)	84 (35.29)	131 (55.04)	21 (8.90)	41 (17.37)	55 (23.31)	114 (48.31)
Day hospital	30 (12.61)	58 (24.37)	83 (34.87)	131 (55.04)	22 (9.32)	38 (16.10)	55 (23.31)	114 (48.31)
Outpatient clinic	31 (13.03)	59 (24.79)	79 (33.19)	127 (53.36)	20 (8.47)	36 (15.25)	52 (22.03)	114 (48.31)
A&E by ambulance	31 (13.03)	60 (25.21)	82 (34.45)	130 (54.62)	22 (9.32)	40 (16.95)	56 (23.73)	114 (48.31)
Ambulance with paramedics only	72 (30.25)	68 (28.57)	84 (35.29)	129 (54.20)	60 (25.42)	56 (23.73)	60 (25.42)	114 (48.31)
A&E by own transport	33 (13.87)	60 (25.21)	85 (35.71)	134 (56.30)	23 (9.75)	43 (18.22)	57 (24.15)	117 (49.58)
Hospitalisation for treatment	1 (0.42)	27 (11.34)	48 (20.17)	117 (49.16)	0 (0)	18 (7.63)	22 (9.32)	99 (41.95)
Hospitalisation for respite care	1 (0.42)	27 (11.34)	48 (20.17)	117 (49.16)	0 (0)	18 (7.63)	22 (9.32)	100 (42.37)

| Data items collected from the trial | Trial group, *n* (%) | | | | | | | |
| | PDSAFE (*N* = 238) | | | | Control (*N* = 236) | | | |
	Baseline	3 months	6 months	12 months	Baseline	3 months	6 months	12 months
Social care resource use								
Home care help	8 (3.36)	33 (13.87)	51 (21.43)	121 (50.84)	5 (2.12)	28 (11.86)	28 (11.86)	109 (46.19)
Meals on wheels	1 (0.42)	27 (11.34)	48 (20.17)	117 (49.16)	0 (0)	19 (8.05)	22 (9.32)	100 (42.37)
Day centre	2 (0.84)	28 (11.76)	48 (20.17)	117 (49.16)	0 (0)	19 (8.05)	23 (9.75)	100 (42.37)
Luncheon club	3 (1.26)	28 (11.76)	48 (20.17)	119 (50.00)	0 (0)	19 (8.05)	25 (10.59)	102 (43.22)
Sitting service	1 (0.42)	28 (11.76)	49 (20.59)	117 (49.16)	1 (0.42)	20 (8.47)	22 (9.32)	100 (42.37)
Night care	1 (0.42)	28 (11.76)	48 (20.17)	117 (49.16)	0 (0)	20 (8.47)	22 (9.32)	100 (42.37)
EQ-5D-3L								
Mobility	1 (0.42)	27 (11.34)	49 (20.59)	117 (49.16)	0 (0)	18 (7.63)	22 (9.32)	100 (42.37)
Self-care	1 (0.42)	27 (11.34)	49 (20.59)	117 (49.16)	0 (0)	18 (7.63)	22 (9.32)	100 (42.37)
Usual activities	1 (0.42)	27 (11.34)	50 (21.01)	117 (49.16)	0 (0)	20 (8.47)	22 (9.32)	100 (42.37)
Pain and discomfort	1 (0.42)	27 (11.34)	48 (20.17)	117 (49.16)	0 (0)	18 (7.63)	23 (9.75)	100 (42.37)
Anxiety and depression	3 (1.26)	28 (11.76)	48 (20.17)	117 (49.16)	1 (0.42)	18 (7.63)	22 (9.32)	100 (42.37)
Visual analogue scale	6 (2.52)	28 (11.76)	50 (21.01)	117 (49.16)	3 (1.27)	19 (8.05)	23 (9.75)	100 (42.37)

TABLE 19 NHS and social care resource use per patient over 6 months (complete case)

| Resource use (number of visits) | Trial group | | | | | | | | | | | p-value |
| | PDSAFE (N = 238) | | | | | Control (N = 236) | | | | | |
	n	Mean	SD	Median	Minimum, maximum	n	Mean	SD	Median	Minimum, maximum		p-value
NHS												
GP	144	2.72	2.47	2	0, 16	177	3.23	2.80	3	0, 15		0.09
Practice nurse	140	1.39	1.67	1	0, 9	170	2.09	4.67	1	0, 43		0.09
Parkinson's nurse	138	1.21	1.45	1	0, 11	177	1.47	1.67	1	0, 11		0.15
Health visitor	138	0.11	0.54	0	0, 5	170	0.17	0.76	0	0, 8		0.42
Social worker	136	0.07	0.38	0	0, 3	170	0.17	0.72	0	0, 7		0.16
NHS physiotherapist	136	2.48	3.64	0	0, 16	170	1.34	2.42	0	0, 14		0.00
Occupational therapist	136	0.35	0.93	0	0, 6	169	0.50	1.44	0	0, 12		0.29
Speech therapist	135	0.89	2.09	0	0, 11	167	0.59	2.03	0	0, 21		0.22
Day hospital	137	0.93	1.89	0	0, 14	170	0.90	1.57	0	0, 10		0.89
Outpatient clinic	142	1.78	2.09	1	0, 13	173	1.78	1.79	1	0, 13		1.00
A&E by ambulance	137	0.14	0.42	0	0, 2	167	0.11	0.33	0	0, 2		0.48
Ambulance with paramedics only	131	0.26	0.83	0	0, 6	153	0.19	0.63	0	0, 5		0.42
A&E by own transport	135	0.16	0.45	0	0, 3	165	0.22	0.59	0	0, 4		0.31
Hospitalisation for treatment	187	0.30	2.51	0	0, 30	208	0.07	0.47	0	0, 5		0.19
Hospitalisation for respite care	187	0	0	0	0, 0	208	0	0	0	0, 0		–

| Resource use (number of visits) | Trial group | | | | | | | | | | p-value |
| | PDSAFE (N = 238) | | | | | Control (N = 236) | | | | | |
	n	Mean	SD	Median	Minimum, maximum	n	Mean	SD	Median	Minimum, maximum	
Social care											
Home care/home help	181	13.43	50.55	0	0, 390	192	29.99	103.30	0	0, 910	0.05
Meals on wheels	187	1.04	12.49	0	0, 169	207	1.00	12.77	0	0, 182	0.98
Day centre	186	0.49	4.35	0	0, 52	206	0.63	4.59	0	0, 52	0.75
Luncheon club	186	0.21	2.86	0	0, 39	204	0.51	6.43	0	0, 91	0.56
Sitting service	186	0.91	7.16	0	0, 65	206	1.33	7.75	0	0, 78	0.58
Night care	186	0.98	13.34	0	0, 182	206	0.06	0.91	0	0, 13	0.33

TABLE 20 Cost of health-care and social care resources per patient over 6-months' follow-up (complete-case analysis and after imputation)

Cost categories	Trial group (£)					p-value		
	PDSAFE (N = 238)		Control (N = 236)					
	Unadjusted mean (SE)	95% CI	Unadjusted mean (SE)	95% CI		OLS	Gamma, log link	Gamma, log link, adjusted for covariates
Complete-case analysis								
NHS excluding hospitalisation	2639.92 (264.95)	2118.72 to 3161.12	2493.00 (202.81)	2094.05 to 2891.95		0.655	0.654	0.246
Hospitalisation	111.11 (67.97)	−22.52 to 244.73	24.87 (11.95)	1.37 to 48.36		0.189	0.052	Did not converge
Social care	309.36 (81.21)	149.70 to 469.01	515.05 (120.15)	278.83 to 751.26		0.166	0.145	0.124
Total cost	2994.41 (303.44)	2397.48 to 3591.35	2871.02 (243.07)	2392.86 to 3349.18		0.748	0.748	0.167
Total baseline cost (3 months pre baseline to baseline)	1827.02 (273.80)	1288.85 to 2365.20	1635.20 (200.00)	1242.08 to 2028.32		0.57	0.565	0.134
After imputation								
NHS excluding hospitalisation	2653.81 (228.53)	2203.81 to 3103.80	2521.66 (188.09)	2151.88 to 2891.44		0.658	0.659	0.499
Hospitalisation	107.36 (63.96)	−18.42 to 233.13	23.39 (11.17)	1.44 to 45.34		0.197	0.00	Did not converge
Social care	376.23 (85.26)	208.66 to 543.80	524.25 (113.39)	301.41 to 747.09		0.295	0.287	0.237
Total cost	3137.39 (272.08)	2602.18 to 3672.61	3069.30 (228.13)	2620.88 to 3517.72		0.849	0.849	Did not converge
Total baseline cost (3 months prior to baseline)	1849.02 (266.16)	1325.82 to 2372.22	1659.16 (194.26)	1277.38 to 2040.95		0.565	0.56	Did not converge

OLS, ordinary least squares; SE, standard error.
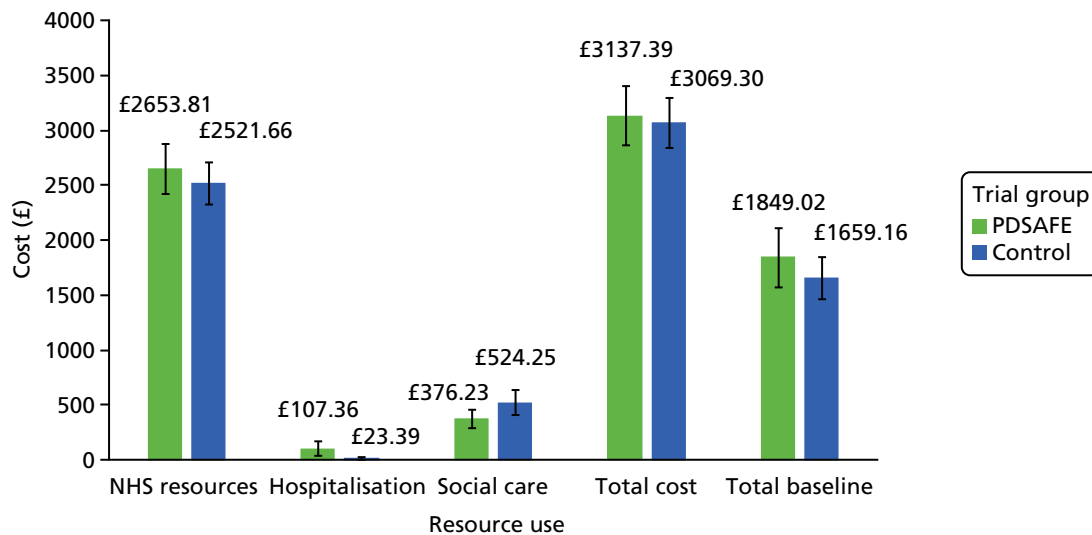
FIGURE 9 Mean cost of NHS and social care resources use per patient over the 6-month follow-up period.

slightly higher in the intervention group than in the control group (but the difference was not statistically significant); however, the total baseline cost (i.e. from 3 months pre baseline to baseline) was also higher in the intervention group. The most commonly used NHS services were GP, NHS physiotherapist, practice nurse, Parkinson's nurse and outpatient clinic, with at least one visit per patient over the 6-month follow-up period. The intervention group was found to have fewer GP visits, practice nurse visits and home care help visits; none of the differences was statistically significant. The most frequently used social service was home care, of which, over the 6-month follow-up period, each participant in the intervention group had an average of 13 visits and each participant in the control group had an average of 30 visits. Medication was not included in the total costs because of the large number of prescriptions identified, the frequent low cost of medications, identified comparability across arms and poorly reported data.

Health-related quality of life

The EQ-5D-3L health utility values for each treatment group at baseline and at 3, 6 and 12 months are shown in *Table 21* (complete case), *Table 22* (after imputation) and visualised in *Figure 10* (after imputation), assuming a linear change between each assessment point. The completeness of the EQ-5D-3L questionnaire at the 6-month follow-up was 79% (188/238) for the intervention group and 90% (213/236) for the control group. The utility values of the intervention group declined slightly less than the control group over the 6-month, as well as the 12-month, period. The differences in utility values between the arms were small (i.e. 0.031 at 6 months and 0.017 at 12 months) given that the full range of the EQ-5D-3L index score was –0.592 (worst) to 1 (full health), and not statistically significant.

Cost-effectiveness base-case analysis

The cost-effectiveness results for the PDSAFE home-based personalised physiotherapy intervention are presented in *Table 23*. Overall, the PDSAFE intervention is more costly within the 6-month time horizon but generates greater HRQoL than the control. The average cost per patient was £4020 (95% CI £3531 to £4510) in the intervention group and £3095 (95% CI £2694 to £3496) in the control group, an incremental cost of £925 (95% CI £428 to £1422). The average QALY gain was 0.34 (95% CI 0.326 to 0.345) QALYs in the intervention group and 0.328 (95% CI 0.319 to 0.337) QALYs in the control group, The intervention group had an incremental 0.008 (95% CI –0.006 to 0.021) QALY gain compared with the control group.

The cost-effectiveness plane for the base-case analysis is shown in *Figure 11*. The dyads come from the 1000 bootstrap iterations. The *x*-axis represents the bootstrapped incremental QALYs between the randomisation groups and the *y*-axis represents the incremental costs. All of the simulated cost–utility dyads were in the north quadrant, indicating that the intervention was always more expensive than the control. Similarly, the

TABLE 21 The EQ-5D-3L visual analogue scale and index value (complete case)

| Time point | Trial group | | | | | | | | | | |
| | PDSAFE (N = 238) | | | | | Control (N = 236) | | | | | |
	n	Mean	SD	SE	Minimum, maximum	n	Mean	SD	SE	Minimum, maximum	p-value
Visual analogue scale											
Baseline	232	60.685	23.595	1.549	3, 100	233	60.811	24.715	1.619	3, 100	0.96
3-month	210	62.486	22.841	1.576	4, 100	217	62.465	23.350	1.585	5, 95	0.99
6-month	188	63.750	21.808	1.590	5, 100	213	63.394	21.872	1.499	3, 100	0.87
12-month	121	64.322	17.209	1.564	25, 99	136	64.331	17.816	1.528	9, 100	1.00
Index score											
Baseline	235	0.657	0.232	0.015	−0.181, 1	235	0.669	0.245	0.016	−0.115, 1	0.60
3-month	210	0.677	0.244	0.017	−0.086, 1	216	0.668	0.247	0.017	−0.077, 1	0.70
6-month	190	0.680	0.217	0.016	−0.016, 1	216	0.644	0.258	0.018	−0.126, 1	0.13
12-month	124	0.643	0.269	0.024	−0.016, 1	141	0.635	0.272	0.023	−0.115, 1	0.81
Utility change											
6 month – baseline	188	0.008	0.239	0.017	−1, 0.795	215	−0.022	0.260	0.018	−0.795, 0.672	0.2266
12 month – baseline	123	−0.039	0.279	0.025	−1, 0.639	140	−0.053	0.295	0.025	−0.883, 0.743	0.7052

SE, standard error.

TABLE 22 The EQ-5D-3L index value (after imputation)

| Time point | Trial group | | | | |
| | PDSAFE (*N* = 238) | | Control (*N* = 236) | |
	Mean (SE)	95% CI	Mean (SE)	95% CI
Baseline	0.657 (0.015)	0.628 to 0.687	0.669 (0.016)	0.637 to 0.700
3 months	0.672 (0.017)	0.638 to 0.705	0.664 (0.017)	0.630 to 0.697
6 months	0.672 (0.016)	0.640 to 0.704	0.641 (0.017)	0.607 to 0.676
12 months	0.644 (0.027)	0.590 to 0.697	0.626 (0.028)	0.571 to 0.681

SE, standard error.
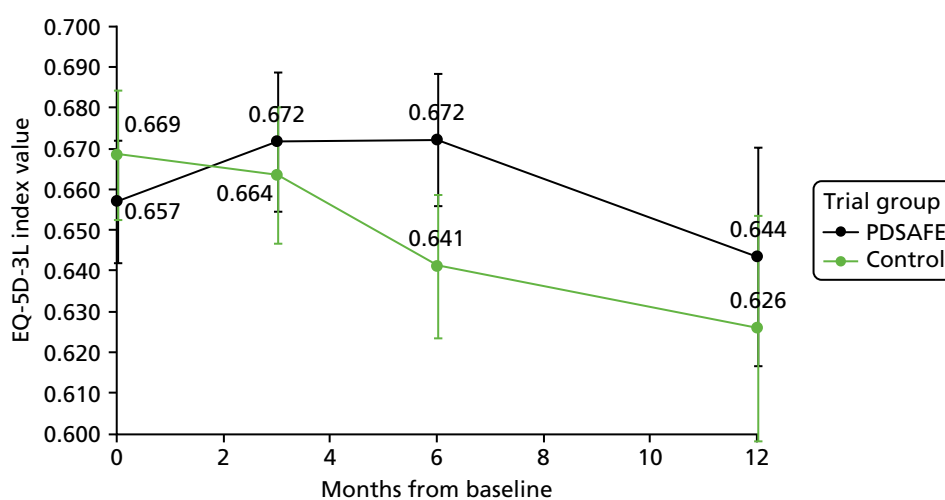
FIGURE 10 The EQ-5D-3L utility values at baseline and at 3, 6 and 12 months (after imputation).

TABLE 23 Cost-effectiveness results (after imputation) with 6-month follow-up

| Trial group | Cost (£)[a] | | | QALY[b] | | |
	Mean	SE	95% CI	Mean	SE	95% CI
PDSAFE (*n* = 238)	4020.3	249.7	3530.7 to 4509.8	0.336	0.005	0.326 to 0.345
Control (*n* = 236)	3095.3	204.5	2694.3 to 3496.2	0.328	0.005	0.319 to 0.337
Difference (95% CI)	925.0	253.5	427.8 to 1422.2	0.008	0.007	−0.006 to 0.021
ICER	120,659 per QALY					
95% CI for ICER (from bootstrap)	−1,056,012.00 to 434,764.80					

SE, standard error.
a Adjusted cost; per-participant intervention cost is included in the cost of the intervention group.
b Adjusted QALY.
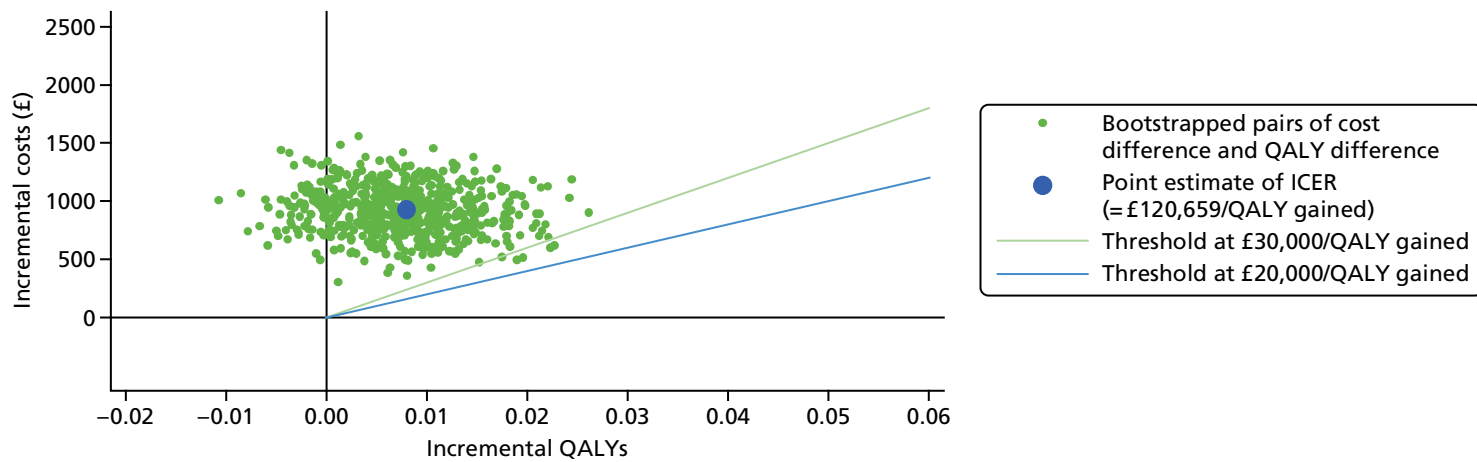
FIGURE 11 Cost-effectiveness plane representing 1000 bootstrapped cost difference and QALY difference pairs.

majority of the simulated cost–utility dyads were in the east quadrant, indicating that the intervention was very likely to improve health outcomes compared with the control. The flat oval shape of the cost-effectiveness plane indicates that there is a higher degree of uncertainty surrounding the estimates of the incremental QALYs than the incremental cost, leading to a wide 95% CI for the estimate of ICER.

The CEAC for the base-case analysis is shown in *Figure 12*. The probability that the intervention was cost-effective at the £30,000 per QALY threshold was 0.5%. This corresponds to the very few dyads under the sand line in the cost-effectiveness plane in *Figure 11*.

Subgroup cost-effectiveness analysis

The results for the subgroups defined according to cognitive function, presence of freezing symptoms, MDS-UPDRS and retrospective falls at baseline are presented in *Table 24*. The results indicated that the ICER was lower in two subgroups (although still above NICE's upper threshold of £30,000): (1) participants who were cognitively impaired (MoCA score of ≤ 25) and (2) participants whose Parkinson's was of moderate severity (MDS-UPDRS score of between 22 and 39). Compared with the control group, those in the cognitively impaired subgroup of the intervention arm (*n* = 184) consumed less resource (–£462.80, excluding the intervention cost) and achieved a similar QALY gain to the control group; therefore, the ICER for the PDSAFE intervention versus control was £39,486. In the subgroup including those participants with Parkinson's moderate severity of (*n* = 161), the PDSAFE intervention was associated with an incremental cost of £500 and an incremental QALY (0.016) that was double the incremental QALY gain of the overall group, leading to an ICER of £30,731.

Although still above the £30,000 per QALY threshold, compared with the base-case analysis the ICER is lower in the following subgroups: participants with moderate cognitive function (£84,925 per QALY gained), participants who had not experienced freezing symptoms (£61,687 per QALY gained) and participants who had had at least two falls in the 12-month period prior to recruitment (£53,860 per QALY gained for participants who had two or three falls and £82,532 per QALY gained for participants who had more than three falls). In addition, the increase in QALYs gained in the PDSAFE intervention arm for the participants who had not experienced freezing episodes was statistically significant [0.021 (95% CI 0.0007 to 0.041) QALYs]. In contrast, the PDSAFE intervention was found to be less effective than usual care and more costly in two subgroups, the subgroup with more severe Parkinson's (i.e. those with a MDS-UPDRS score of ≥ 39) and those who had experienced freezing episodes; therefore, usual care dominated PDSAFE in both of these subgroups.
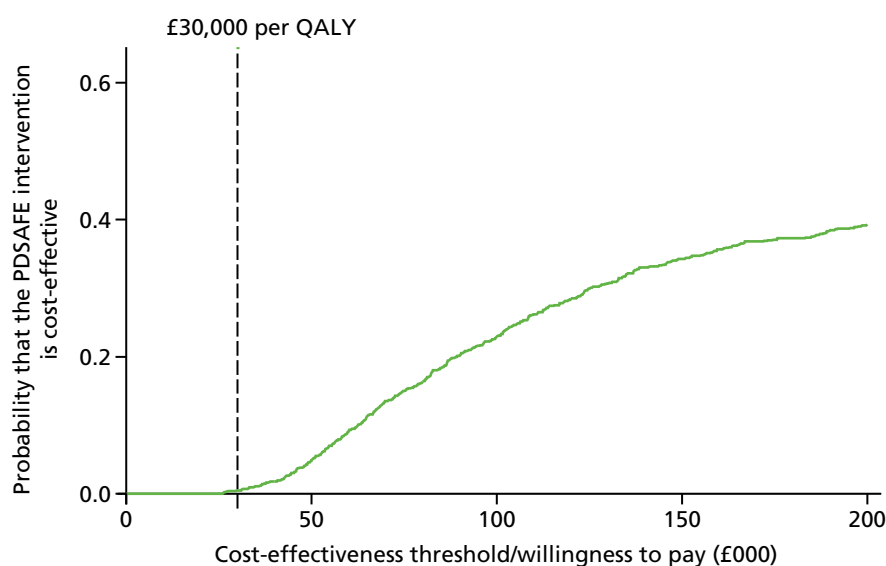
FIGURE 12 Cost-effectiveness acceptability curve.

TABLE 24 Subgroup analysis results (over 6 months)

| Analysis | Incremental (PDSAFE – control) (95% CI) | | ICER (cost per QALY gained) (£) |
	Cost (£)	QALYs	
Base-case analysis			
Base-case	925.0 (427.8 to 1422.2)	0.008 (–0.006 to 0.021)	120,659
Subgroup by MoCA (cognitive function)			
Impaired (MoCA score of ≤ 25) (n = 184)	292.9 (–890.4 to 1476.2)	0.007 (–0.014 to 0.029)	39,486
Not impaired (MoCA score of 26 or 27) (n = 122)	1512.9 (206.9 to 2819.0)	0.018 (–0.008 to 0.043)	84,925
Good cognitive function (MoCA score of ≥ 28) (n = 168)	1513.8 (329.4 to 2698.2)	0.0006 (–0.020 to 0.021)	2,613,629
Subgroup by the presence of freezing symptoms			
No freezing (n = 182)	1284.8 (234.3 to 2335.3)	0.021 (0.0007 to 0.041)	61,687
Freezing (n = 291)	851.5 (–169.9 to 1872.8)	–0.0006 (–0.018 to 0.017)	Control dominates
Subgroup by MDS-UPDRS (Parkinson's severity)			
Lowest disease severity (MDS-UPDRS score of ≤ 22) (n = 153)	1956.2 (746.9 to 3165.6)	0.006 (–0.015 to 0.028)	301,605
Moderate disease severity (MDS-UPDRS score of 23–38) (n = 161)	500.1 (–760.6 to 1760.8)	0.016 (–0.006 to 0.039)	30,731
Highest disease severity (MDS-UPDRS score of ≥ 39) (n = 158)	600.2 (–639.7 to 1840.0)	–0.004 (–0.027 to 0.019)	Control dominates
Subgroup by retrospective falls			
One fall (n = 99)	1201.3 (–117.3 to 2519.8)	0.010 (–0.018 to 0.038)	197,810
Two or three falls (n = 198)	1121.1 (7.4 to 2234.8)	0.009 (–0.011 to 0.030)	53,860
More than three falls (n = 177)	724.8 (–531.5 to 1981.1)	0.007 (–0.014 to 0.029)	82,532

Sensitivity analysis

The results of the sensitivity analysis are presented in *Table 25*. Although the PDSAFE intervention was cost-ineffective compared with the control in all sensitivity analysis, the ICER decreased by more than half when estimated over a 12-month time horizon with around half of the data imputed based on the observed data. This was due to the linearly interpolated increase in QALYs over the 12-month period.

Discussion

The results showed that the PDSAFE home-based personalised physiotherapy intervention was not likely to be cost-effective for the overall Parkinson's population from the NHS and PSS perspective over the 6-month time horizon at a £20,000 to £30,000 threshold for the ICER estimated. There was little difference in the mean cost of NHS and social service use between the treatment groups. The utility values declined slightly less in the intervention group than in the control group over the trial period, but the difference was minimal and not statistically significant.

A high degree of uncertainty over the QALYs gained was observed, leading to a wide CI for the estimate of the ICER, which may be a result of the small mean QALY gained observed and large variation among the participants. Another possible explanation might be related to the limitation of the EQ-5D-3L questionnaire in capturing the impact of the PDSAFE physiotherapy intervention on QoL aspects, such as

TABLE 25 Sensitivity analysis: summary of results

Analysis	Incremental (PDSAFE – control) (95% CI)		ICER (cost per QALY gained) (£)
	Cost (£)	QALYs	
Base-case analysis			
Base case (6 months)	925.0 (427.8 to 1422.2)	0.008 (–0.006 to 0.021)	120,659
Time horizon			
12 months	1176.2 (248.5 to 2103.9)	0.021 (–0.011 to 0.054)	55,176
Cost			
10 sessions (actual number of sessions)	824.7 (327.7 to 1321.8)	0.008 (–0.005 to 0.021)	105,360
Number of sessions reduced to eight	719.2 (225.5 to 1212.9)	0.008 (–0.005 to 0.021)	91,876
Missing data			
Complete-case analysis ($n = 288$)	1138.8 (588.4 to 1689.3)	0.010 (–0.006 to 0.025)	117,226
Routine use of physiotherapist			
Routine physiotherapist visit not included in the overall cost	903.1 (416.4 to 1389.8)	0.008 (–0.005 to 0.020)	120,086

improved falls efficacy and less fear of falling, as identified in the effectiveness results and qualitative study in this report.

Subgroup analyses indicated that the PDSAFE intervention is more likely to be cost-effective in the subgroup of participants who are cognitively impaired. This is due to the slightly lower (albeit non-significant) NHS and social care service costs arising in this subgroup of the intervention arm compared with the control group. The estimated NHS and social resource use costs in the cognitively impaired subgroup were £3916.90 in the control group and £3454.20 in the intervention group, with a marginal £462.70 lower resource use cost in the intervention group. In contrast, the intervention arm was associated with higher resource use in the moderate cognitive function and good cognitive function subgroups (marginal cost £709.20 and £664.20, respectively). In terms of individual service use, among the cognitively impaired subgroup, the intervention group, in comparison with the control group, attended significantly fewer outpatient clinic appointments (1.23 vs. 2.10; $p = 0.02$), received fewer social worker visits (0.02 vs. 0.14; $p = 0.10$). However, statistical significance for the differences between groups was not observed for the other health-care resources. The details of the comparison of resource use between the intervention and control groups among the cognitively impaired subpopulation are presented in *Appendix 19*. The resource use savings arising in this subgroup may be attributed to the unusually high cost of the control arm of this subgroup and the relatively lower cost of the intervention arm as a response to the improved falls efficacy, reduced near-falls and improved balance; however, it could also be due to chance.

The intervention was also more likely to be cost-effective in the subgroup of participants who had a Parkinson's of moderate severity (MDS-UPDRS score of 23–38), owing to the cost savings arising in service use and the larger magnitude of QALY gain. This is in line with the effectiveness results showing that the PDSAFE intervention was associated with a statistically significantly lower risk of falling in this subgroup in the FRR analysis. In addition, the ICER estimate of the PDSAFE intervention was lower than the overall sample in the participants who had moderate cognitive function, those who had not experienced freezing symptoms and those who had had at least two falls in the year prior to recruitment. In terms of the impact on HRQoL, the PDSAFE intervention was shown to be statistically beneficial in participants who had not experienced freezing episodes, whereas in participants who had experienced freezing episodes or had severe Parkinson's, it resulted in a lower mean QALY gain than in the control group.

Sensitivity analyses indicated that the intervention was more likely to be cost-effective when a 12-month time horizon was adopted, although only half of the data at the 12-month follow-up were directly observed. This is because of the difference in HRQoL at the 6-month primary end point, as well as the persistent benefit of the intervention beyond the 6-month intervention period. At 12 months, HRQoL in the intervention group was still higher than in the control group with both observed-only data and imputed data; therefore, it is likely that this difference would last beyond the 12-month follow-up point. This means that the probability of the intervention being cost-effective might increase if the results were extrapolated over a longer time horizon; although it would require a longer follow-up study to test the long-term effect because of the large number (50%) of missing data at the 12-month follow-up.

It was found that there was a statistically significantly higher use of routine NHS physiotherapy in the intervention group than in the control group over 0–3 months (1.3 vs. 0.7 times), 3–6 months (1.0 vs. 0.7 times) and 6–12 months (1.4 vs. 0.8), but not during the 3-month period prior to baseline (1.1 vs. 1.0 times). The intervention lasted for 6 months and the higher use of physiotherapists in the intervention group over 0–6 months is likely to be because some participants included trial therapist visits in their health and social care service use data, despite the distinction being made. Originally, the routine service use of physiotherapists was designed to be collected through assessor interview in which the participants could have had more guidance. However, a risk of unblinding the assessors was identified; therefore, the NHS routine resource use questions were sent by post to the participants and filled in by participants themselves at home. Even so, this does not explain the higher use of physiotherapists from 6 to 12 months. In this situation, it is possible that some of the participants in the intervention group found the intervention effective and therefore continued having physiotherapy visits provided by the routine services. Despite the possible inaccuracy in the reported number of visits, the sensitivity analysis assuming no difference between the use of this routine service found that this had little effect on the magnitude of ICER and, therefore, is not likely to cause any bias.

Overall, the cost-effectiveness analysis results reflect the primary outcomes of the trial, in that there was no difference in the risk of repeat falling, but the intervention was associated with a lower risk of near-falling, better balance and an increased confidence in mobility. This mixed result may contribute to the small mean QALY gain (0.008 years over the 6-month trial period) as well as the large degree of uncertainty surrounding the QALY gain, which led to the wide CI of the ICER. The uncertainty analysis (see *Figure 12*) revealed that the probability of the intervention being cost-effective is 0.5%, which suggested that the PDSAFE intervention was probably not cost-effective from the NHS and PSS perspectives. The large magnitude of ICER was attributed primarily to the very small QALY gains rather than the intervention cost. It was shown in the sensitivity analysis that, even when the number of PDSAFE physiotherapy sessions was reduced from 12 to 8, the ICER (£91,876 per QALY) was still much higher than the NICE threshold (£20,000–30,000 per QALY) because of the unchanged incremental QALY gain. Therefore, cost reduction strategies only, such as changing home-based sessions to group sessions, will not result in the intervention being cost-effective unless the effectiveness improves.

Chapter 8 Discussion and conclusions

Main finding in context

To our knowledge, PDSAFE is the largest trial of physiotherapy for fall prevention among people with Parkinson's; it was novel, with an intervention that was personalised and conducted in the home. The sample was more than double the size of any previous trial in the field. Despite this, the findings failed to demonstrate that PDSAFE was effective in reducing falls in a heterogeneous sample of people with Parkinson's. The non-significant result is similar to that found by previous researchers of trials with > 100 participants.[17,37,40,72,73] The exception is the trial by Morris *et al.*,[72] who in 2015 reported a positive effect of exercise training on fall reduction, largely conducted in an outpatient setting. Interestingly, they did not replicate the finding in 2017 when training was delivered at home and at a lower frequency.[73] Two other research groups found a reduction in falls from interventions outside of normal physiotherapy delivery, with virtual reality and treadmill training[74] and tai chi.[75] A mixed and very small response, with short- and long-term effects, to various exercise interventions for fall reduction emerged from the meta-analysis by Shen *et al.*[76] This PDSAFE trial had a very heterogeneous sample; unlike other fall prevention trials, those with high disease severity or those with more complex symptoms, such as freezing, were not excluded.

Wide spectrum of falling

The wide spectrum of falling experiences among participants in the sample may have contributed to the non-significant finding. People with one fall were included, as were those with multiple falls and those reporting falling every day in the year prior to commencing the trial. This inclusive approach was typical of other trials and a reflection of a Parkinson's population. The PDSAFE treatment was personalised; for this reason, it was believed that the management of the range of profiles would have been addressed. However, in hindsight, multiple falls are not just about the numbers of falls: the complex and varied nature of falling among people with Parkinson's may have been the challenge and the key contributing factor to the non-significant treatment effect in this trial. Among this population, falls are indicative of a changing disease process, the pathway from non-falling to near-falling, to falling and to repeat falling can differ, and falls among established repeat fallers are different from the single-faller experience.[77] People with Parkinson's who have an established pattern of falling will have more global features of decline that may be age- and/or disease-related; Lord *et al.*[77] suggest that these progressive features create additional challenges for implementing appropriate management and research. Other researchers[17,37,40] have previously suggested that those with less severe Parkinson's have responded positively to fall reduction programmes, but that effect has been counterbalanced with the deterioration experienced among those with more severe disease, leading to non-significant results. The analysis of our trial reflects a similar pattern.

Freezing of gait and worse Parkinson's

As with any group of people with Parkinson's, this sample included those with and without FoG. The motor learning potential is reduced in people who freeze[78,79] and there is increasing evidence that FoG is an important risk factor of falls and associated with reduced balance[22] and impaired cognition. The inclusion of people who did or did not experience freezing illustrates the diverse range of motor problems present in a community sample of people with Parkinson's and the range of challenges faced when teaching and learning new skills. Interestingly, all participants in the trial showed overall improvement in impairments such as balance, but no overall significant reduction in falls in response to PDSAFE. The complexity of fall avoidance, it seems, resides in the transition between these two features. More supervised therapy focused around the fall avoidance strategies may have been required, even though a specific strategy for FoG was included in the training

programme. As with those experiencing FoG, people with greater disease severity (more likely to have additional cognitive impairment) may be more restricted in their ability to implement fall avoidance strategies and may also have had greater difficulty in engaging in unsupervised sessions, thus limiting the intensity of practice and the effects.

Cognitive impairment

Participants were screened for cognitive impairment, namely a score of ≥ 24 on the MMSE scale, to ensure that understanding of and compliance with the exercise programme of the trial was not compromised. In spite of this eligibility procedure, some participants were recruited to the trial with cognitive impairment identified later through a low score on the MoCA. The MoCA is known to be more sensitive to specific cognitive deficits linked to frontal and executive function associated with people who fall,[80] but at the time of designing this trial it was still a relatively new test and not widely used. To explore whether or not this was a factor contributing to the lack of benefit overall, we looked at subgroups defined by tertiles of MoCA score at baseline and found a pattern of association between decreasing MoCA score and decreasing PDSAFE benefit with respect to the falling outcomes. As previously highlighted, all participants, even those with cognitive impairments, showed improvements in their balance scores and fall efficacy scales. This is interpreted as indicating that these participants were able to comply with exercise even when their MoCA scores were low but were not able to benefit from the more demanding fall prevention programme, for whatever reason. In future research, including MoCA[81] as an eligibility criterion is recommended, although researchers such as Domingos et al.[82] have called for more studies into fall prevention with people with impaired cognition.

Treatment of fall risk

The fall risk factors of participants in the trial (i.e. the secondary outcome measures of balance, falls efficacy and functional strength) were targeted in the intervention; the analysis demonstrated a consistent improvement across the whole PDSAFE group. A positive PDSAFE effect on near-falls, an indicator of instability and reflective of the improvements in balance, was also reported. These results support those of others,[77] highlighting the benefits of exercise for balance and gait ability. Interventions in previous trials have been delivered largely outside the home, but the results of this study demonstrate similar findings from interventions within the home environment, which is important for those with fewer opportunities for access, those who are unable to regularly travel for training or those who may suffer from fatigue or apathy.

Therapy

A strength of the trial was the evidence-based therapy programme delivered by skilled trained physiotherapists. The training was structured and practice was rigorously tested for fidelity. Participants received, on average, 11 or 12 face-to-face supervised sessions of 1–1.5 hours' duration and were encouraged to complete unsupervised daily practice, meeting the recommendations of Sherrington et al.[83] of at least 50 hours of practice. Previous research has used a range of different interventions, often poorly described, with a great deal of diversity of treatment protocols and dosage.[76] This programme was multidimensional, requiring individuals to progress their activities and to integrate their training into everyday functional tasks; although this would have been manageable for those in the moderate to least severe disease group, it may have been too challenging for those at the more severe end of the spectrum, despite treatment being personalised. Active participation and cognitive reasoning were needed to comply with PDSAFE and progress to self-management for falls avoidance. Participants at the severe end of the disease spectrum with cognitive impairment and FoG may have needed more supervised sessions focused on fall prevention strategy training.

In the longitudinal qualitative inquiry into the expectations and experiences of people with Parkinson's, the first of its type, it was found that many of the participants receiving the treatment had realistic and well-informed expectations about the PDSAFE intervention at the outset. Most had had previous experience of physiotherapy and a variety of other rehabilitation interventions. Participants seemed well motivated to embark on the programme for a variety of personal reasons, including anticipated benefits relating to improved mobility and function, and more general improvements in confidence and independence. People also wanted to participate for altruistic reasons, hoping that the research would benefit others with Parkinson's. This variety of potential motivations for participating in exercise by people with Parkinson's, including the altruistic desire to help others, was also found by O'Brien et al.[84] in exploring views of people with Parkinson's about participation in an exercise group. PDSAFE was valued for its convenience, in being delivered at home, and also for the input from specialist physiotherapists with experience and expertise in Parkinson's.

Participants recalled the exercise programme well at the time of the second visit, and were able to describe, in some detail, specific components. They recognised that the exercise programme was graded, becoming more intense as it progressed, and acknowledged that their programmes were individually tailored. Several also highlighted the strategies in describing the programme, and understood better the process of discussion and negotiation whereby exercises and strategies were designed to meet individual needs and expectations.

The mixed reactions to the equipment were affected by the value that participants placed on the increased intensity that they afforded. The varied responses to the technology used within PDSAFE reflected a continuum of familiarity and use among participants. However, some who were familiar with computers and smartphones felt that the visual images should be offered in alternative formats (e.g. as an app), which they could download and keep with them (e.g. on a tablet). These findings highlight a need to be creative and flexible when using technology, in order that the means of delivery can likewise be tailored to suit individual participants.

Most participants felt that the PDSAFE intervention had been of some benefit, when reflecting on its impact, whether in mobility, balance, strength or freezing, more general functional activities or improved confidence and independence. Similar views were expressed by people with Parkinson's in Quinn et al.,[85] who believed that exercise would keep them 'strong, functional and fit'. A significant minority of our participants mentioned that they experienced fewer falls, or were more aware of triggers for falls. A wide variety of benefits were highlighted, not all of which were captured by the outcome measures used within the main trial.

In terms of barriers to participation, lack of motivation was highlighted as a specific challenge. Participants valued the encouragement, monitoring and feedback provided by the therapists, and missed this once visits became less frequent and eventually stopped. Feedback from physiotherapists was also found by O'Brien et al.[86] to be important to people with Parkinson's in making decisions about exercise engagement. Another barrier was the time required to complete the individualised programmes; several participants mentioned their other competing commitments and difficulties in carrying out the PDSAFE intervention, either in full or at all. Many participants had busy lives including leisure activities, Parkinson's groups and family commitments, particularly those whose symptoms were not so severe.

The social support and encouragement provided by both the treating physiotherapists and others such as spouses, carers and partners seemed to be the biggest facilitator for continued engagement with the programme. Ravenek and Schneider,[87] in the first study exploring factors influencing participation in physical activity by people with Parkinson's, highlighted the significance of social support, and described three types: instrumental, information and emotional support. Participants mentioned that they found written information about the PDSAFE intervention useful; this was offered in blue folders to which many made reference.

Fall recording

The most widely adopted and recommended process for recording fall events is the use of self-reported falls diaries,[88] as used in the trial. The process is dependent on recall but open to error, most likely under-reporting, particularly when someone has multiple falls. For example, participants who did not receive any treatment (i.e. the control group) had very little interaction with the trial team, and thus received fewer reminders to complete falls diaries than the intervention group. It may be that those in the control group, particularly those with cognitive impairment, were less likely to report falls. Conversely, those in the treatment group may perhaps be more likely to report falls. Near-falls are open to similar errors of recording; they are events that would result in a fall if protective moves such as reaching out or stepping were not taken.[26] Near-falls among people with Parkinson's have been reported by a number of researchers, such Gazibara *et al.*[89] and Ashburn *et al.*;[37] they are often related to stumbling or balance loss, and have been observed to predispose the general older population to falling.[90] Gazibara *et al.*[89] describe near-falls as common among people with Parkinson's and particularly among people with FoG. In this trial, participants received guidance on recording fall events, had a 3-month run-in period for recording falls and received reminders to keep records throughout the trial. It is possible that participants in the intervention group were more aware of falling and kept more accurate records. In the future, body-worn sensor technology could be adopted, although the feasibility of this in clinical trials is not yet clear.

Beneficial effects on falls and stratification

As already stated in this discussion, previous researchers[17,37,40] have suspected that those with less severe Parkinson's have responded to fall reduction programmes, whereas, in their trials, deterioration may have occurred among people in the worse categories of Parkinson's. For that reason, disease severity and FoG were prespecified in a secondary subgroup analysis of PDSAFE; that analysis demonstrated a diverse response to the intervention programme. Those with moderate disease severity benefited most from the intervention, with a fall reduction of 30% over 6 months. Those at the severe end of the disease spectrum and those with FoG experienced an increase in falls of between 43% and 50% over the same period. The overall improvements in fall risks suggested that sufficient therapy for learning and responding to an exercise programme was delivered but fall avoidance by those at the severe end of the disease spectrum fell short. A greater understanding of the complexities of the transition from improved movements to fall avoidance in people who are compromised by a progressive condition is needed. At a simplistic level, PDSAFE may have made people more confident in their daily activities that exposed them to greater fall risk, to which the more able could respond effectively, but the more severely affected were unable to implement strategies for fall avoidance. People with more severe disease (i.e. more likely to have additional cognitive impairment and possibly FoG) may be more restricted in their ability to choose how to respond and may also have greater difficulty in engaging in unsupervised sessions, thus limiting the intensity of practice and the effects of fall prevention. Falls management needs to be stratified with careful consideration of the needs of those with multiple challenging issues that come with a progressive condition. The benefits highlighted by the secondary analysis on those with moderate disease severity need to be confirmed in a further trial.

Health economics

The results of the health economics analysis showed that the PDSAFE home-based personalised physiotherapy intervention was not likely to be cost-effective for the overall Parkinson's population from the NHS and PSS perspectives over the 6-month time horizon at a £20,000- to £30,000-per-QALY threshold for the ICER estimated. There was little difference in the mean cost of NHS and social service use between the treatment groups. The utility values of the intervention group declined slightly less than in the control group over the trial period, but the difference was minimal and not statistically significant.

Although not cost-effective in the overall population, subgroup analyses indicated that the PDSAFE intervention appears to be cost-effective in the subgroup of participants with more severe disease. This is because of the substantial saving of NHS and social care services arising in this subgroup of the intervention arm. The intervention was also cost-effective in the subgroup of participants who had Parkinson's of moderate severity (i.e. a MDS-UPDRS score of 23–38), because of the reduction in service use and the larger magnitude of QALY gain. In terms of the impact on HRQoL, the PDSAFE intervention was shown to be statistically significantly beneficial in participants who had not experienced freezing episodes whereas, among participants with severe Parkinson's, it resulted in a lower mean QALY gain than the control group.

Sensitivity analyses indicated that the intervention was more likely to be cost-effective when a 12-month time horizon was adopted; although only half of the data for participants at the 12-month follow-up were directly observed. This is because of the difference in HRQoL at the 6-month primary end point, as well as the persistent benefit of the intervention beyond the 6-month intervention period. At 12 months, HRQoL in the intervention group was still higher than in the control group, with both observed-only data and imputed data; therefore, it is likely that this difference would last beyond the 12-month follow-up point. This means that the probability of the intervention being cost-effective might increase if extrapolating the results to a longer term.

Limitations

Most participants in the trial were followed to 12 months, with the primary outcome measured at 6 months post randomisation; however, the last 132 participants to be recruited could be followed only to the primary outcome point (i.e. 6 months) because of restricted funding. This meant that the numbers of participants in the trial reduced during the period between 6 and 12 months, creating a limitation in the analysis and interpretation of the long-term outcome of the intervention and the health economic sensitivity analysis.

Participants were asked to complete a number of self-recorded diaries. The most important was the falls diaries for the primary outcome. The trial team invested a great deal in facilitating the completion of the falls diaries. Self-recorded data on unsupervised practice of the intervention was incomplete. The demand on the participant meant that recording of unsupervised practice was not always completed and was less of a priority than the falls record.

Implications for practice

- The PDSAFE intervention did not reduce falls in a heterogeneous sample of people with Parkinson's.
- Secondary analysis supported previous research findings that exercise had a positive effect on fall risk.

Future research

- Future fall prevention trials should not target heterogeneous samples but specific groups of people with Parkinson's.
- Primary trials of fall prevention for disease-specific groups are recommended.
- Secondary analysis demonstrated that the PDSAFE intervention did have a positive effect on balance, functional strength, falls efficacy and near-falls.

Conclusion

The PDSAFE intervention did not reduce falls in a heterogeneous sample of people with Parkinson's. There was evidence of improvement in balance, functional strength and falls efficacy, with a reduction in near-falls. Secondary analysis showed diverse responses to the intervention in accordance with disease severity and FoG. Further trials of falls prevention on targeted groups of people with Parkinson's are recommended.

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Publications

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Data-sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

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Appendix 1 Participant invitation letter

<Printed on local headed paper
with address and telephone number>

PARTICIPANT INVITATION LETTER

A randomised controlled trial of the effectiveness of PDSAFE to prevent falls among people with Parkinson's: Main Trial

Dear

I am writing on behalf of Dr, to invite you to take part in a research trial, 'A randomised controlled trial of the effectiveness of PDSAFE to prevent falls among people with Parkinson's. This research is being led by Professor Ann Ashburn, Professor of Rehabilitation at the University of Southampton. We are considering new ways of helping people with Parkinson's to maintain safe balance and walking and we have chosen to do this by studying the benefits of exercises and strategies designed to help people to improve the way they move about. I enclose an Information Sheet that explains more about the trial. If you have any questions that are not answered in the Information Sheet please feel free to contact me using the details above.

If you are interested in taking part in this trial and would like further information, I would be most grateful if you would complete the 'reply slip' enclosed and return it in the pre-addressed Freepost envelope provided. This will not commit you to taking part in the trial.

Thank you.

Yours sincerely,

<Contact details for Local Assessor for the PDSAFE Trial>

Appendix 2 Participant information sheet

PARTICIPANT INFORMATION SHEET

A randomised controlled trial of the effectiveness of PDSAFE to prevent falls among people with Parkinson's: Main Trial

We would like to invite you to take part in our research trial. Before you decide whether or not to take part, we would like you to understand why the research is being carried out and what it would involve for you. Please take time to read the following information carefully and discuss it with friends, relatives, and your GP if you wish. A member of our research team will go through this Information Sheet with you and answer any questions you may have. If you would like further information, please do not hesitate to telephone the number above.

What is the purpose of this trial?
Parkinson's is a common, progressive condition that affects the body's nervous system. Over time people with Parkinson's are likely to become less steady, less able to move around within their homes and outside and more prone to falls. Although drugs are available to treat the symptoms of Parkinson's, reduced balance control and falls do not respond to drugs. There is some evidence that physiotherapy can help, though to date there are insufficient research findings to quantify the benefits for people with Parkinson's. A new exercise and strategy-based intervention for people with Parkinson's, called PDSAFE, has been developed by a research team led by Professor Ann Ashburn in Southampton. PDSAFE is a personalised physiotherapy programme that is aimed to help with balance and movement. The purpose of this trial is to see if the PDSAFE intervention helps people with Parkinson's to fall less often and to assess whether it is cost-effective. More specifically, our main question is: do people with Parkinson's who follow PDSAFE fall less than those who do not follow it?

Why have I been invited?
We are planning to recruit 600 people with Parkinson's to this trial. You have been identified as someone who has been diagnosed with Parkinson's and might be interested in taking part in this research trial. You have been told about this trial either a) by a health professional who is known to you, b) by your Parkinson's support group, or c) because you have previously agreed that we could inform you of further research taking place at the University of Southampton or with the local research network.

Do I have to take part?
It is up to you to decide if you wish to join the trial. By returning the reply slip accompanying this Information Sheet you are only agreeing to be contacted by a researcher at this point. He/she will describe the trial and go through this Information Sheet with you. If you agree to take part, we will then ask you to sign a consent form. You are free to withdraw at any time without giving a reason. Deciding not to take part or withdrawing from the trial at any point will not affect the standard of care you receive.

What will happen to me if I take part?

How long will I be involved with the research?
You will be involved in the research over a period of approximately 15 months.

How many times will I meet the researcher for assessments?
You will meet the researcher on five separate occasions for assessments. The first assessments will take place in the three months before the trial formally starts (a screening visit to obtain your written consent). At the baseline assessment visit (three months later) you will be randomly allocated either to the exercise group, who will receive the PDSAFE intervention, or the control group. The researcher will see you again for assessments at 3, 6 and 12 months after your random group allocation.

Where will I meet the researcher?
The assessments will take place in your own home.

How long will these visits for assessments be?
The assessments will take up to 90 minutes.

What happens during these assessment visits?

During the screening visit, the researcher will talk to you about the research trial and ask you to sign a consent form. The researcher will then ask you to complete two assessments to confirm your eligibility to join the trial. Should you be unable to complete these, the researcher will advise you that, unfortunately, you are not suitable to be included in the trial. If you complete the assessments the researcher will proceed to ask you questions about your balance, ability to move about, stamina, vision, any falls you have had, ability to remember instructions and any medical and/or surgical condition you feel may affect the way you move. They will also ask you whether you have a carer whom we could approach to take part in the trial. Having a carer is not a requirement for you to take part in the trial.

During the assessment visits (at baseline, 3, 6 and 12 months), you will be asked to complete a questionnaire on your quality of life, mood, fear of falling and an ability to complete everyday tasks. You only have to answer the questions you feel comfortable with and if you are unhappy with any of the questions you may stop at any time. The researcher will also ask you questions about your usual leisure activities and ask you to complete tests of your balance, posture, turning and walking. The assessment of turning involves you turning round and may require video recording. The balance tests involve you completing a series of exercises like standing up, reaching forward and attempting to stand on one leg. You may also be asked to complete a hand grip test. You will not be asked to complete any tests you feel you cannot manage. You will be allowed to rest during and between tests. The tests can be stopped at any time if you become tired.

Throughout the duration of the trial, you will be asked to record any falls you may have in a diary, which we will provide. We will explain the falls diary to you during the screening visit and give you a contact number to call if you have any queries about completing the falls diary.

<u>Which group will I be put into?</u>
To date there are insufficient research findings to quantify the benefits of exercise on fall risk for people with Parkinson's. We do not know if taking part in these exercises will reduce your fall risk and how big the benefits of exercising are on other aspects of your wellbeing e.g. your balance. To find out, we need to compare different treatments. We will allocate people to two groups; one group will have the PDSAFE exercises and their usual care, while the other group will only have their usual care. The results are compared to see if one is better. To try to make sure the groups are the same to start with, each patient is put into a group by chance (randomly).

***If you are allocated to the PDSAFE exercise group*:** you will be asked to continue with your usual care and normal day to day life and you will be asked to follow the PDSAFE programme which will be personalised to your needs and ability by a physiotherapist. If you are happy to do so the physiotherapist will ask you to comply with an exercise agreement, but only if you feel that this will encourage you to practice the agreed exercises. The programme includes exercises for *balance* (such as standing still and reaching forwards and back and standing on foam and stepping sideways) *muscle strengthening* (such as standing up from sitting, stepping up and down from a step, these may be progressed by wearing a weighted vest adjusted to your ability) and strategies for improving walking, freezing (unable to move), steadiness and avoiding falls, as well as identifying fall hazards in and around your home. The physiotherapist will discuss the exercise treatment with you, teach you the exercises and together you will identify how often you would practice the exercises during the week. The physiotherapist will come to your house to practice the exercises with you. The frequency of his/her visits will be reduced over a six month period; starting with one hour twice a week for two or three weeks, then once a week for four to six weeks, followed by a visit at three months and a final visit at five months.

In each treatment session, the physiotherapist will illustrate ways of improving means of moving around by showing videos of demonstrations and s/he may video the treatment session, then transfer the film onto DVD and return it to you, so that you can replay it at home. You will be provided with all of the necessary equipment (including lending you a DVD player if you do not have one at home) to allow you to take part in the intervention. The DVD will enable multiple replays of a session as required and act as a reminder of the activity, instructions, information and feedback. PDSAFE will be delivered by physiotherapists in your own home over a period of up to five months. As part of the intervention, the physiotherapist will identify fall hazards in and around your home. If the physiotherapist identifies any fall hazards, we will discuss these issues with you and try to find possible solutions. However, if the hazards cannot be easily rectified by the research team, the physiotherapist will ask you for your permission to contact relevant authorities to address these hazards. You will be asked not to share the

treatment with other Parkinson's friends as it is important that the exercises and videos are only available to those under supervision in the treatment group of this trial.

If you are in the control group: you will be asked to continue with your usual care and normal day to day life. A physiotherapist will visit you to give you a DVD with information about Parkinson's and visit again at the end of the trial to advise about safe mobility and leave a booklet containing general tips on fall prevention and general advice about physical activities and strategies for balance and safety. Participants in the control group play an important role in the success of the trial.

Quality assurance
In order to check the quality of assessments being performed on all participants and the delivery of physiotherapy, advice and information, an additional member of the PDSAFE team may join the assessor and/or physiotherapist on an occasional visit. This will only apply to a very small number of participants.

Personal views interviews:
A small group of trial participants (40 in total) will be invited to take part in interviews to talk about your personal views of the treatment. If you agree to take part in this aspect of the trial, the first interview will be conducted soon after the baseline assessments are completed and prior to the start of the intervention. The second interview will be six months later. The researcher will visit you at home to discuss your experience. Interview visits will last approximately 60 minutes.

What are the possible benefits of taking part?
There will be no direct benefit to you from taking part in the trial although you might enjoy completing the exercises and being more active. However it is hoped that the data collected will allow us to define the benefits of PDSAFE, in terms of reducing falls and improving balance of people with Parkinson's. The cost of PDSAFE will be assessed using information about the treatment delivery costs. This information will be used to further develop the treatment and enhance clinical services.

Are there any risks involved?
Answering questions from questionnaires can sometimes cause distress but we do not anticipate any disadvantage or risks. You do not have to answer any questions or participate in activities you don't wish to and can stop at any point. It is possible that taking part in exercises and/or assessments can cause instability and put you off balance. You do not have to practice any exercises or do any assessments you feel unsure about. A researcher will be present during the assessments to help ensure your safety.

Can you practice the exercises on your own?
Only after you have practiced with the physiotherapist and you both agree that you are happy and safe to do so with the help of your strategy DVD.

What if there is a problem or I have a complaint?
If you feel you have any concerns or complaints about this trial you should contact Professor Ann Ashburn (███ ██). If you remain unhappy and wish to complain, Ann will provide you with details of the University of Southampton and University Hospital Southampton NHS Foundation Trust Complaints Procedure. Alternatively, you may wish to speak to the local Patient Support Services, PALS on *< contact details for local Patient Support Services>*.

Who is organizing the research & reviewing the trial?
The research is being led by Professor Ann Ashburn, Professor of Rehabilitation at the University of Southampton. It has been reviewed by the National Ethics Research Service Committee South Central – Hampshire B Research Ethics Committee and University Hospital Southampton are the sponsors.

Will my participation be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Each person will be allocated an ID number by which any documentation will be identifiable to the researchers only. All information will be kept in a locked filing cabinet in accordance with storage of medical records. The results from the trial will be entered into a University computer, accessible only to the researchers. Any information about you which is used in research reports or publications will have your name and address removed so that you cannot be identified. Nevertheless, the research team is required by law to break confidentiality where cases of malpractice, abuse, or risk to self or others are disclosed. Such cases will be referred to the appropriate authority.

What happens when the research trial stops?

When the research trial stops, the PDSAFE exercises as delivered by a physiotherapist will come to an end and participants will continue to receive their usual care. The group who took part in the PDSAFE exercises can choose to continue the exercises and will be able to keep their personalised PDSAFE exercise DVD. The group who did not take part in the exercises will be able to keep the Parkinson's information DVD and falls prevention booklet. We will disseminate our findings after the completion of the study.

What will happen to the results of the research?

At the end of the research, the data collected will be securely stored at the University of Southampton for 10 years. The results will be presented at conferences and may be published in research papers for scientific journals. If you would like a copy of the published results at the end of the trial please let us know.

Contact for further information:

If you would like any further information please contact:

< LOCAL CONTACT DETAILS>

Or

Dr Kim Chivers Seymour (Trial Manager)

Thank you for taking the time to read this information.

Appendix 3 Participant reply slip

PARTICIPANT REPLY SLIP

A randomised controlled trial of the effectiveness of PDSAFE to prevent falls among people with Parkinson's: Main Trial

I would like further information about this trial and I am happy for the researcher to contact me.

☐ I agree for you to contact me (Please initial the box)

Please use the following details to contact me: (Please Print)

Name: _____

Address: _____

_____

_____

_____

_____

_____

_____

Telephone Number: _____

E-mail: _____

Today's date: _____

Please return this reply slip in the pre-addressed Freepost envelope.

Thank you very much for your interest.

Appendix 4 Falls diaries

PD SAFE

Fall Prevention in Parkinson's disease

How to complete the Falls Diaries

If you have a _FALL_, please:
 a) Mark an "F" on the monthly sheet of your Falls Diary, on the day which you have a fall, and
 b) Use the boxes on the 'Details of Falls' sheets to describe what happened for each fall.

Definition of a FALL
> "When you accidentally lose your balance and cannot save yourself.
> You may land on the ground or on a piece of furniture."

Please make a note of the following details:
- Date and time (use 'morning', 'afternoon', 'evening' or 'night', if you can't recall the exact time).
- Where you fell, e.g. in the bathroom, in the garden, in the street.
- What you were doing or trying to do, e.g. sit down, turn round, open the front door.
- Why you think you fell, e.g. tripped over your feet, froze, misjudged a distance.
- How you landed, e.g. flat on your back, on all fours, on one knee.
- Injuries or treatment , e.g. bruised hip, broken bone, went to A&E, admitted to hospital, saw GP/Nurse.
- Getting up again, e.g. needed help, by yourself, crawled to furniture.

Short (even single word) answers are perfectly acceptable:
- You do not have to write sentences.
- There is space to describe two falls on every Details of Falls sheet.
- If you want to write any more about what happened when you fell, please feel free to do so.

We don't expect you to remember every detail of every fall.
- If you can't be certain, please write, 'Don't know', 'No idea', or 'Can't remember' in any box.
- The trial team are available to answer any questions that you have about your Falls Diary. Contact the PDSAFE Team on: 023 8120 4943.
- You may have to leave a message on the answer phone – please state your name and a contact number and one of the team will get back to you.

If you have a _NEAR FALL_, please:
Mark "NF" in the box on any day of the monthly sheets of your Falls Diary on which you have a near fall.

Definition of a NEAR FALL
> "When you felt you were going to fall but did not and managed to save yourself."

<u>Falls Diary</u>

APRIL 2017

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
					1	2
3	4	5	6	7	8	9
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30

<u>FALL</u> = When you accidentally lose your balance and cannot save yourself. You may land on the ground or on a piece of furniture.

Please mark an "F" in the box on any day on which you have a fall. Then record details of the fall on the 'Details of Falls' sheet.

<u>NEAR FALL</u> = When you felt you were going to fall but did not and managed to save yourself.

Please mark "NF" in the box on any day on which you have a near fall. No need to record further details of near falls.

Thank you

Details of Fall
Date and time of your fall
Where did you fall?
What were you trying to do when you fell?
Why do you think you fell?
How did you land when you fell?
Did you incur any injuries when you fell?
Any treatment/follow-up care? (please tick all that apply) 　　　No　　　　　　　　　　　　Admission to hospital　　 __ (please specify number of days) 　　　Ambulance to A&E　　　　　Others (please specify, e.g. GP)
Getting up again – how did you get up after your fall?

Fall
Date and time of your fall
Where did you fall?
What were you trying to do when you fell?
Why do you think you fell?
How did you land when you fell?
Did you incur any injuries when you fell?
Any treatment/follow-up care? (please tick all that apply) 　　　No　　　　　　　　　　　　Admission to hospital　　 __ (please specify number of days) 　　　Ambulance to A&E　　　　　Others (please specify, e.g. GP)
Getting up again – how did you get up after your fall?

Appendix 5 Recruitment and randomisation
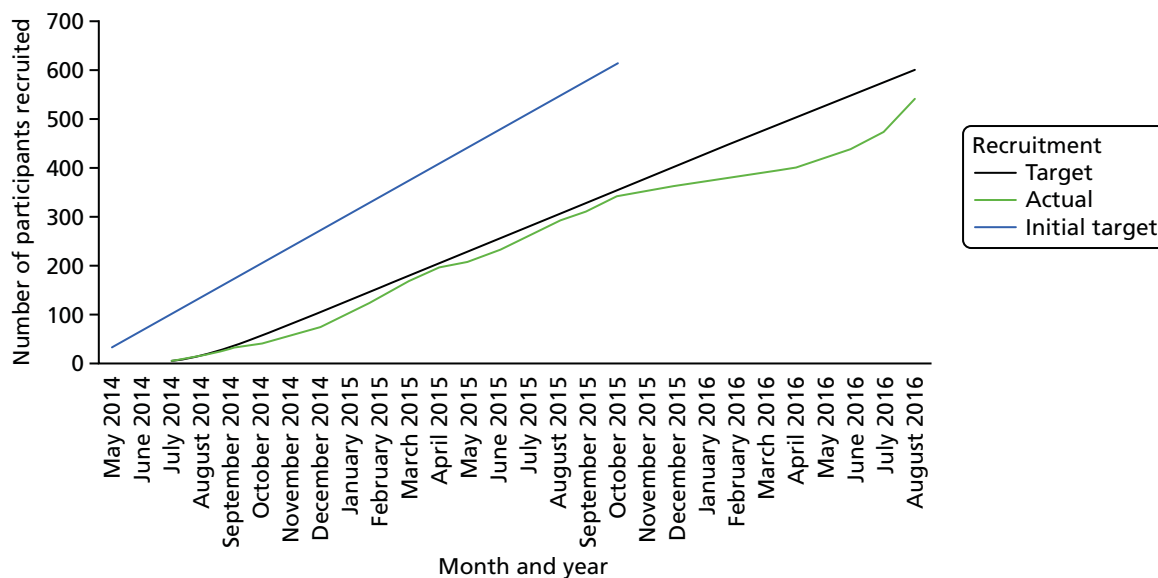
FIGURE 13 PDSAFE recruitment against target.
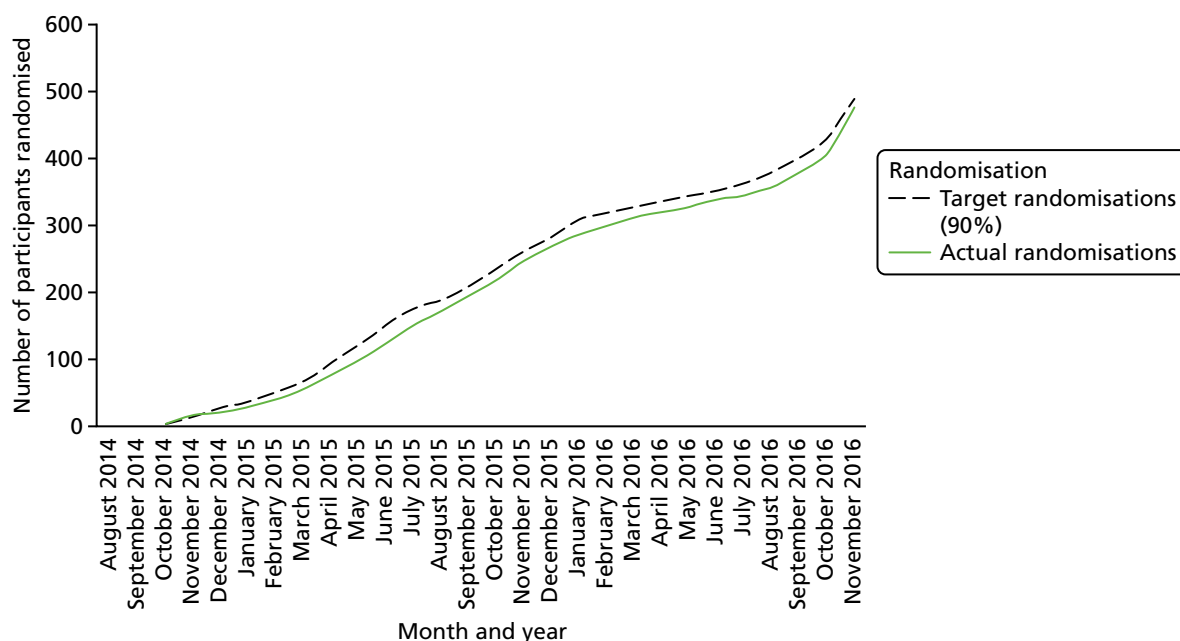
FIGURE 14 PDSAFE randomisation against target (90% of those recruited).

Appendix 6 Power calculations

TABLE 26 Power calculations for primary and secondary falling outcomes: risk of repeat falling

Risk of repeat falling[a]	Trial group (%)		Required in analysis (*n*)		Needed at (*n*)	
	Control	PDSAFE	Per group	Total	Recruitment[b]	Randomisation[c]
0–6 months (5% loss to follow-up)						
13% difference	63	50	228	456	534	480
15% difference	70	55	163	326	382	344
15% difference	60	45	173	346	408	366
13% difference	63	50	228	456	534	480
6–12 months (10% loss to follow-up)						
13% difference	63	50	228	456	564	508
15% difference	70	55	163	326	404	364
15% difference	60	45	173	346	430	386

a In EXSART,[37] risks of repeat falling from 0 to 6 months were 68% for the control group and 56% for the intervention group.
b Numbers needed at recruitment allow for 10% of those agreeing to enter the pre-randomisation falls collection period not to participate in the main trial, and a further loss of 5% of falls information by 6 months and 10% by 12 months. This is conservative in the case of the falls rate models, as participants dropping out during a period will contribute some exposure time to the analysis.
c Numbers needed at randomisation allow for 5% loss of falls information by 6 months and 10% by 12 months.

TABLE 27 Power calculations for secondary falling outcomes: fall rates

Fall rates[a]	Baseline rate per 3 months	Required in analysis (n)		Needed at (n)	
		Per group	Total	Recruitment[b]	Randomisation[c]
FRR 0–6 months (5% loss to follow-up)					
0.75	3	100	200	236	212
0.8	3	164	328	386	346
0.75	2.5	120	240	278	254
0.8	2.5	197	394	464	416
0.75	2	150	300	352	316
0.8	2	246	492	576	518
FRR 6–12 months (10% loss to follow-up)					
0.75	3	100	200	250	224
0.8	3	164	328	408	366
0.75	2.5	120	240	298	268
0.8	2.5	197	394	488	438
0.75	2	150	300	372	334
0.8	2	246	492	610	548

a In EXSART, the FRR over the 6-month follow-up was 0.833; the control group had a rate of falls of 3 over 3 months of follow-up.
b Numbers needed at recruitment allow for 10% of those agreeing to enter the pre-randomisation falls collection period not to participate in the main trial, and a further loss of 5% of falls information by 6 months and 10% by 12 months. This is conservative in the case of the falls rate models, as participants dropping out during a period will contribute some exposure time to the analysis.
c Numbers needed at randomisation allow for 5% loss of falls information by 6 months and 10% by 12 months.

Appendix 7 Sensitivity analysis

TABLE 28 Sensitivity analysis for ITT OR for repeat falling from 0 to 6 months and from 6 to 12 months, whole group, based on three methods: restricted to those with 50% diary completion or more, restricted to full diary and unrestricted to diary completion

Period	Trial group, *n/N* (%)		PDSAFE/control[a] OR (95% CI)	*p*-value[a]
	PDSAFE	**Control**		
Repeat falling restricted to ≥ 50% diaries				
0–6 months	125/203 (62)	116/211 (55)	1.21 (0.74 to 1.98)	0.447
6–12 months	57/114 (50)	71/132 (54)	0.86 (0.45 to 1.65)	0.657
Repeat fallers restricted to full diary completion				
0–6 months	79/130 (61)	83/158 (53)	1.31 (0.72 to 2.39)	0.374
6–12 months	34/64 (53)	37/76 (49)	1.28 (0.47 to 3.52)	0.627
Repeat fallers unrestricted to diary completion				
0–6 months	134/237 (57)	127/236 (54)	1.07 (0.69 to 1.66)	0.759
6–12 months	63/137 (46)	78/150 (52)	0.68 (0.38 to 1.22)	0.200

a　Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, and H&Y scale stage.

Appendix 8 Repeat falling

TABLE 29 The ITT OR for repeat falling from 0 to 6 months and from 6 to 12 months, whole group and subgroups, restricted to those with 50% diary completion or more

| Participant group | Period (months) | Trial group, *n/N* (%) | | PDSAFE/control OR (95% CI)[a] | *p*-value[a] | |
		PDSAFE	Control		PDSAFE within participant group	Interaction
All participants	0 to 6	125/203 (62)	116/211 (55)	1.21 (0.74 to 1.98)	0.447	
	6 to 12	57/114 (50)	71/132 (54)	0.86 (0.45 to 1.65)	0.657	
MDS-UPDRS score of ≤ 58	0 to 6	115/192 (60)	106/195 (54)	1.18 (0.71 to 1.95)	0.521	
	6 to 12	55/111 (50)	66/125 (53)	0.90 (0.47 to 1.74)	0.758	
H&Y scale stage ≤ 3	0 to 6	104/180 (58)	92/179 (51)	1.13 (0.68 to 1.87)	0.651	
	6 to 12	50/106 (47)	54/113 (48)	0.91 (47 to 1.76)	0.785	
MoCA score						
≤ 25	0 to 6	49/74 (66)	45/80 (56)	2.03 (0.91 to 4.54)	0.083	0.111
≥ 26	0 to 6	76/129 (59)	71/131 (54)	0.91 (0.49 to 1.67)	0.754	
≤ 25	6 to 12	20/43 (47)	33/56 (59)	0.71 (0.25 to 2.02)	0.525	0.606
≥ 26	6 to 12	37/71 (52)	38/76 (50)	1.01 (0.44 to 2.29)	0.987	
FoG						
No	0 to 6	27/76 (36)	38/93 (41)	0.66 (0.32 to 1.38)	0.269	0.025
Yes	0 to 6	98/126 (78)	78/118 (66)	2.04 (1.03 to 4.06)	0.042	
No	6 to 12	12/43 (28)	22/58 (38)	0.58 (0.21 to 1.57)	0.282	0.309
Yes	6 to 12	45/70 (64)	49/74 (66)	1.14 (0.48 to 2.70)	0.772	
MoCA score						
≤ 25	0 to 6	49/74 (66)	45/80 (56)	2.04 (0.91 to 4.55)	0.083	0.238
26 or 27	0 to 6	32/55 (58)	27/53 (51)	1.07 (0.42 to 2.79)	0.863	
≥ 28	0 to 6	44/74 (59)	44/78 (56)	0.78 (0.35 to 1.75)	0.352	
≤ 25	6 to 12	20/43 (47)	33/56 (59)	0.71 (0.25 to 2.01)	0.248	0.751
26 or 27	6 to 12	16/32 (50)	14/31 (45)	1.30 (0.38 to 4.43)	0.680	
≥ 28	6 to 12	21/39 (54)	24/45 (53)	0.82 (0.27 to 2.45)	0.720	
MDS-UPDRS score						
≥ 39	0 to 6	44/61 (72)	41/74 (55)	2.55 (1.03 to 6.33)	0.044	0.140
23–38	0 to 6	48/77 (62)	35/60 (58)	0.80 (0.35 to 1.86)	0.609	
≤ 22	0 to 6	33/65 (51)	39/76 (51)	0.97 (0.43 to 2.17)	0.942	
≥ 39	6 to 12	16/29 (55)	29/46 (63)	0.80 (0.23 to 2.80)	0.727	0.943
23–38	6 to 12	24/49 (50)	18/38 (47)	1.02 (0.35 to 2.98)	0.976	
≤ 22	6 to 12	17/36 (47)	23/47 (49)	1.02 (0.35 to 2.98)	0.936	

TABLE 29 The ITT OR for repeat falling from 0 to 6 months and from 6 to 12 months, whole group and subgroups, restricted to those with 50% diary completion or more (*continued*)

| Participant group | Period (months) | Trial group, *n/N* (%) | | PDSAFE/control OR (95% CI)[a] | *p*-value[a] | |
		PDSAFE	Control		PDSAFE within participant group	Interaction
Retrospective falls						
> 3	0 to 6	75/88 (85)	49/63 (78)	1.45 (0.57 to 3.67)	0.436	0.407
2 or 3	0 to 6	35/71 (49)	58/104 (56)	0.79 (0.39 to 1.61)	0.523	
1	0 to 6	15/44 (34)	9/44 (20)	1.68 (0.59 to 4.77)	0.331	
> 3	6 to 12	34/45 (76)	31/41 (76)	1.18 (0.36 to 3.88)	0.780	0.501
2 or 3	6 to 12	17/43 (40)	35/62 (56)	0.57 (0.22 to 1.49)	0.251	
1	6 to 12	6/26 (23)	5/29 (17)	1.36 (0.32 to 5.73)	0.672	

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage, and the interaction term where this is listed.

Appendix 9 Falls rate ratio

TABLE 30 The ITT FRRs from 0 to 6 months and from 6 to 12 months: whole group and subgroups

Participant group	Period (months)	Participants contributing diaries, *n*	PDSAFE/control FRR (95% CI)[a]	*p*-value[a] PDSAFE within participant group	Interaction
All participants	0–6	461	0.98 (0.80 to 1.19)	0.824	
	6–12	274	0.83 (0.62 to 1.11)	0.200	
MDS-UPDRS score of ≤ 58	0–6	429	0.95 (0.77 to 1.18)	0.648	
	6–12	256	0.79 (0.58 to 1.08)	0.142	
H&Y scale stage ≤ 3	0–6	395	0.99 (0.78 to 1.25)	0.915	
	6–12	240	0.80 (0.57 to 1.12)	0.191	
MoCA score					
≤ 25	0–6	178	1.19 (0.88 to 1.61)	0.255	0.088
≥ 26	0–6	283	0.85 (0.66 to 1.09)	0.208	
≤ 25	6–12	112	1.06 (0.67 to 1.66)	0.810	0.154
≥ 26	6–12	162	0.69 (0.48 to 1.00)	0.050	
FoG					
No	0–6	181	0.89 (0.61 to 1.29)	0.527	0.566
Yes	0–6	279	1.01 (0.80 to 1.26)	0.964	
No	6–12	112	0.81 (0.47 to 1.38)	0.766	0.956
Yes	6–12	161	0.82 (0.58 to 1.15)	0.251	
MoCA score					
≤ 25	0–6	178	1.12 (0.89 to 1.61)	0.246	0.089
26 or 27	0–6	119	1.06 (0.71 to 1.58)	0.778	
≥ 28	0–6	164	0.75 (0.55 to 1.02)	0.055	
≤ 25	6–12	112	1.06 (0.67 to 1.67)	0.800	0.361
26 or 27	6–12	70	0.66 (0.37 to 1.16)	0.148	
≥ 28	6–12	92	0.72 (0.45 to 1.17)	0.191	
MDS-UPDRS score					
≥ 39	0–6	152	1.43 (1.04 to 1.95)	0.028	0.009
23–38	0–6	155	0.70 (0.50 to 0.98)	0.038	
≤ 22	0–6	152	0.97 (0.69 to 1.37)	0.866	
≥ 39	6–12	87	1.07 (0.67 to 1.72)	0.773	0.231
23–38	6–12	95	0.60 (0.36 to 1.01)	0.057	
≤ 22	6–12	91	1.00 (0.59 to 1.70)	0.992	

TABLE 30 The ITT FRRs from 0 to 6 months and from 6 to 12 months: whole group and subgroups (*continued*)

Participant group	Period (months)	Participants contributing diaries, *n*	PDSAFE/control FRR (95% CI)[a]	*p*-value[a] PDSAFE within participant group	Interaction
Retrospective falls					
> 3	0–6	168	1.16 (0.88 to 1.52)	0.286	0.050
2 or 3	0–6	196	0.70 (0.50 to 0.96)	0.026	
1	0–6	97	1.03 (0.59 to 1.80)	0.916	
> 3	6–12	96	0.98 (0.64 to 1.49)	0.925	0.402
2 or 3	6–12	119	0.64 (0.40 to 1.04)	0.072	
1	6–12	59	0.69 (0.31 to 1.54)	0.364	

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage, and the interaction term where this is listed.

Appendix 10 Near-falls rate ratio

TABLE 31 The ITT near-falls rate ratio from 0 to 6 months and from 6 to 12 months: whole group and subgroups

Participant group	Period (months)	Participants contributing diaries, n	PDSAFE/control FRR (95% CI)[a]	p-value[a] PDSAFE within participant group	Interaction
All participants	0–6	447	0.67 (0.53 to 0.86)	0.001	
	6–12	280	1.01 (0.67 to 1.52)	0.968	
MDS-UPDRS score of ≤ 58	0–6	415	0.63 (0.49 to 0.80)	0.000	
	6–12	262	0.97 (0.64 to 1.46)	0.881	
H&Y scale stage ≤ 3	0–6	386	0.65 (0.51 to 0.83)	0.001	
	6–12	243	0.92 (0.60 to 1.41)	0.701	
MoCA score					
≤ 25	0–6	169	0.64 (0.43 to 0.96)	0.032	0.755
≥ 26	0–6	281	0.69 (0.51 to 0.93)	0.015	
≤ 25	6–12	113	1.00 (0.53 to 1.88)	0.992	0.981
≥ 26	6–12	168	0.99 (0.59 to 1.68)	0.980	
FoG					
No	0–6	178	0.55 (0.37 to 0.84)	0.005	0.277
Yes	0–6	271	0.74 (0.54 to 0.99)	0.048	
No	6–12	116	1.04 (0.54 to 2.03)	0.899	0.903
Yes	6–12	165	0.99 (0.59 to 1.66)	0.976	
MoCA score					
≤ 25	0–6	169	0.64 (0.43 to 0.96)	0.033	0.885
26 or 27	0–6	119	0.74 (0.47 to 1.17)	0.199	
≥ 28	0–6	162	0.66 (0.45 to 0.98)	0.039	
≤ 25	6–12	113	0.97 (0.52 to 1.81)	0.930	0.407
26 or 27	6–12	71	1.33 (0.63 to 2.82)	0.452	
≥ 28	6–12	97	0.67 (0.33 to 1.35)	0.266	
MDS-UPDRS score					
≥ 39	0–6	148	0.74 (0.49 to 1.12)	0.152	0.364
23–38	0–6	150	0.56 (0.37 to 0.85)	0.007	
≤ 22	0–6	150	0.85 (0.56 to 1.28)	0.429	
≥ 39	6–12	90	1.32 (0.65 to 2.70)	0.446	0.567
23–38	6–12	97	0.77 (0.38 to 1.58)	0.483	
≤ 22	6–12	93	1.11 (0.56 to 2.21)	0.763	

TABLE 31 The ITT near-falls rate ratio from 0 to 6 months and from 6 to 12 months: whole group and subgroups (*continued*)

Participant group	Period (months)	Participants contributing diaries, *n*	PDSAFE/control FRR (95% CI)[a]	*p*-value[a]	
				PDSAFE within participant group	Interaction
Retrospective falls					
> 3	0–6	166	0.74 (0.51 to 1.07)	0.113	0.652
2 or 3	0–6	187	0.70 (0.47 to 1.03)	0.073	
1	0–6	97	0.54 (0.31 to 0.95)	0.032	
> 3	6–12	98	1.17 (0.61 to 2.26)	0.630	0.358
2 or 3	6–12	124	1.21 (0.65 to 2.27)	0.545	
1	6–12	59	0.54 (0.20 to 1.43)	0.215	

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling and log rate of near-falling in the pre-randomisation falls collection period, H&Y scale stage, and the interaction term where this is listed.

Appendix 11 Mini-Balance Evaluation Systems Test

TABLE 32 The ITT Mini-BESTest analysis (0–28, lower values worse) measured at 6 and 12 months: whole group and subgroups

Participant group	Visit (months)	Participants (*n*)	Trial group: change from baseline, mean (SD)		PDSAFE – control mean change (95% CI)[a]	*p*-value[a]	Interaction
			PDSAFE	Control		PDSAFE within participant group	
All participants	6	394	1.1 (3.8)	0.2 (3.8)	0.95 (0.24 to 1.67)	0.009	
	12	241	–0.7 (4.5)	–0.2 (3.8)	–0.41 (–1.48 to 0.66)	0.449	
MDS-UPDRS score of ≤ 58	6	369	1.1 (3.8)	0.1 (3.6)	1.04 (0.32 to 1.77)	0.005	
	12	227	–0.8 (4.4)	–0.1 (3.8)	–0.52 (–1.62 to 0.58)	0.353	
H&Y scale stage ≤ 3	6	345	1.1 (3.7)	0.0 (3.6)	1.01 (0.35 to 1.82)	0.004	
	12	216	–0.7 (4.4)	–0.5 (3.8)	–0.30 (–1.43 to 0.84)	0.607	
MoCA score							
≤ 25	6	140	0.9 (4.0)	0.2 (4.5)	0.73 (–0.46 to 1.91)	0.228	0.654
≥ 26	6	254	1.2 (3.7)	0.2 (3.3)	1.06 (0.18 to 1.95)	0.019	
≤ 25	12	91	–1.2 (5.0)	0 (4.1)	–0.76 (–2.47 to 0.95)	0.384	0.570
≥ 26	12	150	–0.3 (4.1)	–0.2 (4.1)	–0.13 (–1.49 to 1.23)	0.851	
FoG							
No	6	157	0.7 (3.7)	–0.1 (3.5)	0.71 (–0.42 to 1.83)	0.220	0.570
Yes	6	236	1.4 (3.6)	0.5 (4.0)	1.12 (0.20 to 2.04)	0.017	
No	12	101	–0.6 (3.8)	–0.4 (4.1)	0.05 (–1.59 to 1.69)	0.950	0.464
Yes	12	139	–0.8 (4.9)	0.1 (3.7)	–0.74 (–2.13 to 0.66)	0.299	

| Participant group | Visit (months) | Participants (n) | Trial group: change from baseline, mean (SD) | | PDSAFE – control mean change (95% CI)[a] | p-value[a] | |
			PDSAFE	Control		PDSAFE within participant group	Interaction
MoCA score							
≤ 25	6	140	0.9 (4.0)	0.2 (4.5)	0.74 (–0.45 to1.92)	0.225	0.892
	12	91	–1.2 (5.0)	0 (3.4)	–0.75 (–2.47 to 0.97)	0.391	0.786
26 or 27	6	106	1.2 (4.4)	0.1 (3.4)	1.16 (–0.21 to 2.53)	0.096	
	12	63	–0.3 (4.6)	–0.6 (5.0)	0.24 (–1.84 to 2.31)	0.822	
≥ 28	6	148	1.2 (3.2)	0.3 (3.2)	1.01 (–0.14 to 2.16)	0.086	
	12	87	–0.4 (3.8)	0 (3.5)	–0.35 (–2.12 to 1.43)	0.701	
MDS-UPDRS score							
≥ 39	6	126	1.28 (4.2)	0.6 (4.4)	0.77 (–0.49 to 2.04)	0.231	0.255
	12	73	0.1 (4.9)	1.5 (3.5)	–1.49 (–3.44 to 0.45)	0.132	0.493
23–38	6	126	1.9 (3.9)	0.4 (3.3)	1.64 (0.40 to 2.87)	0.010	
	12	80	–0.5 (4.6)	–0.6 (3.4)	0.07 (–1.74 to 1.88)	0.939	
≤ 22	6	139	0 (3.2)	–0.3 (3.4)	0.21 (–0.98 to 1.40)	0.729	
	12	85	–1.46 (3.8)	–1.2 (4.0)	–0.41 (–2.14 to 1.33)	0.647	
Retrospective falls							
> 3	6	147	1.1 (3.8)	0.6 (3.5)	0.70 (–0.46 to 1.86)	0.236	0.162
	12	85	–1.1 (5.2)	0.1 (3.7)	–1.31 (–3.09 to 0.47)	0.149	0.195
2 or 3	6	168	1.2 (4.1)	0 (4.1)	1.78 (0.66 to 2.90)	0.002	
	12	104	–0.4 (3.9)	–0.6 (4.2)	0.78 (–0.90 to 2.46)	0.360	
1	6	79	0.9 (3.3)	0.1 (3.4)	0 (–1.58 to 1.58)	0.998	
	12	52	–0.2 (4.0)	0.5 (3.0)	–1.14 (–3.44 to 1.16)	0.330	

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage, covariate value at baseline and the interaction term where this is listed.

Appendix 12 Falls Efficacy Scale – International

TABLE 33 The ITT FES-I analysis (16–64, higher values worse) measured at 6 and 12 months: whole group and subgroups

Participants group	Visit (months)	Participants (n)	Trial group: change from baseline, mean (SD)		PDSAFE – control mean change (95% CI)[a]	p-value[a]	
			PDSAFE	Control		PDSAFE within participant group	Interaction
All participants	6	400	–0.7 (7.9)	1.1 (7.2)	–1.60 (–3.0 to –0.19)	0.026	
	12	354	1.3 (8.2)	3.5 (9.3)	–1.40 (–3.41 to 0.66)	0.184	
MDS-UPDRS score of ≤ 58	6	376	–0.8 (7.9)	1.1 (7.0)	–1.44 (–2.85 to –0.02)	0.047	
	12	241	1.3 (8.3)	3.1 (8.8)	–0.93 (–2.97 to 1.12)	0.372	
H&Y scale stage ≤ 3	6	352	–0.9 (7.9)	1.2 (6.7)	–1.5 (–2.97 to 0.04)	0.045	
	12	228	0.9 (8.1)	3.7 (9.1)	–1.50 (–3.63 to 0.65)	0.170	
MoCA score							
≤ 25	6	145	–0.4 (7.7)	1.8 (8.3)	–1.89 (–4.16 to 0.37)	0.101	0.724
≥ 26	6	255	–0.9 (8.0)	0.6 (6.3)	–1.39 (–3.11 to 0.34)	0.115	
≤ 25	12	99	1.9 (8.1)	4.3 (10.3)	–2.20 (–5.41 to 1.02)	0.180	0.534
≥ 26	12	155	1.0 (8.2)	2.9 (8.6)	–0.91 (–3.49 to 1.67)	0.489	
FoG							
No	6	159	0.1 (6.5)	0.3 (5.8)	–0.18 (–2.33 to 1.98)	0.872	0.085
Yes	6	240	–1.2 (8.6)	1.7 (8.0)	–2.60 (–4.37 to –0.82)	0.004	
No	12	105	1.1 (6.5)	2.6 (7.6)	–0.89 (–3.96 to 2.18)	0.569	0.580
Yes	12	148	1.5 (9.1)	4.2 (8.6)	–2.01 (–4.63 to 0.61)	0.132	

| Participants group | Visit (months) | Participants (n) | Trial group: change from baseline, mean (SD) | | PDSAFE – control mean change (95% CI)[a] | p-value[a] | |
			PDSAFE	Control		PDSAFE within participant group	Interaction
MoCA score							
≤ 25	6	145	–0.4 (7.7)	1.8 (8.3)	–1.92 (–4.18 to 0.33)	0.095	0.448
	12	99	1.9 (8.1)	4.3 (10.3)	–2.23 (–5.43 to 0.97)	0.170	0.112
26 or 27	6	107	0.2 (9.4)	0.6 (6.9)	–0.21 (–2.83 to 2.41)	0.873	
	12	67	2.9 (8.6)	1.9 (7.4)	1.93 (–1.92 to 5.77)	0.325	
≥ 28	6	148	–1.7 (6.6)	0.7 (6.0)	–2.33 (–4.56 to -0.09)	0.041	
	12	88	–0.6 (7.6)	3.6 (9.4)	–3.26 (–6.66 to 0.13)	0.060	
MDS-UPDRS score							
≥ 39	6	140	–0.5 (9.3)	1.5 (5.9)	–1.68 (–3.97 to 0.60)	0.149	0.929
	12	86	3.4 (7.2)	2.7 (8.6)	–1.89 (–5.22 to 1.44)	0.256	0.507
23–38	6	132	–0.3 (7.6)	0.4 (6.5)	–1.12 (–3.47 to 1.23)	0.349	
	12	88	0.6 (8.7)	2.4 (9.3)	0.07 (–3.24 to 3.38)	0.967	
≤ 22	6	124	–1.6 (6.4)	0.7 (6.4)	–1.67 (–4.14 to 0.80)	0.185	
	12	77	0.7 (9.3)	4.8 (11.4)	–2.72 (–6.44 to 1.00)	0.151	
Retrospective falls							
> 3	6	146	–1.7 (8.5)	0.4 (6.5)	–2.15 (–4.44 to 0.14)	0.065	0.834
	12	87	0.6 (8.7)	2.4 (9.3)	–1.58 (–5.00 to 1.84)	0.364	0.994
2 or 3	6	170	–0.3 (6.4)	1.1 (8.2)	–1.32 (–3.51 to 0.87)	0.238	
	12	110	1.17 (7.2)	3.3 (9.8)	–1.33 (–4.54 to 1.88)	0.415	
1	6	84	0.6 (8.1)	1.9 (5.4)	–1.21 (–4.20 to 1.78)	0.426	
	12	58	2.8 (8.6)	5.2 (8.3)	–1.43 (–5.67 to 2.82)	0.509	

a   Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage, covariate value at baseline and the interaction term where this is listed.

Appendix 13 Repeat falling

TABLE 34 The ITT and per-protocol OR for the primary outcome, repeat falling, from 0 to 6 months and from 6 to 12 months, restricted to those with 50% diary completion or more: whole group and subgroups

Participant group	Period (months)	ITT			Per protocol		
		PDSAFE/control OR (95% CI)[a]	PDSAFE within participant group p-value[a]	Interaction p-value[a]	PDSAFE/control OR (95% CI)[a]	PDSAFE within participant group p-value[a]	Interaction p-value[a]
All participants	0–6	1.21 (0.74 to 1.98)	0.447		1.16 (0.71 to 1.92)	0.538	
	6–12	0.86 (0.45 to 1.65)	0.657		0.92 (0.47 to 1.77)	0.793	
MDS-UPDRS score of ≤ 58	0–6	1.18 (0.71 to 1.95)	0.521		1.14 (0.69 to 1.89)	0.616	
	6–12	0.90 (0.47 to 1.74)	0.758		0.96 (0.49 to 1.86)	0.896	
H&Y scale stage ≤ 3	0–6	1.13 (0.68 to 1.87)	0.651		1.10 (0.66 to 1.83)	0.723	
	6–12	0.91 (47 to 1.76)	0.785		0.97 (47 to 1.76)	0.918	
MoCA score							
≤ 25	0–6	2.03 (0.91 to 4.54)	0.083	0.111	1.96 (0.88 to 4.41)	0.101	0.113
≥ 26	0–6	0.91 (0.49 to 1.67)	0.754		0.87 (0.47 to 1.63)	0.672	
≤ 25	6–12	0.71 (0.25 to 2.02)	0.525	0.606	0.75 (0.26 to 2.12)	0.583	0.561
≥ 26	6–12	1.01 (0.44 to 2.29)	0.987		1.10 (0.48 to 2.55)	0.819	
FoG							
No	0–6	0.66 (0.32 to 1.38)	0.269	0.025	0.66 (0.32 to 1.39)	0.280	0.039
Yes	0–6	2.04 (1.03 to 4.06)	0.042		1.90 (0.95 to 3.81)	0.068	
No	6–12	0.58 (0.21 to 1.57)	0.282	0.309	0.59 (0.22 to 1.63)	0.311	0.304
Yes	6–12	1.14 (0.48 to 2.70)	0.772		1.25 (0.52 to 2.83)	0.620	

Participant group	Period (months)	ITT			Per protocol		
		PDSAFE/control OR (95% CI)[a]	PDSAFE within participant group p-value[a]	Interaction p-value[a]	PDSAFE/control OR (95% CI)[a]	PDSAFE within participant group p-value[a]	Interaction p-value[a]
MoCA score							
≤ 25	0–6	2.04 (0.91 to 4.55)	0.083	0.238	1.96 (0.88 to 4.41)	0.101	0.264
26 or 27	0–6	1.07 (0.42 to 2.79)	0.863		0.94 (0.36 to 2.45)	0.902	
≥ 28	0–6	0.78 (0.35 to 1.75)	0.352		0.81 (0.36 to 1.81)	0.608	
≤ 25	6–12	0.71 (0.25 to 2.01)	0.248	0.751	0.74 (0.25 to 2.01)	0.575	0.820
26 or 27	6–12	1.30 (0.38 to 4.43)	0.680		1.23 (0.38 to 4.43)	0.745	
≥ 28	6–12	0.82 (0.27 to 2.45)	0.720		1.00 (0.27 to 2.45)	0.994	
MDS-UPDRS							
≥ 39	0–6	2.55 (1.03 to 6.33)	0.044	0.140	2.45 (0.98 to 6.18)	0.055	0.149
23–38	0–6	0.80 (0.35 to 1.86)	0.609		0.79 (0.33 to 1.84)	0.588	
≤ 22	0–6	0.97 (0.43 to 2.17)	0.942		0.92 (0.41 to 2.08)	0.839	
≥ 39	6–12	0.80 (0.23 to 2.80)	0.727	0.943	0.95 (0.26 to 3.43)	0.940	0.989
23–38	6–12	1.02 (0.35 to 2.98)	0.976		1.08 (0.37 to 3.16)	0.895	
≤ 22	6–12	1.02 (0.35 to 2.98)	0.936		1.01 (0.33 to 3.05)	0.989	
Retrospective falls							
> 3	0–6	1.45 (0.57 to 3.67)	0.436	0.407	1.38 (0.54 to 3.52)	0.497	0.453
2 or 3	0–6	0.79 (0.39 to 1.61)	0.523		0.79 (0.39 to 1.61)	0.511	
1	0–6	1.68 (0.59 to 4.77)	0.331		1.61 (0.56 to 4.66)	0.379	
> 3	6–12	1.18 (0.36 to 3.88)	0.780	0.501	1.12 (0.34 to 3.71)	0.853	0.575
2 or 3	6–12	0.57 (0.22 to 1.49)	0.251		0.64 (0.24 to 1.68)	0.365	
1	6–12	1.36 (0.32 to 5.73)	0.672		1.53 (0.36 to 6.50)	0.568	

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage, and the interaction term where this is listed.

Appendix 14 Falls rate ratio

TABLE 35 The ITT and per-protocol FRRs from 0 to 6 months and from 6 to 12 months: whole group and subgroups

| Participant group | Visit (months) | Participants (n) | Trial group: change from baseline, mean (SD) | | PDSAFE – control mean change (95% CI)[a] | p-value[a] | |
			PDSAFE	Control		PDSAFE within participant group	Interaction
All participants	6	402	1.9 (10.7)	1.0 (11.7)	0.16 (–1.83 to 2.15)	0.876	
	12	254	7.2 (13.5)	3.3 (13.4)	3.86 (0.99 to 6.73)	0.009	
MDS-UPDRS score of ≤ 58	6	378	2.4 (10.3)	2.2 (10.6)	–0.08 (–2.08 to 1.93)	0.938	
	12	241	7.6 (13.2)	4.3 (12.8)	3.86 (0.94 to 6.78)	0.010	
H&Y scale stage ≤ 3	6	352	2.4 (10.4)	1.7 (10.8)	0.25 (–1.77 to 2.27)	0.809	
	12	227	7.3 (13.2)	3.9 (14.5)	3.67 (0.76 to 6.58)	0.014	
MoCA score							
≤ 25	6	145	2.1 (10.6)	1.2 (12.5)	–0.06 (–3.32 to 3.20)	0.968	0.860
≥ 26	6	257	1.8 (10.8)	0.9 (11.2)	0.29 (–2.17 to 2.75)	0.812	
≤ 25	12	98	5.3 (13.6)	3.6 (12.8)	1.45 (–3.09 to 6.00)	0.529	0.186
≥ 26	12	156	8.2 (13.4)	3.1 (13.9)	5.32 (1.69 to 8.94)	0.004	
FoG							
No	6	160	2.9 (11.2)	2.0 (10.6)	0.42 (–2.69 to 3.53)	0.791	0.844
Yes	6	241	1.4 (10.3)	0.4 (12.4)	0.02 (–2.53 to 2.58)	0.987	
No	12	102	6.5 (14.7)	3.2 (13.0)	3.34 (–1.03 to 7.72)	0.133	0.846
Yes	12	148	7.6 (12.8)	3.4 (13.8)	3.90 (0.19 to 7.61)	0.039	

| Participant group | Visit (months) | Participants (n) | Trial group: change from baseline, mean (SD) | | PDSAFE – control mean change (95% CI)[a] | p-value[a] | |
			PDSAFE	Control		PDSAFE within participant group	Interaction
MoCA score							
≤ 25	6	145	2.0 (10.5)	1.1 (12.5)	–0.06 (–3.32 to 3.20)	0.970	0.401
	12	98	5.2 (13.6)	3.6 (12.7)	1.40 (–3.10 to 5.90)	0.540	0.448
26 or 27	6	107	3.4 (10.7)	0.1 (11.5)	2.22 (–1.56 to 5.99)	0.249	
	12	67	12.1 (12.6)	6.2 (14.2)	5.66 (0.27 to 11.05)	0.040	
≥ 28	6	150	0.5 (10.7)	1.4 (11.0)	–1.13 (–4.32 to 2.07)	0.488	
	12	89	4.9 (13.1)	0.9 (13.3)	4.37 (–0.38 to 9.11)	0.071	
MDS-UPDRS score							
≥ 39	6	128	–1.2 (10.5)	–6.2 (12.5)	4.20 (0.71 to 7.69)	0.018	0.007
	12	79	–0.6 (13.5)	–6.2 (13.2)	6.89 (1.70 to 12.09)	0.009	0.295
23–38	6	132	–0.3 (9.7)	3.1 (9.1)	–3.47 (–6.83 to –0.11)	0.043	
	12	87	6.5 (13.1)	5.7 (9.7)	1.36 (–3.4 to 6.12)	0.574	
≤ 22	6	140	7.1 (10.2)	6.3 (9.2)	0.12 (–3.15 to 3.40)	0.941	
	12	86	14.1 (10.2)	11.1 (10.3)	4.07 (–0.69 to 8.82)	0.093	
Retrospective falls							
> 3	6	148	2.2 (11.9)	–0.9 (12.6)	1.90 (–1.34 to 5.14)	0.249	0.403
	12	87	7.3 (14.0)	0 (16.1)	7.00 (2.21 to 11.79)	0.004	0.277
2 or 3	6	171	2.6 (10.2)	1.5 (12.1)	–0.68 (–3.80 to 2.44)	0.668	
	12	109	9.4 (10.5)	4.8 (13.5)	3.07 (–1.41 to 7.54)	0.179	
1	6	83	–0.1 (8.6)	2.9 (8.6)	–1.18 (–5.49 to 3.14)	0.592	
	12	58	3.2 (16.2)	4.3 (7.9)	1.29 (–4.64 to 7.22)	0.668	

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage, covariate value at baseline and the interaction term where this is listed.

Appendix 15 Physical Activity Scale for the Elderly

TABLE 36 The PASE analysis (0–400, lower values worse) measured at 6 and 12 months: whole group and subgroups

| Participant group | Visit (months) | Participants (n) | Trial group: change from baseline, mean (SD) | | PDSAFE – control mean change (95% CI)[a] | p-value[a] | |
			PDSAFE	Control		PDSAFE within participant group	Interaction
All participants	6	331	2.6 (51.0)	1.3 (49.5)	1.27 (–9.0 to 11.5)	0.808	–
	12	253	–8.7 (53.0)	–11.0 (48.5)	0.52 (–12.8 to 13.8)	0.939	–
MDS-UPDRS score of ≤ 58	6	312	2.4 (52.0)	0.9 (50.0)	1.19 (–9.52 to 11.89)	0.828	–
	12	200	–8.1 (54.3)	–10.6 (48.8)	0.78 (–13.28 to 14.82)	0.914	–
H&Y scale stage ≤ 3	6	292	2.4 (52.0)	3.2 (51.3)	3.50 (–7.85 to 14.84)	0.545	–
	12	189	–7.1 (53.7)	–9.3 (50.3)	0.36 (–13.94 to 14.64)	0.961	–
MoCA score							
≤ 25	6	111	5 (46.5)	5.9 (45.8)	–1.94 (–19.39 to 15.52)	0.827	0.904
≥ 26	6	219	1.2 (52.9)	–2.5 (50.1)	–0.64 (–13.12 to 11.84)	0.920	
≤ 25	12	79	–7.6 (44.1)	–2.7 (38.5)	–9.26 (–31.10 to 12.59)	0.404	0.347
≥ 26	12	134	–9.3 (57.8)	–16.2 (53.4)	3.73 (–12.99 to 20.46)	0.660	
FoG							
No	6	139	3.1 (55.7)	5.7 (48.9)	–2.34 (–17.85 to 13.16)	0.766	0.799
Yes	6	190	1.7 (47.8)	–3.5 (48.1)	0.28 (–13.13 to 13.68)	0.968	
No	12	96	–14.6 (61.2)	–11.2 (53.7)	–3.05 (–22.81 to 16.72)	0.761	0.732
Yes	12	116	–4.4 (46.8)	–10.9 (43.7)	1.52 (–16.44 to 19.48)	0.867	

| Participant group | Visit (months) | Participants (n) | Trial group: change from baseline, mean (SD) | | PDSAFE – control mean change (95% CI)[a] | p-value[a] | |
			PDSAFE	Control		PDSAFE within participant group	Interaction
MoCA score							
≤ 25	6	111	5 (46.5)	5.9 (45.8)	–1.90 (–19.39 to 15.58)	0.831	0.881
	12	79	–7.6 (44.1)	–2.7 (38.5)	–9.26 (–31.1 to 12.59)	0.404	0.501
26 or 27	6	90	–3.8 (52.9)	9.3 (45.3)	–5.27 (–24.90 to 14.35)	0.597	
	12	55	–12.1 (45.1)	–30 (49.5)	9.29 (–17.0 to 35.18)	0.480	
≥ 28	6	129	4.9 (53)	1.9 (52.8)	1.20 (–15.0 to 17.39)	0.885	
	12	79	–7.3 (66.2)	–7.2 (54.5)	1.27 (–20.54 to 23.1)	0.908	
MDS-UPDRS score							
≥ 39	6	104	7.1 (35.6)	–6.6 (46.2)	2.31 (–16.16 to 20.71)	0.809	0.387
	12	60	0.4 (47.8)	–18.1 (51.5)	4.93 (–21.17 to 30.02)	0.710	0.881
23–38	6	109	–6.4 (53.6)	9.6 (55.3)	–10.63 (–28.25 to 7.30)	0.247	
	12	74	–17.5 (60.9)	–5.3 (56.7)	–3.83 (–15.99 to 20.61)	0.804	
≤ 22	6	104	7.9 (59.5)	–0.3 (45.5)	5.82 (–12.86 to 21.98)	0.607	
	12	77	–4.5 (45.6)	–10.8 (39.4)	0.30 (–22.12 to 22.71)	0.979	
Retrospective falls							
> 3	6	118	6.1 (50.7)	–6.6 (42)	10.48 (–6.32 to 27.28)	0.221	0.194
	12	72	–2.4 (47.5)	–11.3 (49.8)	9.95 (–12.47 to 32.37)	0.382	0.423
2 or 3	6	142	–0.8 (54.1)	3.9 (46.8)	–8.48 (–24.43 to 7.47)	0.296	
	12	95	–10.5 (50.7)	–7 (46.3)	–10.99 (–31.58 to 9.59)	0.293	
1	6	70	2.4 (50.8)	0.5 (48.6)	–3.99 (–25.84 to 17.84)	0.719	
	12	46	–18.1 (68.1)	–19 (52.0)	3.21 (–25.80 to 32.21)	0.830	

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage, covariate value at baseline and the interaction term where this is listed.

Appendix 16 Parkinson's Disease Questionnaire

TABLE 37 The ITT PDQ-39 analysis (0–100, higher values worse) measured at 6 and 12 months: whole group and subgroups

Participant group	Visit (months)	Participants (n)	Trial group: change from baseline, mean (SD)		PDSAFE – control mean change (95% CI)[a]	p-value[a]	Participant group
			PDSAFE	Control			
All participants	6	279	0.8 (8.3)	0.9 (9.0)	–0.12 (–2.28 to 2.0)	0.911	–
	12	177	2.0 (8.6)	2.8 (11.2)	–0.48 (–3.49 to 2.53)	0.754	–
MDS-UPDRS score of ≤ 58	6	268	0.9 (8.4)	0.9 (9.0)	–0.07 (–2.28 to 2.14)	0.952	–
	12	166	1.8 (8.5)	2.9 (11.5)	–0.4 (–3.55 to 2.74)	0.800	–
H&Y scale stage ≤ 3	6	251	1.2 (8.0)	0.2 (8.9.0)	0.91 (–1.32 to 3.14)	0.423	
	12	159	1.7 (8.6)	2.1 (11.0)	–0.35 (–3.4 to 2.7)	0.820	
MoCA score							
≤ 25	6	90	0.7 (9.6)	0.3 (9.6)	0.69 (–3.02 to 4.40)	0.715	0.594
≥ 26	6	189	0.9 (7.7)	1.1 (8.7)	–0.51 (–3.11 to 2.07)	0.697	
≤ 25	12	61	2.2 (10.8)	4.2 (11.2)	–0.86 (–5.87 to 4.15)	0.734	0.947
≥ 26	12	116	1.8 (7.3)	2.0 (11.2)	–0.65 (–4.39 to 3.09)	0.732	
FoG							
No	6	124	1.2 (7.5)	1.4 (8.7)	–0.77 (–4.0 to 2.46)	0.639	0.710
Yes	6	154	0.6 (8.9)	0.3 (9.2)	0.25 (–2.59 to 3.1)	0.864	
No	12	79	2.8 (8.1)	4.5 (12.7)	–0.91 (–5.43 to 3.60)	0.689	0.732
Yes	12	97	1.3 (9.0)	1.3 (9.5)	0.12 (–3.85 to 3.48)	0.952	

| Participant group | Visit (months) | Participants (n) | Trial group: change from baseline, mean (SD) | | PDSAFE – control mean change (95% CI)[a] | p-value[a] | Participant group |
			PDSAFE	Control			
MoCA score							
≤ 25	6	90	0.7 (9.6)	0.3 (9.6)	0.67 (–3.02 to 4.36)	0.721	0.441
	12	61	2.2 (10.8)	4.2 (11.2)	–0.84 (–5.86 to 4.18)	0.742	0.532
26 or 27	6	76	2.3 (7.1)	1.7 (8)	1.04 (–3.0 to 5.11)	0.611	
	12	47	2 (5.5)	1 (10.3)	1.74 (–3.92 to 7.39)	0.546	
≥ 28	6	103	–0.2 (8.1)	0.8 (9.1)	–1.93 (–5.24 to 1.39)	0.254	
	12	69	1.7 (8.6)	2.6 (11.8)	–2.47 (–7.42 to 2.48)	0.326	
MDS-UPDRS score							
≥ 39	6	75	1.9 (10.5)	0.9 (9.8)	–0.85 (–4.32 to 2.62)	0.631	0.492
	12	46	0.7 (11)	6 (12.2)	0.91 (–4.19 to 5.98)	0.723	0.270
23–38	6	95	–0.1 (7.7)	0.6 (8.7)	–1.11 (–4.72 to 2.52)	0.548	
	12	63	3 (8.1)	1.3 (11.9)	1.03 (–3.81 to 5.87)	0.674	
≤ 22	6	107	1.1 (7.3)	1.3 (8.7)	2.00 (–2.22 to 6.24)	0.352	
	12	65	1.4 (7.4)	1.6 (10)	–4.73 (–10.76 to 1.29)	0.123	
Retrospective falls							
> 3	6	99	0.3 (8)	2 (11.5)	–1.49 (–4.99 to 2.01)	0.403	0.512
	12	65	0.6 (7.9)	5.3 (12.5)	–4.77 (–9.50 to –0.37)	0.048	0.090
2 or 3	6	122	1 (8)	–0.7 (6.4)	1.09 (–2.17 to 4.36)	0.511	
	12	75	3.7 (9.3)	1.3 (8.7)	2.33 (–2.40 to 7.06)	0.333	
1	6	58	1.6 (9.8)	2.5 (9.1)	–1.23 (–5.84 to 3.39)	0.601	
	12	37	1.4 (8.4)	2.3 (13.6)	1.10 (–5.3 to 7.52)	0.736	

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage, covariate value at baseline and the interaction term where this is listed.

Appendix 17 Geriatric Depression Scale

TABLE 38 The ITT GDS analysis (0–15, higher values worse) measured at 6 and 12 months: whole group and subgroups

Participant group	Visit (months)	Participants (*n*)	Trial group: change from baseline, mean (SD)		PDSAFE – control mean change (95% CI)[a]	*p*-value[a]	Participant group
			PDSAFE	**Control**			
All participants	6	337	0.3 (1.8)	0.2 (1.9)	–0.02 (–0.42 to 0.39)	0.942	–
	12	214	0.2 (2.0)	0.4 (1.7)	–0.21 (–0.72 to 0.31)	0.421	–
MDS-UPDRS score of ≤ 58	6	318	0.2 (1.8)	0.3 (1.9)	–0.10 (–0.52 to 0.32)	0.636	–
	12	200	0.2 (2.1)	0.4 (1.8)	–0.26 (–0.79 to 0.28)	0.354	–
H&Y scale stage ≤ 3	6	301	0.3 (2.2)	0.2 (1.9)	–0.02 (–0.47 to 0.40)	0.923	–
	12	192	0.2 (2.0)	0.5 (1.7)	–0.26 (–0.79 to 0.30)	0.344	–
MoCA score							
≤ 25	6	115	0 (1.5)	0.4 (2.0)	–0.42 (–1.10 to 0.26)	0.229	0.151
≥ 26	6	222	0.4 (1.9)	0.1 (1.8)	0.19 (–0.30 to 0.68)	0.456	
≤ 25	12	79	0.2 (2.2)	0.2 (2.0)	0.16 (–0.69 to 1.01)	0.713	0.302
≥ 26	12	135	0.2 (2.0)	0.6 (1.6)	–0.40 (–1.05 to 0.25)	0.231	
FoG							
No	6	145	0.4 (1.9)	0.2 (1.7)	0.19 (–0.41 to 0.80)	0.528	0.379
Yes	6	192	0.2 (2.2)	0.3 (2.0)	–0.16 (–0.69 to 0.37)	0.552	
No	12	99	0.7 (2.1)	0.5 (2.0)	0.24 (–0.62 to 1.08)	0.526	0.105
Yes	12	113	–0.2 (1.9)	0.3 (1.6)	–0.59 (–1.38 to 0.04)	0.100	

Participant group	Visit (months)	Participants (n)	Trial group: change from baseline, mean (SD)		PDSAFE – control mean change (95% CI)[a]	p-value[a]	Participant group
			PDSAFE	Control			
MoCA score							
≤ 25	6	115	0 (1.5)	0.4 (2.0)	−0.41 (−1.08 to 0.27)	0.237	0.009
	12	79	0.2 (2.2)	0.2 (2.0)	0.16 (−0.70 to 1.02)	0.715	0.450
26 or 27	6	93	0.8 (2.1)	−0.2 (2.0)	0.97 (0.22 to 1.72)	0.011	
	12	56	0.2 (2.4)	0.4 (1.6)	−0.12 (−1.10 to 0.87)	0.814	
≥ 28	6	130	0.1 (1.8)	0.3 (1.7)	−0.38 (−1.01 to 0.25)	0.241	
	12	78	0.2 (1.5)	0.7 (1.6)	−0.61 (−1.47 to 0.26)	0.168	
MDS-UPDRS score							
≥ 39	6	106	0.3 (1.7)	0.4 (1.9)	−0.06 (−0.74 to 0.63)	0.868	0.841
	12	64	−0.1 (1.8)	0.4 (1.7)	−0.23 (−1.30 to 0.68)	0.605	0.944
23–38	6	112	0.1 (1.4)	0.1 (1.7)	−0.14 (−0.83 to 0.55)	0.691	
	12	72	0.2 (1.9)	0.2 (1.5)	−0.09 (−0.96 to 0.78)	0.837	
≤ 22	6	125	0.2 (2.2)	0.1 (1.9)	0.15 (−0.58 to 0.88)	0.684	
	12	77	0.2 (2.2)	0.5 (0.5	−0.31 (−1.30 to 0.68)	0.537	
Retrospective falls							
> 3	6	62	0.3 (2.0)	0.7 (2.2)	−0.06 (−0.92 to 0.79)	0.889	0.441
	12	71	−0.3 (2.3)	0.8 (1.6)	−0.01 (−1.10 to 1.08)	0.987	0.019
2 or 3	6	147	0.2 (1.8)	−0.1 (1.5)	0.23 (−0.36 to 1.23)	0.471	
	12	97	0.4 (2.0)	0 (1.6)	0.44 (−0.65 to 1.48)	0.278	
1	6	71	1.8 (1.8)	0.3 (1.9)	−0.36 (−1.02 to 0.31)	0.293	
	12	46	0.5 (1.2)	0.8 (1.9)	−1.21 (−2.07 to -0.35)	0.006	

a Controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage, covariate value at baseline and the interaction term where this is listed.
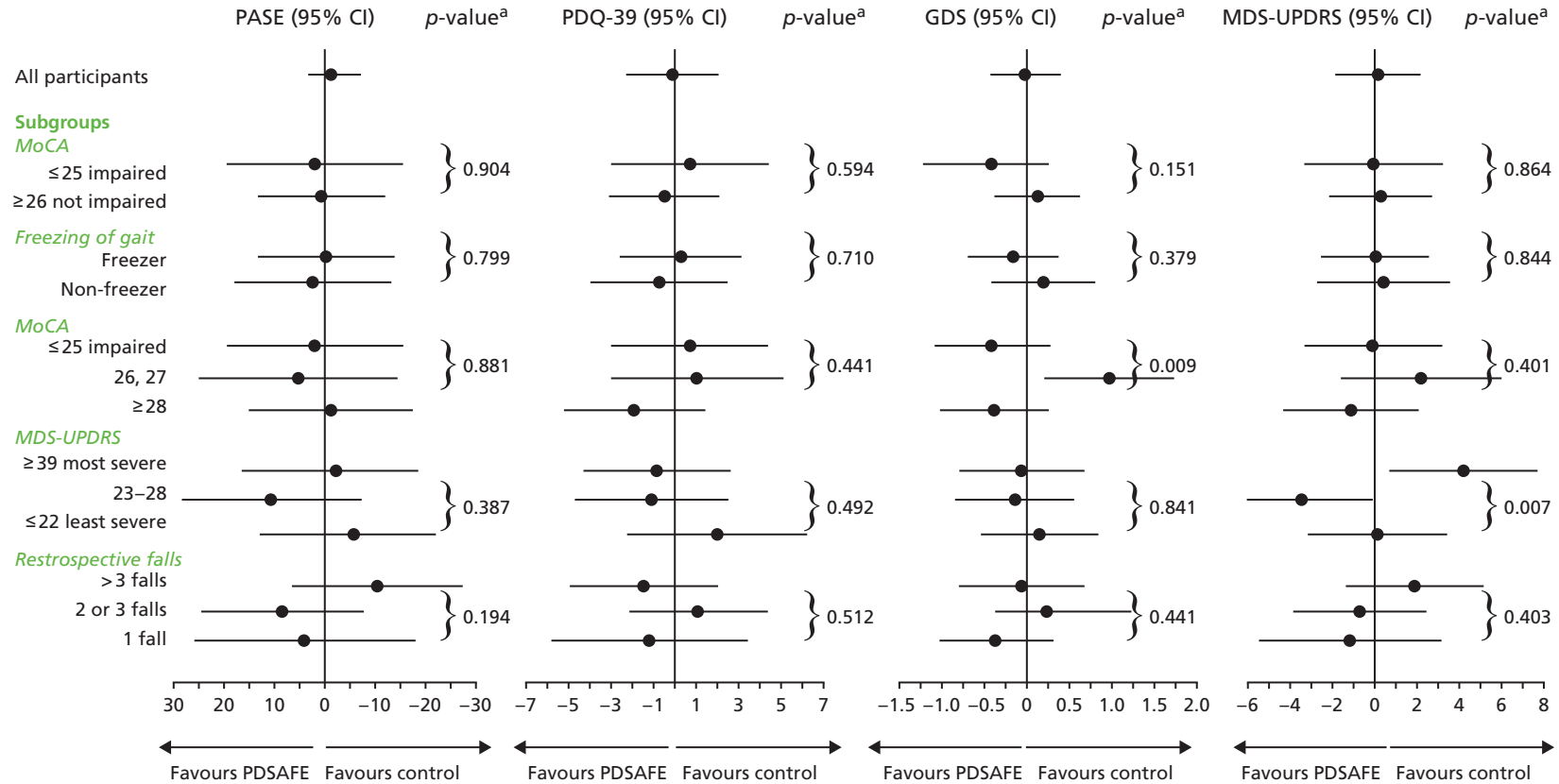
Appendix 18 Secondary outcomes

FIGURE 15 Overall and subgroup analysis of the secondary outcomes measured at 6 months (PASE, PDQ-39, GDS and MDS-UPDRS). a, Test for interaction of PDSAFE contrast differing across subgroups controlled for site, age, gender, repeat falling or not in the year prior to screening, log number of falls in the year prior to screening, log rate of falling in the pre-randomisation falls collection period, H&Y scale stage, and the outcome in question assessed at baseline.

Appendix 19 Further exploration

TABLE 39 Subgroup analysis further exploration: resource use of the intervention and control groups in the cognitively impaired group

| Resource | p-value | Trial group | | | | | | | | | | |
| | | PDSAFE (N = 91) | | | | | Control (N = 93) | | | | |
		Mean	Median	Minimum, maximum	SD	n	Mean	Median	Minimum, maximum	SD	n
GP	0.44	3.02	2.5	0, 11	2.61	44	3.45	3	0, 12	2.96	62
Practice nurse	0.23	1.73	1	0, 9	2.05	44	3.11	1	0, 43	7.44	61
Parkinson's nurse	0.33	1.30	1	0, 11	1.87	43	1.69	1	0, 11	2.11	64
Health visitor	0.56	0.20	0	0, 5	0.81	45	0.13	0	0, 2	0.42	62
Social worker	0.10	0.02	0	0, 1	0.15	44	0.14	0	0, 2	0.47	63
NHS physiotherapist	0.48	1.86	0	0, 12	3.52	43	1.45	0	0, 9	2.32	60
Occupational therapist	0.41	0.37	0	0, 5	0.98	43	0.64	0	0, 12	1.95	61
Speech therapist	0.13	0.95	0	0, 11	2.33	43	0.42	0	0, 7	1.27	62
Day hospital	0.25	0.82	0	0, 14	2.31	44	1.28	0.5	0, 8	1.77	60
Outpatient clinic	0.02	1.23	1	0, 6	1.38	44	2.10	2	0, 13	2.16	62
A&E by ambulance	0.84	0.11	0	0, 2	0.44	44	0.10	0	0, 2	0.35	61
Ambulance with paramedics only	0.58	0.26	0	0, 5	0.94	42	0.37	0	0, 5	0.94	54
A&E by own transport	0.18	0.18	0	0, 3	0.54	44	0.37	0	0, 4	0.81	62
Home care/home help	0.11	23.58	0	0, 390	66.44	59	52.00	0	0, 728	122.76	73
Meals on wheels	0.82	3.10	0	0, 169	21.49	63	2.30	0	0, 182	20.48	79
Day centre	0.54	1.44	0	0, 52	7.42	63	0.83	0	0, 26	4.36	78
Luncheon club	0.37	0.00	0	0, 0	0.00	63	0.17	0	0, 13	1.48	77
Sitting service	0.77	1.68	0	0, 52	9.26	62	2.17	0	0, 78	10.35	78
Night care	0.29	2.94	0	0, 182	23.11	62	0.17	0	0, 13	1.47	78
Hospitalisation for treatment[a]	0.14	0.71	0	0, 30	4.20	63	0.03	0	0, 2	0.22	80
Hospitalisation for respite care[a]	/	0	0	0, 0	0	63	0	0	0, 0	0	80

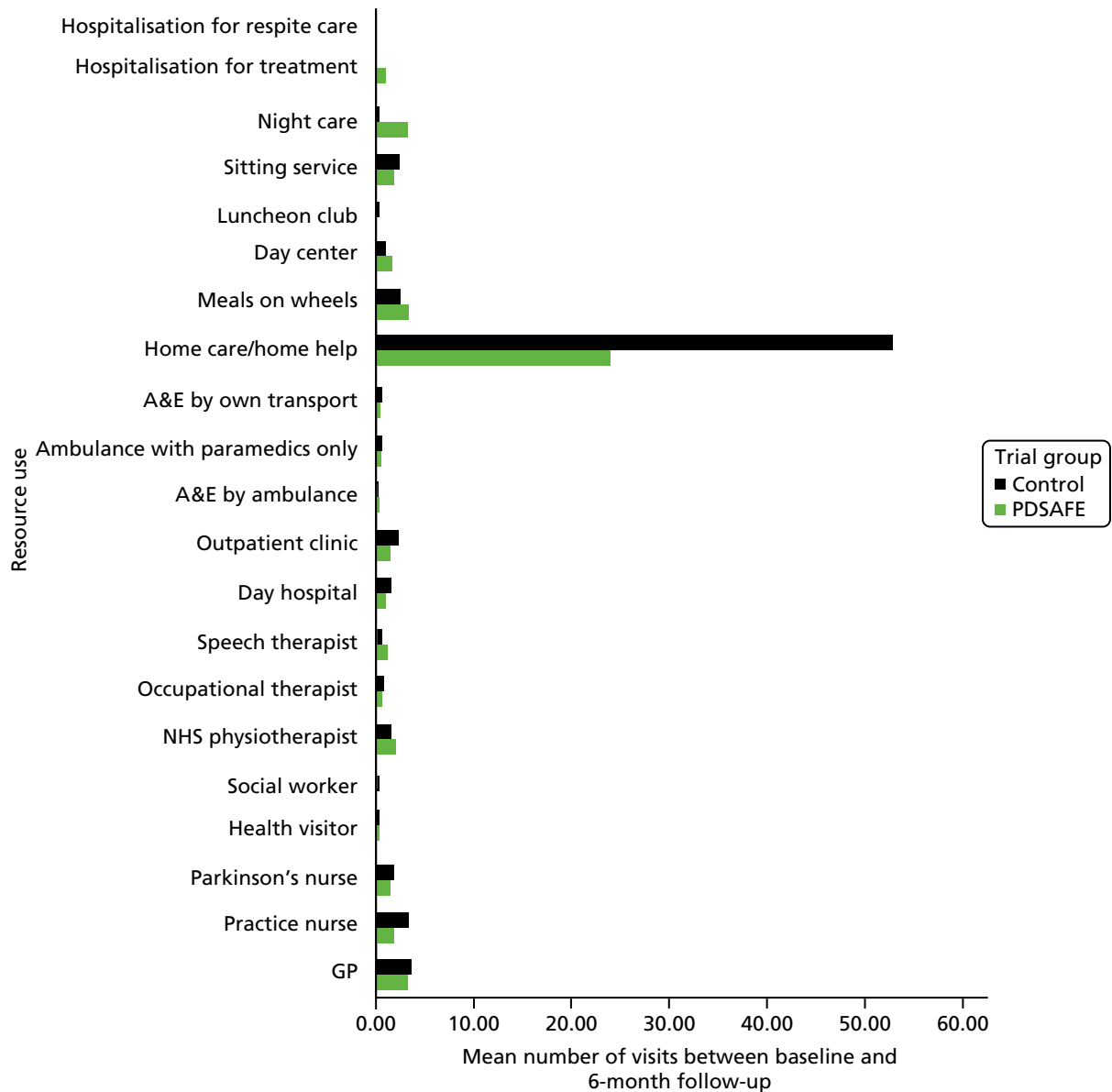a The table can be visualised in the bar graph, as in *Figure 16*.

FIGURE 16 Six months' resource use of the intervention ($n = 91$) and control ($n = 93$) groups in the cognitively impaired group.

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