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Abstract

Clinical effectiveness and cost-effectiveness of physiotherapy and occupational therapy versus no therapy in mild to moderate Parkinson's disease: a large pragmatic randomised controlled trial (PD REHAB)

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Background: Cochrane reviews of physiotherapy (PT) and occupational therapy (OT) for Parkinson's disease found insufficient evidence of effectiveness, but previous trials were methodologically flawed with small sample size and short-term follow-up.

Objectives: To evaluate the clinical effectiveness and cost-effectiveness of individualised PT and OT in Parkinson's disease.

Design: Large pragmatic randomised controlled trial.

Setting: Thirty-eight neurology and geriatric medicine outpatient clinics in the UK.

Participants: Seven hundred and sixty-two patients with mild to moderate Parkinson's disease reporting limitations in activities of daily living (ADL).

Intervention: Patients were randomised online to either both PT and OT NHS services ($n = 381$) or no therapy ($n = 381$). Therapy incorporated a patient-centred approach with individual assessment and goal setting.

Main outcome measures: The primary outcome was instrumental ADL measured by the patient-completed Nottingham Extended Activities of Daily Living (NEADL) scale at 3 months after randomisation. Secondary outcomes were health-related quality of life [Parkinson's Disease Questionnaire-39 (PDQ-39); European Quality of Life-5 Dimensions (EQ-5D)], adverse events, resource use and carer quality of life (Short Form questionnaire-12 items). Outcomes were assessed before randomisation and at 3, 9 and 15 months after randomisation.

Results: Data from 92% of the participants in each group were available at the primary time point of 3 months, but there was no difference in NEADL total score [difference 0.5 points, 95% confidence interval (CI) –0.7 to 1.7; $p = 0.4$] or PDQ-39 summary index (0.007 points, 95% CI –1.5 to 1.5; $p = 1.0$) between groups. The EQ-5D quotient was of borderline significance in favour of therapy (–0.03, 95% CI –0.07 to –0.002; $p = 0.04$). Contact time with therapists was for a median of four visits of 58 minutes each over 8 weeks (mean dose 232 minutes). Repeated measures analysis including all time points showed no difference in NEADL total score, but PDQ-39 summary index (curves diverging at 1.6 points per annum, 95% CI 0.47 to 2.62; $p = 0.005$) and EQ-5D quotient (0.02, 95% CI 0.00007 to 0.03; $p = 0.04$) showed significant but small differences in favour of the therapy arm. Cost-effective analysis showed that therapy was associated with a slight but not significant gain in quality-adjusted life-years (0.027, 95% CI –0.010 to 0.065) at a small incremental cost (£164, 95% CI –£141 to £468), resulting in an incremental cost-effectiveness ratio of under £4000 (£3493, 95% –£169,371 to £176,358). There was no difference in adverse events or serious adverse events.

Conclusions: NHS PT and OT did not produce immediate or long-term clinically meaningful improvements in ADL or quality of life in patients with mild to moderate Parkinson's disease. This evidence does not support the use of low-dose, patient-centred, goal-directed PT and OT in patients in the early stages of Parkinson's disease. Future research should include the development and testing of more structured and intensive PT and OT programmes in patients with all stages of Parkinson's disease.

Trial registration: Current Controlled Trials ISRCTN17452402.

Funding: This project was funded by the NIHR Health Technology Assessment programme and will be published in full in *Health Technology Assessment*; Vol. 20, No. 63. See the NIHR Journals Library website for further project information. The Birmingham Clinical Trials Unit, University of Birmingham, received support from the UK Department of Health up to March 2012. Catherine Sackley was supported by a NIHR senior investigator award, Collaboration for Leadership in Applied Health Research and Care East of England and West Midlands Strategic Health Authority Clinical Academic Training award.

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List of abbreviations

ADL	activities of daily living
BCTU	Birmingham Clinical Trials Unit
CEAC	cost-effectiveness acceptability curve
CI	confidence interval
CONSORT	Consolidated Standards of Reporting Trials
EQ-5D	European Quality of Life-5 Dimensions
GP	general practitioner
HADS	Hospital Anxiety and Depression Scale
HRG	health-care resource group
ICER	incremental cost-effectiveness ratio
MCIC	minimal clinically important change
NEADL	Nottingham Extended Activities of Daily Living Scale
OT	occupational therapy
PD	Parkinson's disease
PD OT	pilot study of occupational therapy in Parkinson's disease
PDQ-39	Parkinson's Disease Questionnaire-39
PSSRU	Personal Social Services Research Unit
PT	physiotherapy
QALY	quality-adjusted life-year
QoL	quality of life
RCT	randomised controlled trial
RMI	Rivermead Mobility Index
SD	standard deviation
SF-12	Short Form questionnaire-12 items
UPDRS	Unified Parkinson's Disease Rating Scale

Plain English summary

Parkinson's disease (PD) is a degenerative condition of the brain of uncertain cause that mainly affects older people. Shaking is a distinctive feature of the disease, but slowness, poverty of movement and stiffness interfere with everyday life. Drug treatment helps with only some aspects of the condition, so other therapies are considered.

Physiotherapy (PT) promotes and maintains mobility and activity by treating physical problems with task-related practice. Core work areas are gait, balance, posture and transfers. Occupational therapy (OT) addresses personal rehabilitation goals through activity and participation, helping patients to remain independent and to reduce carer strain. When delivered at home, OT includes equipment provision and environmental adaptations to facilitate independence.

There is not enough evidence of the value of PT and OT in PD, so we performed the PD REHAB trial to assess the benefits of both therapies.

In total, 762 patients with mild to moderate PD and limitations in activities of daily living (ADL) from 38 neurology/geriatric medicine outpatient clinics across the UK were randomised to either both therapies or no therapy. Patients reported no meaningful benefit of therapy at 3, 9 and 15 months after joining the trial in ADL or quality of life. Economic evaluation showed a small increase in costs for a small gain in quality-adjusted life-years, but these results were uncertain.

We conclude that NHS low-dose, patient-centred, goal-directed PT and OT do not produce immediate or long-term improvements in ADL or quality of life in mild to moderate PD.

Scientific summary

Background

Parkinson's disease (PD) affects over 1% of people older than 60 years and the prevalence is set to rise with the ageing population. It causes significant problems with activities of daily living (ADL) that are only partially treated by medication and occasionally surgery. Despite treatment, patients go on to develop intractable motor problems (e.g. imbalance and falls), along with mental-health problems and other non-motor symptoms.

Physiotherapy (PT) and occupational therapy (OT) are traditionally used later in the course of PD and both therapies are frequently offered together. PT aims to promote and maintain mobility and activity by treating motor impairments with exercise and task-related practice. OT works in partnership with patients to address personal rehabilitation goals through activity and participation. Both forms of therapy aim to help patients remain as independent as possible and to reduce carer strain.

Cochrane reviews of PT and OT for PD found insufficient evidence of their individual effectiveness, but previous trials were methodologically flawed with small sample size and short-term follow-up. The UK National Institute for Health and Care Excellence guidelines, although recognising these shortcomings and recommending further trials, stated that all patients should have access to both therapies.

Before commencing the PD REHAB trial, we initially performed a pilot study of OT in PD (PD OT), as considerable evidence was already available on outcome measures from PT trials in PD. PD OT provided us with invaluable information on recruitment rate, outcome measures and data to inform the sample size for the main trial.

Objectives

The objective of the PD REHAB trial was to evaluate the clinical effectiveness and cost-effectiveness of individualised PT and OT in patients with PD.

Methods

PD REHAB was a large pragmatic randomised controlled trial performed in 38 neurology and geriatric medicine outpatient clinics in the UK.

Patients

We recruited patients with idiopathic PD (defined by the UK Parkinson's Disease Society Brain Bank Criteria) who had limitations in ADL. We ensured that investigators were uncertain that the patients would require PT and/or OT during the 15 months of the trial, that is that equipoise about the need for therapy existed. We excluded patients with dementia, as locally defined, and those in receipt of PT or OT for PD in the last 12 months. All patients gave written informed consent before randomisation.

Outcome measures

The primary outcome was instrumental ADL measured by the Nottingham Extended Activities of Daily Living (NEADL) scale at 3 months after randomisation. Secondary outcomes were health-related quality of life [Parkinson's Disease Questionnaire-39 (PDQ-39); European Quality of Life-5 Dimensions (EQ-5D)], adverse events, and carer quality of life (Short Form questionnaire-12 items).

Outcomes were assessed before randomisation and at 3, 9 and 15 months after randomisation.

Intervention

Patients were randomised (1 : 1) to combined PT and OT (therapy group) or no therapy (control group) using an online randomisation service at the Birmingham Clinical Trials Unit (BCTU), University of Birmingham. PT and OT were delivered in the community and/or outpatients clinics by qualified therapists working within the NHS. A framework for therapy content was developed and agreed by expert therapist groups based on previous work on standards of NHS PT and OT and European guidelines. Following initial assessments by both a physiotherapist and an occupational therapist, therapy was tailored to the individual patient's requirements using a joint goal-setting approach. Interactions between therapists and patients were quantified using pre-defined recording forms.

Sample size

The sample size was based on detecting a 2.5-point clinically meaningful difference in the 66-point NEADL scale at 3 months, using the observed standard deviation from the PD OT pilot trial of 10.1 points with a 5% significance level and 90% power. This required 340 patients in each group, which was increased to 750 participants (375 per group) to allow for around 10% non-compliance and dropout.

Economic evaluation

An incremental economic analysis was conducted from a NHS and Personal Social Services perspective. This combined prospectively collected data on resource use, costs and the important consequences in terms of quality of life (EQ-5D). We performed a cost–utility analysis over 15 months, examining the cost per quality-adjusted life-year (QALY) gained.

Results

Recruitment

Between October 2009 and June 2012, a total of 762 patients with mild to moderate Parkinson's disease and limitations in ADL were recruited to the study.

Loss to follow-up

In total, 92% of the 381 patients randomised to the therapy arm completed the NEADL at 3 months compared with 92% of 381 patients randomised to the no therapy arm. The equivalent completion rates at 15 months were 85% in the therapy arm and 88% in the no therapy arm.

Therapy content

In the therapy group, the median number of therapy sessions, including initial assessments, was four, with a mean time per session of 58 minutes. The mean duration of therapy was 8 weeks. The intervention logs provided by the therapists demonstrated an eclectic approach consistent with NHS practice.

Physiotherapists prescribed a range of exercise programmes tailored to their assessment of the patient's physical strength and range of movement. Detailed content analysis of a 10% sample revealed that only three centres provided a specific PD exercise programme accompanied by a booklet, and there was no evidence of a formal exercise progression protocol for any patient. PT included the prescription of walking aids.

Occupational therapy assessed the full range of ADL including leisure activity and work. However, the predominant interventions were equipment provision (such as bed levers or adaptive cutlery) and onward referral (such as speech and language therapy and cognitive assessment), with other advice including recommendations on how to manage sleep problems and how to apply for state benefits. At some centres there was a limit on the funding of prescribed aids; however, the trial was able to fund some of them to improve parity. There was little task-related practice.

Effectiveness

At the primary time point of 3 months, there was no difference in NEADL total score [difference 0.5 points, 95% confidence interval (CI) –0.7 to 1.7 points; $p = 0.4$] or PDQ-39 summary index (0.007 points, 95% CI –1.5 to 1.5 points; $p = 1.0$) between groups. The EQ-5D quotient was of borderline significance in favour of therapy (–0.03, 95% CI –0.07 to –0.002; $p = 0.04$).

Repeated measures analysis including all time points showed no difference in NEADL total score, but PDQ-39 summary index (curves diverging at 1.6 points per annum, 95% CI 0.47 to 2.62 points; $p = 0.005$) and EQ-5D quotient (0.02, 95% CI 0.00007 to 0.03; $p = 0.04$) showed significant but small differences in favour of the therapy arm.

There was no difference in adverse events or serious adverse events.

Economic analysis

The economic analysis showed no statistically significant differences in incremental costs (£164, 95% CI –£141 to £468) or QALYs (0.027 QALYs, 95% CI –0.010 to 0.065 QALYs). The incremental cost per QALY was under £4000 but highly uncertain (£3493, 95% CI –£169,371 to £176,358).

Conclusions

Overall, NHS PT and OT did not produce immediate or long-term clinically meaningful improvements in ADL or quality of life in mild to moderate PD. This evidence does not support the use of low-dose, patient-centred, goal-directed PT and OT in patients in the early stages of PD. Future research should include the development and testing of more structured and intensive physical therapy programmes in patients with all stages of PD.

Trial registration

This trial is registered as ISRCTN17452402.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research. The Birmingham Clinical Trials Unit, University of Birmingham, received support from the UK Department of Health up to March 2012. Catherine Sackley was supported by a NIHR senior investigator award, Collaboration for Leadership in Applied Health Research and Care East of England and West Midlands Strategic Health Authority Clinical Academic Training award.

Chapter 1 Background

Introduction

Parkinson's disease

Parkinson's disease (PD) affects over 1% of people older than 60 years and the prevalence is set to rise with the ageing population.[1] PD causes significant problems with activities of daily living (ADL) that are only partially treated by medication and occasionally surgery. Despite treatment, patients go on to develop intractable motor problems (e.g. imbalance and falls), along with mental-health problems and other non-motor symptoms.

Physiotherapy and occupational therapy

Physiotherapy (PT) and occupational therapy (OT) are traditionally used later in the course of PD.[2] PT aims to promote and maintain mobility and activity by treating motor impairments with task-related practice and exercise. Core work areas are motor practice and exercise prescription for gait, balance, posture and transfers.[3] A recent summary of the role of PT included the prevention of inactivity and falls.[4]

Occupational therapists work in partnership with patients to address personal rehabilitation goals through activity and participation, helping them to remain as independent as possible and to reduce carer strain. When delivered in a domiciliary setting, OT includes equipment provision and environmental adaptations to facilitate independence in the home. Therapists provide task-related training and educate patients and carers.[5,6]

Evidence for physiotherapy and occupational therapy in Parkinson's disease

Cochrane reviews of PT and OT for PD found insufficient evidence of their individual effectiveness, but the trials included in the reviews were methodologically flawed with small size and short-term follow-up.[7–9] Despite this lack of evidence, the UK National Institute for Health and Care Excellence guidelines, although recognising these shortcomings and recommending further trials, stated that all patients should have access to both therapies.[2]

Objective of the PD REHAB trial

The objective of this large-scale pragmatic multicentre randomised controlled trial (RCT) was to evaluate the clinical effectiveness and cost-effectiveness of individualised PT and OT in patients with PD. The current trial (PD REHAB) design was informed by our pilot study of OT in PD (PD OT).[10]

Systematic reviews

Physiotherapy versus no or placebo intervention

This review was published by the trial team in The Cochrane Library[8] and subsequently in the *British Medical Journal*[9]

Methods

A systematic search of the literature to the end of January 2012 was undertaken using a highly sensitive search strategy as recommended by Cochrane. We combined text and, where appropriate, medical subject headings terms for PT, physical therapy, exercise or rehabilitation and for Parkinson, PD or Parkinsonism. No language restrictions were applied. Relevant trials were identified by electronic searches of general biomedical and science electronic databases, English-language databases of foreign-language research and

third-world publications, conference and grey literature databases and trial registries. Hand searching of general and specific journals in the field, abstract books and conference proceedings was also undertaken, as well as examination of the reference lists of identified papers and other reviews.

Studies eligible for this review were RCTs (including the first phase of crossover trials) in PD patients comparing a PT intervention with no intervention or placebo control. PT encompasses a wide range of techniques, so we were inclusive in our definition of PT intervention, with trials of general PT, exercise, treadmill training, cueing, dance and martial arts versus no intervention being included. We excluded trials of multidisciplinary team interventions, as it was difficult to ascertain the amount of PT input.

All articles were read by two independent review authors and data extracted according to pre-defined criteria, with any discrepancies resolved by discussion. In addition, publications were assessed for methodological quality.

Results of each trial were combined using standard meta-analytic methods to estimate an overall effect for PT versus no intervention. All outcomes were continuous variables so weighted mean difference methods were used with a fixed-effects model.

The primary analysis was a comparison of PT and no intervention (control) using change from baseline to the first assessment after the treatment period (which in most cases was immediately after the intervention). This was chosen as the primary analysis, as in most trials this was the main data analysis, and few trials reported data at longer-term assessment points (i.e. after 6 months).

To assess for differences between the different interventions used, indirect comparisons using tests of heterogeneity were used to investigate whether or not the treatment effect differed across the different interventions.

Results

We identified 76 potentially relevant studies; 31 were excluded (e.g. not properly randomised, crossover trial with data not reported for first intervention period) and six were ongoing trials for which no data were available. Therefore, 39 RCTs involving 1827 patients were included in the systematic review. These 39 trials contributed data to 44 comparisons within the six different PT interventions (PT, $n = 7$; exercise, $n = 14$; treadmill training, $n = 8$; cueing, $n = 9$; dance, $n = 2$; and martial arts, $n = 4$) (*Table 1*).

The amount of methodological detail reported in the trials was variable, with several quality indicators not fully discussed in many publications. Only six studies (15%) reported a sample size calculation. Fewer than half of the trials described the randomisation method used, and information on concealment of treatment allocation was also poorly reported (36%). 62% of the studies used blinded assessors. Only nine trials stated intention to treat as the primary method of analysis. Three trials stated per protocol as the primary method of analysis and in the remaining trials the method of analysis was not described.

The effects of the various PT techniques are summarised in *Table 2*.

Only one outcome, Unified Parkinson's Disease Rating Scale (UPDRS) motor subscore, showed significant heterogeneity between the treatment effects of the different classes of intervention. An outlying trial was the cause of this heterogeneity; when this trial was excluded, the result remained statistically significant [–3.77 points, confidence interval (CI) –5.15 to –2.39 points; $p \leq 0.00001$], but the test for between-trial and between-subgroup heterogeneity was no longer significant ($p = 0.44$ and $p = 0.08$, respectively).

For one trial, 60 patients who were split between PT and treadmill categories are not included in the table, as group split was not given. For multiple-arm trials, the control-arm patients are counted twice ($n = 59$).

All results (except for the 10- or 20-m walk test) favoured PT intervention.

TABLE 1 Physiotherapy intervention classifications and trial characteristics in the Cochrane systematic review of PT in PD

PT intervention	Number of trials	Total number of participants (% male)	Mean age (years)	Mean Hoehn and Yahr	Mean duration of PD (years)	Duration of treatment sessions (minutes)	Trial period	Examples of types of therapy
PT	7	244 (69)	65	2.4	4	30–60	4–12 months	Bobath training, gait and balance exercises, hands-on techniques, education and advice on transfer, posture and physical fitness
Exercise	14	769 (61)	69	2.6	6	30–120	3–24 weeks	Strengthening and balance training, walking, falls prevention, neuromuscular facilitation, resistance exercise, aerobic training, education and relaxing techniques
Treadmill	8	179 (61)	68	2.4	5	30–60	4–8 weeks	Walking on treadmill with speed or incline adjustments. Body weight-supported treadmill training, step and gait training
Cueing	9	371 (59)	67	2.6	7	4–30	Single session–13 weeks	Three types of cueing: audio (music, spoken instructions), visual (computer images), sensory (vibration)
Dance	2	120 (63)	69	2.3	7	60	12–13 weeks	Tango, waltz and foxtrot
Martial arts	4	143 (74)	65	2.1	6	60	12–24 weeks	Tai chi and qigong

TABLE 2 Summary of results of Cochrane systematic review of PT in PD

Outcome	Number of trials; comparisons	PT interventions	Number of participants	Mean difference (95% CI)	Heterogeneity between trials	Indirect comparison between subgroups
Gait outcomes						
Speed (m/s)	15; 19	General PT, exercise, treadmill, cueing, dance, martial arts	814	0.04 (0.02 to 0.06), $p = 0.0002$	$p = 0.55$	$p = 0.25$
2- or 6-minute walk test (m)	6; 7	Exercise, treadmill, dance, martial arts	242	13.37 (0.55 to 26.20), $p = 0.04$	$p = 0.44$	$p = 0.19$
10- or 20-metre walk test (s)	4; 4	Exercise, treadmill	169	0.40 (0.00 to 0.80), $p = 0.05$	$p = 0.19$	$p = 0.51$
Freezing of Gait questionnaire	4; 4	Exercise, cueing, dance	298	–1.41 (–2.63 to –0.19), $p = 0.02$	$p = 0.74$	$p = 0.55$
Cadence (steps/minute)	7; 9	General PT, exercise, treadmill, cueing	350	–1.57 (–3.81 to 0.67), $p = 0.17$	$p = 0.73$	$p = 0.97$
Stride length (m)	6; 9	General PT, exercise, treadmill, cueing, dance, martial arts	225	0.03 (–0.02 to 0.08), $p = 0.24$	$p = 0.33$	$p = 0.23$
Step length (m)	5; 6	General PT, exercise, treadmill, cueing	383	0.02 (0.00 to 0.04), $p = 0.06$	$p = 0.71$	$p = 0.47$
Functional mobility and balance outcomes						
Timed Up and Go test (seconds)	9; 10	Exercise, cueing, dance, martial arts	639	–0.63 (–1.05 to –0.21), $p = 0.003$	$p = 0.12$	$p = 0.33$
Functional reach (cm)	4; 4	Exercise, cueing	393	2.16 (0.89 to 3.43), $p = 0.0008$	$p = 0.15$	$p = 0.48$
Berg Balance Scale	5; 6	Exercise, treadmill, dance, martial arts	385	3.71 (2.30 to 5.11), $p < 0.00001$	$p = 0.06$	$p = 0.47$
Activity-specific balance confidence	3; 3	Exercise, cueing	66	2.40 (–2.78 to 7.57), $p = 0.36$	$p = 0.61$	$p = 0.32$

Outcome	Number of trials; comparisons	PT interventions	Number of participants	Mean difference (95% CI)	Heterogeneity between trials	Indirect comparison between subgroups
Falls						
Falls Efficacy Scale	4; 4	Exercise, treadmill, cueing	353	–1.91 (–4.76 to 0.94), $p = 0.19$	$p = 0.44$	$p = 0.28$
Clinician-rated disability – Unified Parkinson's Disease Rating Scale						
Total	3; 4	General PT, exercise, treadmill	207	–6.15 (–8.57 to –3.73), $p < 0.00001$	$p = 0.03$	$p = 0.01$
Subscore – mental	2; 3	General PT, treadmill	105	–0.44 (–0.98 to 0.09), $p = 0.10$	$p = 0.80$	$p = 0.82$
Subscore – ADL	3; 4	General PT, treadmill, dance	157	–1.36 (–2.41 to –0.30), $p = 0.01$	$p = 0.28$	$p = 0.19$
Subscore – motor	12; 14	General PT, exercise, treadmill, cueing, dance, martial arts	593	–5.01 (–6.30 to –3.72), $p < 0.00001$	$p < 0.001$	$p < 0.001$
Patient-rated quality of life – Parkinson's Disease Questionnaire-39						
Summary index	7; 8	General PT, exercise, treadmill, cueing, dance, martial arts	405	–0.38 (–2.58 to 1.81), $p = 0.73$	$p = 0.89$	$p = 0.87$
Subscore – mobility	2; 3	General PT, dance, martial arts	105	–1.43 (–8.03 to 5.18), $p = 0.67$	$p = 0.11$	$p = 0.11$

CI, confidence interval.

Conclusions

This review provides evidence on the short-term (mean follow-up < 3 months) efficacy of PT in the treatment of PD. Significant benefit of PT was reported for nine outcomes: gait speed; 2- or 6-minute walk test; Freezing of Gait questionnaire; Timed Up and Go test; Functional Reach Test; Berg Balance Scale; and UPDRS total, ADL and motor subscores. The relevance of these differences to PD patients must be put into the context of what is considered a minimal clinically important change (MCIC). What few data are available on MCIC for the impairment measures suggest the differences are below those relevant for patients. The benefits in UPDRS total, ADL and motor scores approach the MCIC, suggesting that a PT intervention is beneficial in improving clinician-rated symptoms. However, the only patient-rated quality of life (QoL) outcome measure (Parkinson's Disease Questionnaire-39; PDQ-39) showed no statistically significant benefit from treatment with PT and was reported in only eight trials.

The review also highlights the wide range of PT techniques being used in the treatment of PD. Indirect comparisons provided no evidence that differences in the treatment effect existed between the different types of PT.

The majority of the studies in this review were small and had a short follow-up period. Larger RCTs are required, particularly focusing on improving trial methodology and reporting. Rigorous methods of randomisation should be used and allocation of treatment should be adequately concealed. Data should be analysed according to intention-to-treat principles and trials should be reported according to the guidelines set out in the Consolidated Standards of Reporting Trials (CONSORT) statement. This review also illustrates the need for the universal employment of relevant, reliable and sensitive outcome measures. Further, only three trials looked at the longer-term benefit of PT intervention. In order to assess whether or not and how long any improvement due to PT intervention may last, it is important that long-term follow-up is performed without crossover from control to active intervention. Finally, the review highlights the variety of PT interventions used in the treatment of PD. There is a need for more specific trials with improved treatment strategies to underpin the most appropriate choice of PT intervention.

Considering the low methodological quality, small size and short duration of many of the included trials, this evidence supporting the use of PT for people with PD must be balanced against the lack of long-term evidence currently available.

Physiotherapy versus alternative physiotherapy intervention

This review was published by the trial team in The Cochrane Library.[11]

Methods

See review in previous section: *Physiotherapy versus no or placebo intervention*.

Results

In total, 78 randomised trials of PT intervention in PD patients were identified. Twenty-nine studies were excluded because they were not properly randomised ($n = 12$), they were a crossover trial with data not adequately separated ($n = 4$), the treatment in the trial was not usually used by physiotherapists (such as Whole Body Vibration technique) ($n = 4$), they had no outcome measures relevant to our review ($n = 2$), they were a multidisciplinary therapy rehabilitation trial ($n = 2$), the trial was under 1 day ($n = 1$), they had insufficient information available for inclusion in review ($n = 1$), they had an unsuitable comparator arm ($n = 1$), the study was confounded ($n = 1$) or they were a comparison of PT delivery rather than technique ($n = 1$). There were also six ongoing trials for which data were not yet available. Therefore, there were 43 trials available for inclusion in the review.

The number of participants randomised in the 43 trials ranged from 8 to 210, with 1673 participants randomised in total (giving an average trial size of 39 participants). The assessment period ranged from 2 weeks to 24 months. The mean age of participants in the trials was 67 years, 62% were male, the mean Hoehn and Yahr stage was 2.4 and participants had had PD for approximately 7 years.

Physiotherapy interventions were placed into one of the six categories (general PT, exercise, treadmill training, cueing, dance and martial arts) according to the type of treatment administered. However, the content and delivery of the interventions within each category was diverse. Further, a wide variety of validated and customised outcome measures were used to assess the effectiveness of PT interventions. Consequently, it was inappropriate to combine the results of studies or perform any statistical analysis.

Conclusions

Considering the small number of participants, the methodological flaws in many of the studies, the wide variety of PT interventions and the outcome measures used, there is insufficient evidence to support the use of one approach of PT intervention over another for the treatment of PD. Larger RCTs with longer follow-up are required, particularly focusing on improving trial methodology and reporting. Rigorous methods of randomisation should be used and the allocation adequately concealed. Data should be analysed according to intention-to-treat principles and trials should be reported according to the guidelines set out in the CONSORT statement. There is a need for more specific trials with improved treatment strategies to underpin the most appropriate choice of PT intervention and the outcomes measured. This review also reinforces the need for the universal employment of clinically relevant, reliable and sensitive outcome measures with a predefined outcome in each trial. Future trials should be designed such that the interventions are transferable and cost-effective in mainstream care.

Occupational therapy versus no or placebo intervention

This Cochrane review was published by collaborators of the trial team.[7]

Methods

Relevant trials were identified by electronic searches of general biomedical and science electronic databases, English-language databases of foreign-language research and third-world publications, conference and grey literature databases and trial registries.

Only RCTs were included; however, those trials that allowed quasi-random methods of allocation were allowed. Data were abstracted independently by two authors and differences were settled by discussion.

Results

Two trials were identified, with 84 patients in total. Although both trials reported a positive effect from OT, all of the improvements were small. The trials did not have adequate placebo treatments, they used small numbers of patients and, in one trial, the method of randomisation and concealment of allocation was not specified. These methodological problems could potentially lead to bias from a number of sources.

Conclusions

Considering the significant methodological flaws in the studies, the small number of patients examined and the possibility of publication bias, there is insufficient evidence to support or refute the efficacy of OT in PD. There is now a consensus as to UK current and best practice in OT when treating people with PD. Large, well-designed, placebo-controlled RCTs are required to demonstrate the effectiveness of OT in PD. Outcome measures with particular relevance to patients, carers, occupational therapists and physicians should be chosen and the patients monitored for at least 6 months to determine the duration of benefit. The trials should be reported using CONSORT guidelines.

Parkinson's disease occupational therapy pilot trial

The PD OT pilot trial was done to inform the design of the PD REHAB trial and was published in the *Journal of Neurology, Neurosurgery and Psychiatry*[10]

Method

This pilot study was a RCT with masked assessment of standard community-based individual OT targeting functional independence and mobility versus usual NHS care with OT deferred until the end of the trial.

We aimed to recruit 50 patients with idiopathic PD, defined by the UPDRS,[12] with Hoehn and Yahr stages 3–4. We excluded patients with dementia, since they would be unable to complete trial forms, and those who had received OT in the last 2 years or PT in the last year, to avoid carry-over effects.

Patients were recruited from four neurology and elderly care PD clinics in the West Midlands. After patients were identified and informed about the study, written consent was taken and baseline information was collected. Patients were randomised by the therapist between the two trial groups (1 : 1) using a computer-generated random number list via a telephone call to the University of Birmingham Clinical Trials Unit. Patients were informed of their treatment allocation. The trial manager and chief investigator were masked to treatment allocation.

The intervention was developed by combining existing evidence from our surveys of current and best-practice OT in PD[5,6] and the consensus of a group of expert occupational therapists.[13] The intervention was provided by an experienced occupational therapist and was delivered at the level of the individual. Primary interventions were targeted towards limitations in ADL (self-care and instrumental); mobility (indoor and outdoor); and home safety. Six sessions of 45 minutes each were administered over 2 months. Content was dependent on the patient's and therapist's agreed goals. OT followed a routine process using a 'client-centred approach',[14] with a continuous process of assessment, treatment and re-evaluation.

The content of the OT intervention addressed specific tasks (e.g. eating, mobilising) within the participant's home. Techniques employed by the therapist included task-specific practice (e.g. dressing, transfers, mobility training), reducing the complexity or demands of tasks and/or altering the environment through provision of aids and adaptations. The therapist also provided advice and information to patients and carers and referral to other health-care workers when appropriate. When time allowed, secondary interventions addressed fatigue management, leisure therapy, continence, speech and communication interventions, and relaxation techniques.

Since the intervention was targeted towards improving functional ability, we assessed instrumental ADL with the Nottingham Extended Activity of Daily Living Scale (NEADL). This has been validated in stroke[15] and has been shown in other community OT trials to be relevant and sensitive to change.[16] We also explored the use of the Rivermead Mobility Index (RMI); the patient-completion UPDRS ADL scale; PDQ-39; European Quality of Life-5 Dimensions (EQ-5D); and Hospital Anxiety and Depression Scale (HADS).

For economic analysis, resource-use data were collected in a patient-completed questionnaire at the end of the trial to estimate the costs associated with treatment and management over the previous 6 months.

At baseline (before randomisation), patients completed assessments by interview. At 2 and 8 months after randomisation, assessments were posted to all patients for self-completion.

As this was a pilot study, definitive answers to the randomised comparison were not expected, so formal statistical hypothesis testing was not performed. Differences between the two arms in change from baseline at 2 and 8 months were calculated with 95% CI. Pearson correlation coefficients were calculated to correlate outcome measures. Statistical analysis was performed using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA).

The PD OT trial was approved by Sandwell and West Birmingham Local Research Ethics Committee, funded by the Parkinson's Disease Society and sponsored by the University of Birmingham. Professor Sackley was funded by a National Primary Care Career Scientist award.

Results

Over 16 months (July 2005 to October 2006), 39 patients were recruited from four centres (25 male; mean age 73 years). Patient eligibility was assessed in one centre's movement disorders clinics (City Hospital, Birmingham) over 9 months. Only 11 patients (6%) attending 196 PD patient visits (some patients attended more than once) were eligible for the trial. The reasons for exclusion were early PD without significant difficulties with ADL (61%), recent OT or PT (21%), dementia (7%), advanced PD (1%) and other (10%).

In the treatment group (11 male; mean age 73 years), 15 were living with someone, three were living alone and one was living in a care home. The mean number of treatment visits was 5.7 (range 3–9). The interval between visits varied from 3 to 63 days. The total time spent by the therapist with patients was 103.1 hours (mean 5.4 hours per patient).

The differences between the OT and no OT arms at 2 and 8 months for the main outcome measures are shown in *Table 3*. There were strong correlations between the mobility, ADL and emotional well-being domains of PDQ-39 and RMI, UPDRS ADL subscale and anxiety and depression subscores of the HADS.

The health economics questionnaire piloted in the trial adequately captured data on health service utilisation.

TABLE 3 Changes in outcome measures in the PD OT trial

Outcome measure	Baseline to 2 months, mean difference in outcome measures (95% CI)	Baseline to 8 months, mean difference in outcome measures (95% CI)
Nottingham Extended ADL	0.04 (–4.74 to 4.82)	3.50 (–3.24 to 10.24)
RMI	–0.46 (–1.89 to 0.97)	–0.70 (–2.87 to –1.47)
UPDRS ADL Score	–1.46 (–5.36 to 2.44)	0.39 (–3.32 to 4.10)
PDQ-39 Summary Index	1.69 (–5.17 to 8.55)	3.82 (–4.94 to 12.57)
EQ-5D score	–0.01 (–0.17 to 0.16)	0.08 (–0.04 to 0.21)
HADS Anxiety Score	1.53 (–0.72 to 3.78)	1.44 (–1.20 to 4.09)
HADS Depression Score	–0.50 (–2.31 to 1.30)	–1.42 (–3.66 to 0.82)

A negative change in NEADL, RMI and EQ-5D scores indicates deterioration from baseline. A positive change in PDQ-39, UPDRS ADL and HADS scores indicates deterioration from baseline. In this table, a positive mean difference in NEADL, RMI and EQ-5D is in favour of deferred therapy, while a positive mean difference in PDQ-39, UPDRS ADL and HADS is in favour of immediate therapy.

Conclusions

Recruitment

We aimed to recruit 50 PD patients over 12 months, but succeeded in recruiting only 39 patients over 16 months. This stemmed from patients with early disease not having significant problems with ADL, patients recently undergoing OT or PT and, rarely, dementia.

Future trials of OT and PT in PD may require better co-ordination with service user groups, longer recruitment periods of incident cases and a large number of centres. Consideration should be given to combining PT and OT in a future trial to better reflect standard NHS practice and to allow inclusion of PD patients with a wider spectrum of disease, particularly earlier-stage patients who may not currently be automatically referred.

Intervention

The intervention was successfully delivered to all 19 patients randomised to OT. The 5 hours' dose of therapy was similar to that described in other trials.[17–20] Loss to follow-up was small, with data missing for one patient at 2 months and for two patients at 8 months. This is similar to another community study of PT (8% loss at 6 months),[21] but higher retention than an outpatient rehabilitation study (30% loss at 6 months).[22] Delivery of OT to the control arm after the trial may have helped with retention.

Outcome measures

The NEADL and PDQ-39 measures were well completed by patients. The NEADL score showed strong correlation with the UPDRS ADL subscale and has the benefit of being used in a variety of conditions including stroke and ageing. There were strong correlations between the mobility, ADL and emotional well-being domains of PDQ-39 and RMI, UPDRS ADL subscale and HADS anxiety and depression subscale scores. Therefore, PDQ-39 could be used as a single scale replacing a collection of scales that are often used in PD trials.

Sample size calculation

Minimally clinically relevant changes in NEADL and PDQ-39 are probably 1–2 points[19] and 1.6 points,[23] respectively. Such minimal changes may be of only small benefit to patients, so we view a clinically meaningful change as around double this, that is 2.5 points for NEADL and 3.5 points for PDQ-39. To detect such differences, at two-tailed $p = 0.05$ with 90% power, at the end of treatment will require 340 patients in each arm for NEADL [standard deviation (SD) from PD OT 10.1] and 310 patients in each arm for PDQ-39 Summary Index (SD from PD OT 13.5). To allow for around 10% dropout rate, we suggest randomising 750 patients.

Parkinson's disease occupational therapy trial intervention

We described the intervention delivered in the PD OT pilot trial in a paper published in the *British Journal of Occupational Therapy*[24]

Method

The development of the PD OT intervention followed a three-step approach:

1. Published trial evidence was gathered (until recruitment commenced in July 2005) to ensure that the PD OT intervention was evidence-based where possible; the evidence considered included OT-specific PD studies, multidisciplinary PD interventions which incorporated OT, studies from the wider PD rehabilitation literature and clinical guidelines.
2. Current UK practice was examined through two published surveys.[25,26]
3. The expert steering group met to evaluate and synthesise the findings of the first two steps with expert opinion consensus, formalising the PD OT intervention.

The aim was to provide treatment that was informed by best practice but could be delivered within the structure and format of the NHS: an enhanced current practice intervention.

Results

All 19 participants completed both their initial assessments and the treatment sessions required to address the goals identified. Treatment was delivered by one occupational therapist. The mean number of visits was 5.7 (range 3–9). A total of 108 therapist visits were carried out. The interval between visits varied from 3 days to 63 days. The initial assessment took a median of 60 minutes (range 45–90 minutes). Subsequent visits lasted a median of 50 minutes (range 5–180 minutes). On average, the occupational therapist spent a mean of 5.4 hours in total with each patient. The mean duration of the complete intervention (from first to last visit inclusive) was 60.3 days.

The content of the intervention for each patient was categorised and recorded as time (minutes) spent under the appropriate headings by the treating therapist. Two hundred and seventy-four interventions were delivered in total. The most common types of intervention were adaptive equipment ($n = 56$), transfers/mobility training ($n = 46$), environmental adaptations ($n = 38$), daily living activities training ($n = 35$), techniques/education ($n = 25$) and goal setting ($n = 15$).

Following completion of the trial, the treating therapist provided feedback on the intervention log. The log was reported as easy to use and was seen to contain categories that were relevant to the treatment being delivered. Difficulties in using the tool were also noted; overlap between categories and issues in identifying the primary aim of an intervention both led to problems with accurate categorisation.

Health economics literature review

We reviewed the literature for economic evaluations involving PT and PD to identify the existing economic evidence. Three studies were identified through the search.[27–29] Previous economic evaluations involving PT or exercise-based interventions in PD have typically focused on multicomponent interventions. Of the included studies, only one provided information in terms of cost-effectiveness on an exercise intervention versus a do-nothing comparator.[27] The results of this study were promising in terms of cost-effective acceptability, but the primary outcome showed no statistically significant improvement and the economic study was uncertain. As with the other two studies,[28,29] the time horizons of the evaluations were short, such that it is unclear whether or not any improvement in patient physical functioning was sustained over the long term (i.e. beyond 6 months).

Chapter 2 Methods

The PD REHAB trial protocol is available at www.birmingham.ac.uk/pdrehab-docs (accessed 28 July 2016). Reproduced with permission from *JAMA Neurology* 2016; doi: 10.1001/jamaneurol.2015.4452. [30]

Patients

Patients with idiopathic PD as defined by the UK Parkinson's Disease Society Brain Bank Criteria[12] were eligible for PD REHAB if they reported limitations in ADL and the investigator was uncertain that they would require PT and/or OT during the 15 months of the trial, that is if equipoise about the need for therapy existed. Exclusion criteria included dementia, as locally defined, and receipt of PT or OT for PD in the past 12 months. All patients gave written informed consent before randomisation. Ethics approval was granted by the West Midlands Research Ethics Committee (08/H1211/168) and local research and development approval was obtained at each participating centre.

Randomisation and therapy allocation

Patients were randomised (1 : 1) to combined PT and OT (therapy group) or no therapy (control group) using an online randomisation service at the Birmingham Clinical Trials Unit (BCTU), University of Birmingham, Randomisation used a computer-based algorithm with minimisation by baseline NEADL total score (severe 0–21; moderate 22–43; and mild 44–66), Hoehn and Yahr stage (≤ 2; 2.5; 3; and ≥ 4) and age (< 60 years; 60–69 years; 70–79 years; and ≥ 80 years) to ensure balance of patients with differing disability levels between the two groups.

Procedures

Inclusion criteria were broad to allow inclusion of a wide spectrum of PD patients to provide a generalisable result. PT and OT were delivered in the community and/or outpatients by qualified therapists. A framework for therapy content was developed and agreed by expert therapist groups based on previous work on standards of UK NHS PT and OT and European guidelines.[3–6] A standard rehabilitation approach was used. Following initial assessments by both a physiotherapist and an occupational therapist, therapy was tailored to the individual patient's requirements using a joint goal-setting approach. Interactions between therapists and patients were described and quantified using pre-defined recording forms, and included non-contact time. Control patients consented to have therapies deferred until the end of their 15 months' trial participation, unless pressing reasons for therapy developed. As therapies may have been arranged outside the trial, control patients were asked whether or not they had received any therapy at the 15-month assessment.

The primary outcome measure was the total score on the NEADL scale at 3 months after randomisation.[15] The NEADL measures instrumental ADL which is specifically addressed by PT and OT, and addresses more complex ADL issues such as making a meal, cleaning and travelling on public transport. The NEADL scale was developed for stroke trials but is now used widely as a generic outcome measure for rehabilitation trials of older people and has been used in PD trials before. It has been shown to be sensitive to change in trials of OT[16] and was successfully used in our pilot study of OT for PD.[10] Secondary outcome measures included patient-rated QoL using the PDQ-39,[31] which is the most widely used disease-specific QoL rating scale for PD; the EQ-5D (3-level version), a generic QoL scale; adverse events; and carer well-being using Short Form questionnaire-12 items (SF-12; version 2). Following a risk assessment, targeted adverse event reporting was deemed to be

appropriate, so only therapy-related adverse events and serious adverse events were recorded, such as falls or equipment failure leading to injury requiring a hospital, general practitioner (GP) or ambulance visit. Outcomes were collected in person at baseline before randomisation, and then by post at 3, 9 and 15 months after randomisation. Antiparkinsonian medication dosage was converted into levodopa dose equivalents using a standard formula.[32]

Statistical analysis

In stroke patients, the MCIC in NEADL is 1–2 points.[19] However, such a small change may be of only little benefit to PD patients; a clinically meaningful change in NEADL for PD patients is likely to be around double this, at 2.5 points. A 2-point change on the NEADL represents becoming independent in one item (e.g. stair climbing, crossing roads or feeding oneself) or improvement in two items (e.g. from being dependent on another person with help to being fully independent). To detect a 2.5-point difference in NEADL at 3 months (using the observed SD from the PD OT pilot trial[10] of 10.1 points; $p < 0.05$ two-tailed; 90% power) required 340 patients in each group, increased to 750 participants (375 per group) to allow for around 10% non-compliance and dropout.

The primary analysis was change in NEADL total score in the therapy group at the 3-month assessment (immediately after the therapy period) compared with that in the no therapy group. An independent two-sample *t*-test compared changes between baseline and 3 months in the NEADL score between the two groups. Results are presented as mean difference between groups with 95% CI. This analysis was repeated for individual NEADL domains and for the QoL secondary outcome measures using the PDQ-39, EQ-5D and carer-completed SF-12.

The different questionnaires included in PD REHAB are interpreted differently. For example, for the NEADL scale higher scores are better, so a positive change over time is an improvement in score. However, for the PDQ-39 lower scores are better, so a negative change over time is an improvement in score. To aid interpretation of the mean differences and CI, regardless of scale, a positive mean difference favours the no therapy group and a negative mean difference favours the therapy group.

The long-term effect or whether or not any benefit of treatment persisted beyond the initial intervention period was compared at 9 and 15 months after randomisation, using both *t*-tests at each time point and a mixed-model repeated-measures analysis across all time points for all outcomes.

Analyses were performed on an intention-to-treat basis, whereby patients were analysed according to the group to which they were randomised, regardless of whether or not they complied with their allocation. Missing data in PDQ-39 domain scores were imputed using an expectation maximisation algorithm.[33,34] There is no established imputation method for the NEADL scale; therefore, the primary analyses used available data only, with no imputation for missing values. However, sensitivity analyses using a best (score 3), worst (score 0), middle (score 1.5) and average (at participant level) case score for missing items on the NEADL were explored.

Three a priori subgroup analyses were planned to compare the effect of combined PT and OT at different levels of ADL disability (analysis stratified by the patient's baseline NEADL total score: severe, 0–21; moderate, 22–43; and mild, 44–66), disease stage (Hoehn and Yahr stage ≤ 2, 2.5, 3 and ≥ 4) and age (< 60 years, 60–69 years, 70–79 years and ≥ 80 years). Subgroup analyses employed a test of interaction to explore whether or not there was evidence that any effect of therapy differed across these subgroups at 3-month follow-up. However, as with all subgroup analyses, these results were interpreted cautiously.

Analyses were performed using SAS version 9.2. Interim analyses of unblinded efficacy and safety data were reviewed annually by an independent data monitoring committee.

Economic evaluation

The study compared the costs and cost-effectiveness of combined PT and OT with no therapy in the treatment of patients with PD from the NHS and Personal Social Services perspective over 15 months.

Data collection

The PD REHAB trial prospectively collected resource-use data as an integral part of the clinical trial using a collection instrument adapted from the PD MED[35] and PD SURG trials.[36] The resources monitored include use of therapy services, primary care consultations including GP and practice nurse appointments, hospital inpatient stays, outpatient visits and accident and emergency attendances. For patients admitted to hospital, the length of stay and reason for admission were noted. All resource use relevant to PD was collected. The use of OT and PT services were recorded in detail by the therapists using the data acquisition forms; use of other primary and secondary care services was collected after randomisation using a postal resource-utilisation questionnaire for patient completion. All resource-use data were collected at 3, 9 and 15 months. PD-related medication was recorded by the clinician at baseline and at 15 months. Health-related QoL was measured by the EQ-5D at baseline and at 3, 9 and 15 months.

Estimating the costs

Primary care visits

Primary care costs including GP and nurse visits were obtained from the Personal Social Services Research Unit 2012 (PSSRU; *Table 4*).[37]

TABLE 4 Unit costs of primary care, therapy services and social care[37]

Resource item	Unit cost (£)	Basis of estimate
Therapy services		
Physiotherapist/occupational therapist/ speech and language therapist time (minutes)	0.55	Derived from the cost per hour of face-to-face contact time from PSSRU (2012)[37] including qualifications
Primary care		
GP clinic appointment	43.00	Per patient contact lasting 11.7 minutes from PSSRU (2012)[37] including qualifications and direct care staff costs
GP home visits	110.00	Per out of surgery visit lasting 23.4 minutes from PSSRU (2012)[37] (including travel time/cost)
Practice nurse clinic appointment[a]	13.69	Per face-to-face patient contact lasting 15.5 minutes, at £53 per hour from PSSRU (2012)[37] including qualifications
Practice nurse home visits	20.67	Per home visit lasting 27 minutes (duration based on most recently available estimate of a nurse home visit duration, i.e. PSSRU 2010), unit cost derived using cost per minute of £0.88 from PSSRU (2012)[37] including qualifications
Social care		
Health visitor	21.00	Per visit lasting 20 minutes (PSSRU 2012)
Social worker	214.00	Per hour face-to-face consultation, including qualifications (PSSRU 2012)

a Advanced nurse specialist unit costs (includes lead specialist, senior specialist) were used, as these relate to the same NHS pay band (band 7) as a Parkinson's Disease Nurse Specialist.

Therapy services

Staff time for PT and OT involved in the delivery of the intervention was recorded via treatment record forms completed by the therapist after each treatment session. Although the control patients consented to have the therapies deferred until the end of their 15 months' participation in the trial, some control patients still did receive therapy during the trial. The number of appointments with therapists for the control patients was reported by patient-completed questionnaire. For control patients whose contact time with therapists was not available, the average contact time was used. Costs per minute of both PT and OT were derived from PSSRU (see *Table 4*). We multiplied the therapist time by unit cost per minute to estimate cost per consultation.

Aids and adaptations

Aids and adaptations acquired during the trial were recorded through treatment logs or patient-completed questionnaires. The unit costs of these were extracted from the PSSRU (2012).[37] The value of the aid or adaptation was annuitised over a period of 10 years (reflecting an assumed typical lifetime of that aid or adaptation) and discounted at the recommended rate of 3.5%.[37] When such information was not available in PSSRU, we looked for an equivalent or similar cost item in the PSSRU to impute an appropriate median annuitised cost (*Table 5*).

Hospital costs

For costs relating to secondary (i.e. inpatient) care, a health-care resource group (HRG) applicable to patients with PD, HRG code AA25Z, descriptor 'Cerebral degenerations of the nervous system or miscellaneous', was identified from discussion with the trial investigators as relevant (*Table 6*). As the National Reference Costs (2011/12) did not record activity data under this HRG,[38] the cost of an inpatient hospital spell was extracted from the National Tariff.[39]

Medication

Use of medication was recorded by clinicians via entry forms when patients were recruited into the trial and at the time of trial exit. The main medications included levodopa, dopamine agonists, monoamine oxidase type B inhibitors, catechol-O-methyltransferase inhibitors, amantadine, apomorphine and intrajejunal levodopa–carbidopa gel infusion. However, we did not include medication costs in our cost

TABLE 5 Unit costs of aids and adaptation (PSSRU 2012)[37]

Aid or adaptation	Median annual equipment cost (£)
Wheelchair (self- or attendant-propelled)	86.00
Wheelchair (active user)	172.00
Wheelchair (powered)	400.00
Grab rail	6.00
Hoist	319.00
Walking stick	4.44
Low-level bath	81.00
New bath/shower room	1820.00
Relocation of bath/shower room	247.00
Relocation of toilet	211.00
Shower over bath	107.00
Shower replacing bath	107.00
Stair lift	402.00
Single concrete ramp	47.00

TABLE 6 Secondary care costs

Resource item	Unit cost (£)	Basis of estimate
Hospital inpatient stay, HRG code AA25Z	3159.00	2011–2012 NHS National Tariff[39] non-elective spell tariff 'Cerebral degenerations of the nervous system or miscellaneous', HRG code AA25Z (for stays up to the trim point of 31 days, long stay per day payment of £209 applied)
Outpatient attendance	106.00	2011–2012 NHS National Reference Costs publication[38] (average unit cost, all outpatient attendances)
Accident and emergency attendance	143.00	2011–2012 NHS National Reference Costs publication,[38] Category 2 Investigation with Category 2 Treatment
Day care admission (per day)	641.00	Based on National Tariff 2011–2012,[39] 'Cerebral degenerations of the nervous system or miscellaneous', HRG code AA25Z
Parkinson's disease nurse (in clinic)	23.67	Based on an advanced nurse specialist and a 20-minute consultation[37]

analysis for several reasons: PD is a long-term condition and there is a low likelihood that patients with early disease would change their medication in the 15 months of the trial. Although drug use data were collected at baseline and at 15 months, no interim data on medication were collected at other assessment points.

Analysis

The analysis followed that specified in the health-economic analysis plan in the protocol. The economic analysis was based on patient-specific resource use and costs, and patient-specific outcome and QoL data. The base-case analysis was framed in terms of costs and consequences, reporting the incremental costs and consequences in a disaggregated manner. As stated in the protocol, if this convincingly identified a situation of dominance (i.e. one arm is associated with both better outcomes and a lower cost), then further analysis would not be required. If no dominance was found, then cost–utility analysis [i.e. cost per quality-adjusted life-year (QALY)] would be employed.

Accumulated total costs per patient were calculated by the sum of the products of resources used and the associated unit costs, aggregated over the study period. The mean costs associated with the therapy and control group were evaluated and the differences in costs were compared according to the intention-to-treat allocation. No discounting rate was applied, as the follow-up period was 15 months.

Quality-of-life data were measured using EQ-5D questionnaires, which were collected at baseline and at 3, 9 and 15 months. The UK Tariff was used to produce utility scores. QALYs for each patient were calculated based on the utility scores at different points using area-under-the-curve. We assumed linear interpolation between two points of measurements.

Missing data because of non-completion in the resource use and EQ-5D questionnaires were imputed by substituting the mean adjusted by treatment groups. We did not employ multiple imputation, as there were few missing values. The costs and QALYs for the cases of death and withdrawals were assumed to cease at the time points when such event occurs.

The bias-corrected bootstrap method was used to estimate mean costs, QALYs and the incremental cost-effectiveness ratio (ICER) with the associated 95% CI. Uncertainty around the costs and effectiveness estimates was illustrated using scatterplots with confidence ellipses and addressed by plotting cost-effectiveness acceptability curves (CEACs).

All analyses were based on the principle of intention to treat. The analyses were conducted in SAS 9.2.

Patient and public involvement

Patient and carer involvement was incorporated at all levels of the PD REHAB trial. A representative from the charity Parkinson's UK (Miss Ramilla Patel, Regional Manager, Parkinson's UK) was a co-applicant on the grant, being involved in the design of the study and a member of the Trial Management Group. With the initial leadership of Dr Sandy Herron-Marx and then Ms Sunil Shah and Dr Caroline Rick, we and Parkinson's UK developed a Patient Advisory Group of PD patients and carers. This was a virtual e-network following an initial face-to-face meeting. Members were supported by Mrs Ramilla Patel and the person leading the group at the time.

The Patient Advisory Group contributed to the development of the participant information sheets, consent forms and resource use questionnaire. It was planned for the group to be involved with the interpretation of the findings through the development of recommendations for practice and patient information leaflets (top-tip leaflet) about therapy choices, although the results have not required such input. The group will also be involved with the dissemination of the findings through existing patient networks, mainly through the auspices of Parkinson's UK and its newsletter service.

Chapter 3 Results

Patients

Between October 2009 and June 2012, 762 people with PD from 38 neurological or geriatric medicine outpatients centres across the UK were randomised to either combined PT and OT or no therapy (381 per group; *Figure 1*). Baseline characteristics were similar between the two groups (*Table 7*). The mean age was 70 years, 65% were male and the median duration of disease was 3.1 years (mean 4.6 years). The majority of patients had mild to moderate disease, with 67% in Hoehn and Yahr stage 2 or less, and the median NEADL total score was 54 (mean 51).

Loss to follow-up

In total, 350 (92%) of 381 patients randomised to the therapy arm completed the NEADL at 3 months, compared with 349 (92%) of 381 patients randomised to the no therapy arm (see *Figure 1*). Of 381 patients randomised in the therapy arm, 311 (82%) completed the NEADL at 15 months, compared with 322 of 381 patients randomised in the control arm (85%). Overall, by 15 months, 48 (6%) patients had exited the trial (eight patients had withdrawn, 17 had partially withdrawn and 23 had died).

Compliance

In total, 25 patients (6%) allocated to PT and OT did not receive therapy by 3 months after randomisation (12 started PT and/or OT after 3 months and 13 never received any therapy; *Figure 1*). Nine patients (2%) allocated to no therapy received therapy for PD-related problems within 3 months, mainly because of worsening PD symptoms including falls and imbalance.

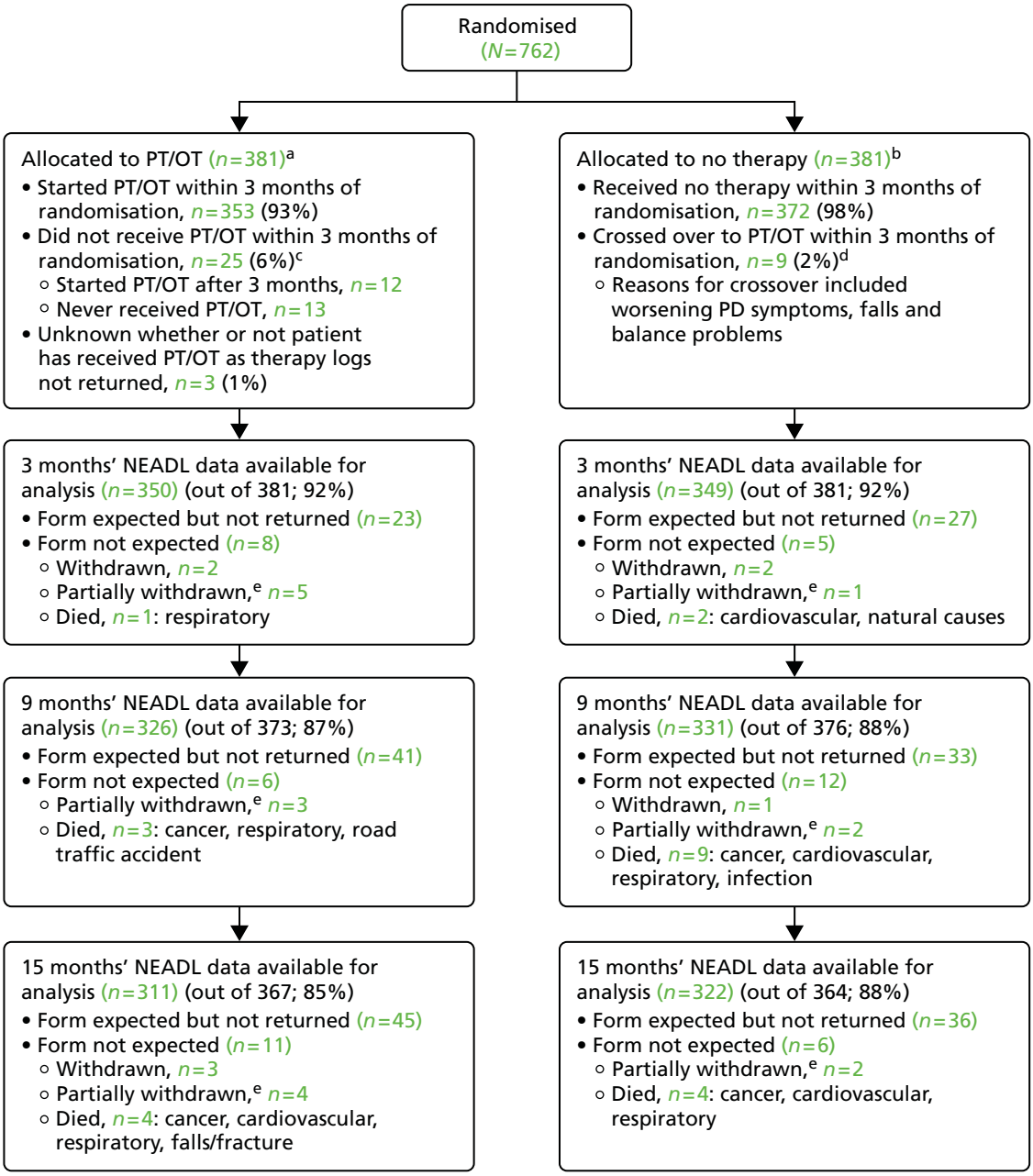

FIGURE 1 Consolidated Standards of Reporting Trials diagram for PD REHAB: patient recruitment and follow-up. a, Eight patients randomised to the PT and OT group were later found to be ineligible, as they had received PT and/or OT for PD in the 12 months prior to randomisation (exclusion criteria). One patient did not receive any PT or OT post randomisation (crossover: only baseline data available – diagnosed with cancer and died at 5 months post randomisation). One patient did not receive PT or OT within 3 months, but was referred for PT outside the trial at 6 months (3-, 9- and 15-month data available). The other six patients all received PT and/or OT post randomisation (baseline and 3-month data available, except for one patient for whom only baseline data are available). b, Three patients randomised to the no therapy group were subsequently found to be ineligible as they had received PT and/or OT for PD in the 12 months prior to randomisation (exclusion criteria). One patient received PT and/or OT within 3 months of randomisation (crossover). For all three patients, baseline and 3-month data were available. c, Thirteen patients randomised to the PT and OT group are known to have not received any PT or OT. Baseline and 3-month data are available for two of these patients (for the other 11 patients, only baseline data are available). Twelve patients did not receive PT or OT by 3 months post randomisation, but did start therapy after 3 months; baseline and 3-month data are available for all patients (except two: one has baseline data only and one has 3-month data only). d, Nine patients randomised to no therapy had some PT and/or OT before their 3-month NEADL form was completed; all patients had baseline and 3-month data available. e, Partially withdrawn patients did not wish to complete patient forms but agreed to clinical follow-up.

TABLE 7 Demographics and baseline characteristics

Characteristic/demographic	PT/OT	No therapy
Number of patients randomised	381	381
Demographics *Age (years)*		
Mean (SD)	70 (9.1)	70 (9.3)
Range	35–90	35–91
Age category (years)		
< 60	47 (12%)	46 (12%)
60–69	129 (34%)	129 (34%)
70–79	148 (39%)	151 (40%)
≥ 80	57 (15%)	55 (14%)
Sex		
Male, *n* (%)	240 (63%)	258 (68%)
Body mass index (kg/m²)		
n	327	333
Mean (SD)	27.2 (5.4)	26.9 (4.4)
Range	16.5–54.9	16.8–44.0
Stage of Parkinson's disease *Duration of PD (years)*		
n	381	379
Mean (SD)	4.5 (4.9)	4.6 (4.5)
Median (IQR)	3.0 (1.0–6.1)	3.3 (1.3–6.4)
Range	0.01–29.9	0–25.6
Hoehn and Yahr stage		
≤ 2.0	254 (67%)	254 (67%)
2.5	46 (12%)	46 (12%)
3.0	61 (16%)	61 (16%)
≥ 4.0	20 (5%)	20 (5%)
Levodopa equivalent dose (mg/day)		
n	381	381
Mean (SD)	453 (357.9)	498 (372.8)
Range	0–1877	0–2181
NEADL scale total score		
n	381	381
Mean (SD)	51 (12.9)	51 (13.3)
Median (IQR)	53 (43–61)	54 (42–62)
Range	6–66	8–66

continued

TABLE 7 Demographics and baseline characteristics (*continued*)

Characteristic/demographic	PT/OT	No therapy
NEADL total score category		
0–21 (severe)	14 (4%)	14 (4%)
22–43 (moderate)	88 (23%)	88 (23%)
44–66 (mild)	279 (73%)	279 (73%)
PDQ-39 summary index		
n	380	377
Mean (SD)	23.8 (14.5)	23.7 (14.4)
Median (IQR)	22.4 (12.6–32.3)	21.1 (12.2–33.0)
Range	2.4–78.4	1.9–67.4

IQR, interquartile range.
Age, Hoehn and Yahr and NEADL total score were minimisation variables in the randomisation algorithm. NEADL total score ranges from 0 to 66, where higher scores are better. PDQ-39 summary index ranges from 0 to 100, where lower scores are better (i.e. better QoL).

Therapy content

In those who received therapy in the PT and OT group, the median total number of therapy sessions was four (range 1–21) (*Table 8*), with a mean time per session of 58 minutes. The mean duration of therapy was 8 weeks. The mean total dose of both therapies was 263 minutes (range 38–1198 minutes; *Table 8*). Most PT was performed in an outpatient setting (53%) rather than in the community (39%) or other setting (8%), whereas OT was more commonly performed in the community (69%) than outpatients (29%) or other (2%).

The PT logs (*Table 9*) showed that the most frequent interventions were for gait (96% of patients), posture (93%), balance (90%), physical conditioning (81%) and transfers (78%). The OT logs (*Table 10*) showed that the most frequent interventions were for transfers (45%), dressing and grooming (36%), sleep and fatigue (31%), indoor mobility (28%), household tasks (28%) and other environmental issues (27%).

A further validation of PT and OT treatment logs was done by comparing them with the full-text patient notes for 38 patients chosen at random from 10 geographically diverse centres. Therapist interventions were listed and thematically grouped into five categories: assessment, equipment and adaptation prescription, exercise recommendations, referral to other specialists and 'other advice'. Physiotherapists prescribed a range of exercise programmes tailored to their assessment of the patient's physical strength and range of movement. Only three physiotherapists provided a specific PD exercise programme accompanied by a booklet, and there was no evidence of a formal progression protocol. PT included the prescription of walking aids. OT assessed the full range of ADL activities including socialising and work. However, the predominant interventions were equipment provision (such as bed levers or adaptive cutlery), onward referral (such as speech and language therapy and cognitive assessment), with 'other advice' including recommendations on how to manage sleep problems and how to apply for state benefits. There was little task-related practice.

TABLE 8 Therapy duration

Item	PT/OT ($n = 381$)	Control ($n = 381$)
Patients who received PT and/or OT during 15-month trial		
n (%)	365 (96%)	53 (14%)
Patients with treatment logs available		
n	355[a]	12[b]
Sessions		
n	355	12
Median (IQR)	4 (3–6)	2 (1–6)
Range	1–21	1–11
Total time (minutes)		
n	355	12
Mean (SD)	263 (178.6)	246 (332.6)
Range	38–1198	60–1070
Time per session (minutes)		
n	355	12
Mean (SD)	58 (27.2)	58 (19.2)
Range	19–399	30–97
Treatment duration (weeks)		
n	355	10
Mean (SD)	8 (9.0)	7 (11.1)
Range	0.1–62	0.1–35
Intervention location (OT)		
n	274	4
Community	188 (69%)	3 (75%)
Outpatient	80 (29%)	1 (25%)
Other	6 (2%)	0 (–)
Intervention location (PT)		
n	318	9
Community	124 (39%)	3 (33%)
Outpatient	170 (53%)	4 (44%)
Other[a]	24 (8%)	2 (23%)

IQR, interquartile range.

a Treatment logs were not returned for 10 patients randomised to the therapy group. These patients are known to have received PT and/or OT through correspondence with the therapist at the centre, but further details of the therapy received are not available.

b Logs were available for 12 patients randomised to the no therapy (control) group who received PT and/or OT for their PD during the 15-month trial (9 patients within 3 months of randomisation; see *Figure 1*).

TABLE 9 Physiotherapy content

Activity	Number[a]		% [b]	
	Treatment	Assessment	Treatment	Assessment
Gait and indoor mobility	330	122	96	36
Posture	318	100	93	29
Balance and falls	309	99	90	29
Physical conditioning	277	61	81	18
Transfers	268	41	78	12
Upper limb function	259	54	76	16
Outdoor mobility	183	35	54	10
Leisure-related activities	184	21	54	6
Domestic ADL	135	13	39	4
Self-care	131	5	38	1
Other (e.g. handwriting practice)	123	20	36	6
Work-related activities	60	3	18	1

a Total number in treatment arm with returned logs = 342.
b In descending order of treatment frequency.

TABLE 10 Occupational therapy content

Activity	Number[a]		% [b]	
	Treatment	Assessment	Treatment	Assessment
Transfers	145	294	45	91
Dressing and grooming	118	274	36	85
Sleeping and fatigue	101	245	31	76
Indoor mobility	91	290	28	90
Household tasks	90	258	28	80
Environmental issues	88	262	27	81
Eating and drinking	86	251	27	77
Communication	82	227	25	70
Emotional support	77	212	24	65
Cognition	73	246	23	76
Social activities	65	248	20	77
Falls	57	224	18	69
Employment	15	144	5	44

a Total number in treatment arm with returned logs = 324.
b In descending order of treatment frequency.

Primary outcome

The mean NEADL total score deteriorated from baseline to 3 months by 1.5 points in the therapy group compared with 1.0 point in the no therapy group (difference 0.5 points, 95% CI –0.7 to 1.7 points; $p = 0.4$) (*Table 11*). No difference was seen in any of the individual categories of the NEADL scale (see *Table 11*). Repeated measures analysis of the NEADL across all time points showed no difference between the treatment arms (*Table 12* and *Figure 2a*).

Secondary outcomes

The mean PDQ-39 summary index deteriorated by 2.4 points in both groups from baseline to 3 months (difference 0.007 points, 95% CI –1.5 to 1.5 points, $p = 1.0$; *Table 11*). No difference was seen in any of the eight domains of the PDQ-39 (*Table 11*). The slight improvement of 0.002 points in the EQ-5D quotient in the therapy group between baseline and 3 months compared with a 0.03-point deterioration in the no therapy group was of borderline significance (difference –0.03, 95% CI –0.07 to –0.002; $p = 0.04$; see *Table 11*). There was no difference in the EQ-5D visual analogue score (difference –0.2, 95% CI –2.6 to 2.2; $p = 0.9$; see *Table 11*).

Repeated measures analysis over the whole 15 months found significant divergence in PDQ-39 summary index (curves diverging at 1.55 points per annum, 95% CI 0.47 to 2.62 points; $p = 0.005$; see *Figure 2b*) and the ADL, emotional well-being and social support domains in favour of therapy but no difference in the mobility domain. There was also a borderline significant difference in the EQ-5D quotient in favour of the therapy arm over time (0.02 points, 95% CI 0.00007 to 0.03; $p = 0.04$; see *Figure 2c*).

Sensitivity analyses

Sensitivity analysis with imputation of missing values on the NEADL scale [assuming a best (score 3), worst (score 0), middle (score 1.5) and average (at participant level) case score for missing items] did not change the results. Therefore, we can be reasonably confident that the results are robust and that missing data do not influence the results at any time point. Similarly, repeating the PDQ-39 analysis without imputation of missing values using the expectation maximisation algorithm also did not affect the results at any time point.

We also analysed the primary outcome of mean change between baseline and 3 months for the NEADL total score data using analysis of covariance adjusting for baseline NEADL score and the minimisation variables used in the randomisation algorithm, and for both analyses this made no difference to the results (difference 0.5; 95% CI –0.7 to 1.7; $p = 0.4$).

TABLE 11 Patient ADL and QoL scores at 3 months

	Baseline		3 months		Mean change from baseline			
Subscale	PT/OT	No therapy	PT/OT	No therapy	PT/OT	No therapy	Mean difference (95% CI)[a]	*p*-value
NEADL								
Total score	381	381	294	304	294	304	–	–
	50.5 (12.9)	50.9 (13.3)	49.6 (14.0)	50.3 (14.5)	–1.5 (7.8)	–1.0 (7.4)	0.5 (–0.7 to 1.7)	0.4
Mobility	376	372	338	338	334	330	0.1 (–0.3 to 0.5)	0.6
	13.9 (4.0)	13.8 (4.2)	13.6 (4.2)	13.6 (4.4)	–0.4 (2.6)	–0.2 (2.4)		
Kitchen activities	379	373	337	337	335	329	0.005 (–0.3 to 0.3)	1.0
	13.0 (2.7)	13.0 (2.9)	13.0 (3.0)	12.9 (3.2)	–0.2 (2.2)	–0.2 (1.9)		
Domestic tasks	374	370	330	332	325	323	0.5 (–0.06 to 1.0)	0.08
	10.9 (4.2)	11.1 (4.3)	10.4 (4.5)	10.8 (4.4)	–0.8 (3.4)	–0.3 (3.2)		
Leisure activities	376	365	318	329	316	318	0.01 (–0.4 to 0.4)	0.9
	12.9 (4.1)	13.0 (4.0)	13.0 (4.1)	13.1 (4.0)	–0.2 (2.4)	–0.1 (2.4)		
PDQ-39								
n	380	377	349	351	348	347	–	–
Mobility	32.7 (26.1)	31.3 (25.8)	33.2 (27.3)	33.3 (28.0)	1.1 (17.1)	2.6 (15.8)	–1.5 (–3.9 to 1.0)	0.2
ADL	31.3 (23.1)	30.6 (21.8)	32.1 (23.8)	31.5 (23.8)	1.6 (14.3)	1.0 (16.7)	0.7 (–1.7 to 3.0)	0.6
Emotional well-being	23.9 (18.5)	23.0 (18.1)	25.9 (19.8)	25.5 (20.3)	2.6 (13.1)	3.0 (16.8)	–0.5 (–2.7 to 1.8)	0.7
Stigma	18.3 (22.9)	17.1 (21.0)	19.8 (23.1)	17.6 (21.3)	1.6 (17.7)	0.9 (17.5)	0.7 (–2.0 to 3.3)	0.6
Social support	6.6 (14.0)	5.7 (11.0)	10.3 (17.4)	9.3 (15.1)	3.6 (15.6)	3.8 (14.9)	–0.2 (–2.5 to 2.0)	0.8
Cognition	26.6 (20.1)	27.3 (21.1)	28.8 (20.6)	29.6 (21.6)	2.2 (16.5)	2.2 (17.0)	–0.05 (–2.6 to 2.4)	1.0
Communication	16.5 (18.2)	18.5 (19.8)	20.8 (20.1)	21.8 (21.1)	4.8 (15.7)	3.0 (17.4)	1.8 (–0.7 to 4.2)	0.2
Bodily discomfort	34.8 (23.4)	35.9 (24.0)	36.5 (24.4)	38.6 (24.1)	2.0 (20.7)	2.8 (21.1)	–0.8 (–3.9 to 2.3)	0.6
Summary index	23.8 (14.5)	23.7 (14.4)	25.9 (16.5)	25.9 (16.5)	2.4 (9.5)	2.4 (10.8)	0.007 (–1.5 to 1.5)	1.0

Subscale	Baseline		3 months		Mean change from baseline		Mean difference (95% CI)[a]	*p*-value
	PT/OT	No therapy	PT/OT	No therapy	PT/OT	No therapy		
EQ-5D quotient								
n	378	374	345	345	342	338	–	–
Score	0.64 (0.27)	0.66 (0.25)	0.65 (0.25)	0.63 (0.26)	0.002 (0.23)	–0.03 (0.21)	–0.03 (–0.07 to –0.002)	0.04
EQ-5D visual analogue scale								
n	376	376	346	347	341	342	–	–
Score	68.5 (17.5)	68.6 (17.0)	67.4 (18.2)	66.8 (17.8)	–1.8 (17.1)	–1.9 (14.3)	–0.2 (–2.6 to 2.2)	0.9

a To aid interpretation, regardless of scale, a positive mean difference favours no therapy group and a negative mean difference favours PT/OT group.
Data are mean (SD). NEADL total score: ranges from 0 to 66 where higher scores are better and a positive change is an improvement in score. PDQ-39: ranges from 0 to 100 where lower scores are better and a negative change is an improvement in score. EQ-5D quotient: ranges from –0.59 to 1 where higher scores are better and a positive change is an improvement in score. EQ-5D visual analogue scale: ranges from 0 to 100 where higher scores are better and a positive change is an improvement in score.

TABLE 12 Long-term changes in ADL and QoL scores

Subscale	Baseline vs. 3 months		Mean difference (95% CI)[a]	Baseline vs. 9 months		Mean difference (95% CI)[a]	Baseline vs. 15 months		Mean difference (95% CI)[a]
	PT/OT	No therapy		PT/OT	No therapy		PT/OT	No therapy	
NEADL									
Total score	294	304	–	289	303	–	268	283	–
	–1.5 (7.8)	–1.0 (7.4)	0.5 (–0.7 to 1.7), $p = 0.4$	–3.6 (8.1)	–3.0 (8.4)	0.6 (–0.7 to 1.9), $p = 0.4$	–3.8 (8.6)	–5.0 (9.8)	–1.2 (–2.8 to 0.3), $p = 0.1$
Mobility	334	330	–	314	315	–	294	301	–
	–0.4 (2.6)	–0.2 (2.4)	0.1 (–0.3 to 0.5), $p = 0.6$	–1.0 (2.6)	–0.7 (2.7)	0.3 (–0.1 to 0.7), $p = 0.1$	–1.1 (2.7)	–1.3 (3.1)	–0.2 (–0.6 to 0.3), $p = 0.4$
Kitchen activities	335	329	–	321	319	–	306	312	–
	–0.2 (2.2)	–0.2 (1.9)	0.005 (–0.3 to 0.3), $p = 1.0$	–0.5 (2.5)	–0.6 (2.2)	–0.04 (–0.4 to 0.3), $p = 0.8$	–0.6 (2.5)	–0.9 (2.5)	–0.3 (–0.7 to 0.05), $p = 0.4$
Domestic tasks	325	323	–	307	314	–	292	302	–
	–0.8 (3.4)	–0.3 (3.2)	0.5 (–0.06 to 1.0), $p = 0.08$	–1.0 (3.3)	–0.8 (3.5)	0.1 (–0.4 to 0.6), $p = 0.7$	–1.1 (3.6)	–1.4 (3.7)	–0.3 (–0.9 to 0.2), $p = 0.2$
Leisure activities	316	318	–	302	307	–	292	291	–
	–0.2 (2.4)	–0.1 (2.4)	0.01 (–0.4 to 0.4), $p = 0.9$	–0.9 (2.4)	–0.8 (2.5)	0.04 (–0.3 to 0.4), $p = 0.8$	–1.1 (2.7)	–1.3 (2.9)	–0.3 (–0.7 to 0.2), $p = 0.2$
PDQ-39									
n	348	347	–	325	327	–	310	319	–
Mobility	1.1 (17.1)	2.6 (15.8)	–1.5 (–3.9 to 1.0), $p = 0.2$	4.5 (17.5)	5.9 (16.7)	–1.3 (–4.0 to 1.3), $p = 0.3$	6.4 (19.4)	9.3 (20.5)	–2.9 (–6.0 to 0.2), $p = 0.07$
ADL	1.6 (14.3)	1.0 (16.7)	0.7 (–1.7 to 3.0), $p = 0.6$	3.1 (15.5)	4.1 (16.7)	–1.0 (–3.5 to 1.5), $p = 0.4$	4.1 (17.1)	7.0 (18.9)	–2.8 (–5.7 to –0.02), $p = 0.05$
Emotional well-being	2.6 (13.1)	3.0 (16.8)	–0.5 (–2.7 to 1.8), $p = 0.7$	3.5 (15.0)	6.0 (15.3)	–2.5 (–4.9 to –0.2), $p = 0.03$	4.6 (16.1)	7.7 (17.5)	–3.1 (–5.7 to –0.5), $p = 0.02$

Subscale	Baseline vs. 3 months		Mean difference (95% CI)[a]	Baseline vs. 9 months		Mean difference (95% CI)[a]	Baseline vs. 15 months		Mean difference (95% CI)[a]
	PT/OT	No therapy		PT/OT	No therapy		PT/OT	No therapy	
Stigma	1.6 (17.7)	0.9 (17.5)	0.7 (–2.0 to 3.3), $p = 0.6$	2.5 (16.1)	3.3 (17.8)	–0.8 (–3.4 to 1.8), $p = 0.5$	2.8 (18.0)	4.5 (18.0)	–1.6 (–4.5 to 1.2), $p = 0.3$
Social support	3.6 (15.6)	3.8 (14.9)	–0.2 (–2.5 to 2.0), $p = 0.8$	3.9 (14.7)	5.6 (15.3)	–1.8 (–4.1 to 0.5), $p = 0.1$	4.3 (14.7)	6.3 (15.8)	–2.0 (–4.4 to 0.4), $p = 0.09$
Cognition	2.2 (16.5)	2.2 (17.0)	–0.05 (–2.6 to 2.4), $p = 1.0$	3.0 (16.7)	4.4 (17.7)	–1.4 (–4.1 to 1.2), $p = 0.3$	4.2 (17.7)	6.0 (18.5)	–1.8 (–4.7 to 1.0), $p = 0.2$
Communication	4.8 (15.7)	3.0 (17.4)	1.8 (–0.7 to 4.2), $p = 0.2$	5.1 (15.9)	5.0 (17.2)	0.1 (–2.4 to 2.7), $p = 0.9$	6.0 (16.2)	5.9 (17.1)	0.1 (–2.5 to 2.7), $p = 0.9$
Bodily discomfort	2.0 (20.7)	2.8 (21.1)	–0.8 (–3.9 to 2.3), $p = 0.6$	2.2 (20.6)	2.3 (22.1)	–0.07 (–3.3 to 3.2), $p = 1.0$	2.3 (20.9)	5.6 (22.9)	–3.3 (–6.7 to 0.2), $p = 0.06$
Summary index	2.4 (9.5)	2.4 (10.8)	0.007 (–1.5 to 1.5), $p = 1.0$	3.5 (9.7)	4.6 (10.7)	–1.1 (–2.7 to 0.5), $p = 0.2$	4.3 (10.6)	6.5 (11.4)	–2.2 (–3.9 to –0.5), $p = 0.01$
EQ-5D quotient									
n	342	338	–	321	322	–	304	313	–
Score	0.002 (0.23)	–0.03 (0.21)	–0.03 (–0.07 to –0.002), $p = 0.04$	–0.02 (0.26)	–0.05 (0.22)	–0.03 (–0.07 to 0.008), $p = 0.1$	–0.05 (0.27)	–0.09 (0.23)	–0.04 (–0.08 to 0.004), $p = 0.08$
EQ-5D visual analogue scale									
n	341	342	–	319	323	–	305	309	–
Score	–1.8 (17.1)	–1.9 (14.3)	–0.2 (–2.6 to 2.2), $p = 0.9$	–3.5 (16.6)	–4.5 (16.1)	–1.0 (–3.5 to 1.6), $p = 0.4$	–4.7 (7.3)	–5.8 (16.3)	–1.1 (–3.7 to 1.6), $p = 0.4$

a To aid interpretation, regardless of scale, a positive mean difference favours no therapy group and a negative mean difference favours PT/OT group.
Data are mean (SD). NEADL total score: a positive change is an improvement in score. PDQ-39: a negative change is an improvement in score. EQ-5D quotient: a positive change is an improvement in score. EQ-5D visual analogue scale: a positive change is an improvement in score.

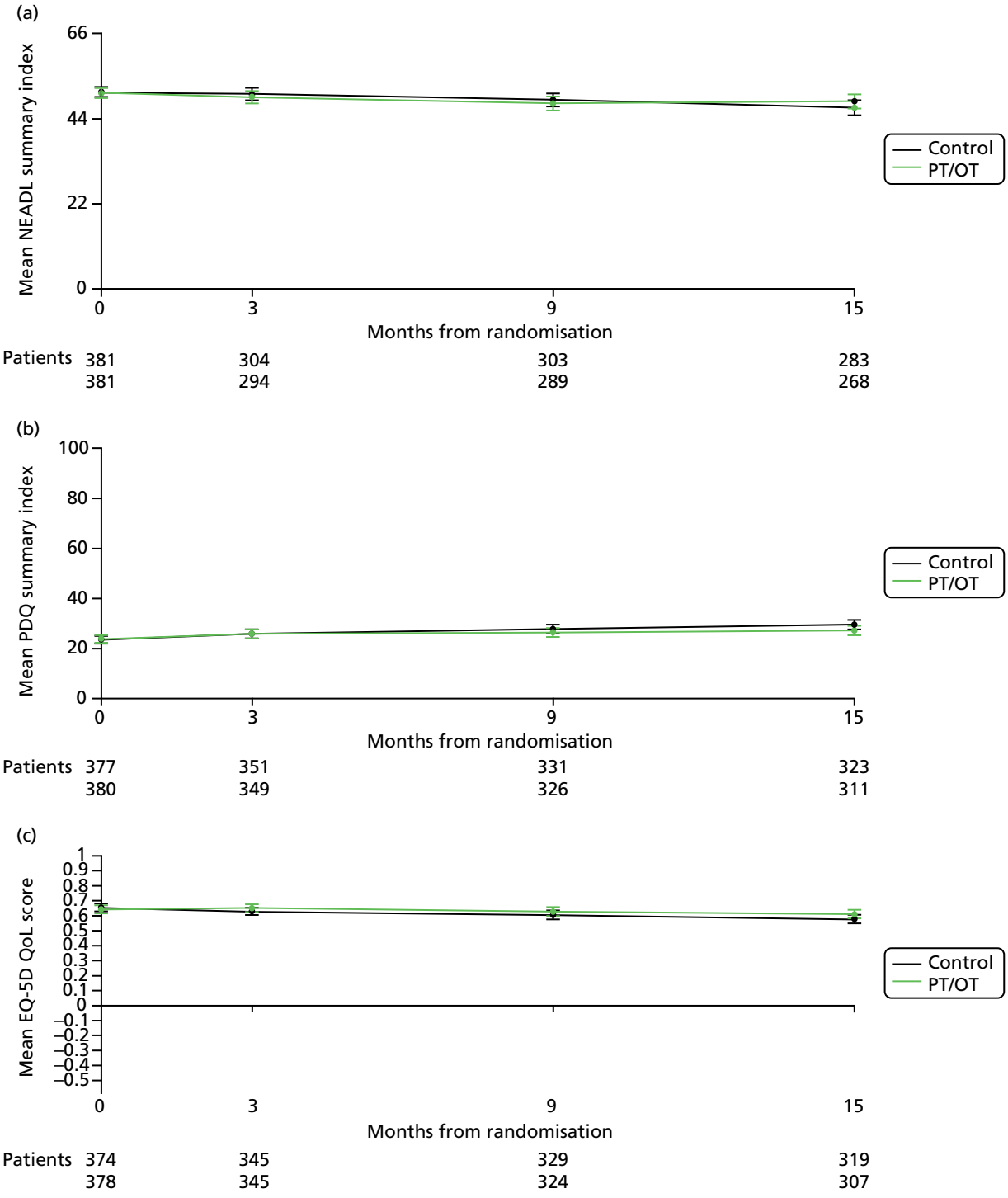

FIGURE 2 Long-term changes in ADL and QoL scores. (a) Mean NEADL summary index over time by treatment. Test for increasing difference over time: $p = 0.3$. Average difference (favours PT/OT): 0.07 points (–0.64 to 0.77 points); $p = 0.9$; (b) mean PDQ-39 summary index over time by treatment. Test for increasing difference over time: $p = 0.005$. Slopes diverge in favour of PT/OT: –1.55 (–2.62 to –0.47); $p = 0.005$; and (c) mean EQ-5D QoL score over time by treatment. Test for increasing difference over time: $p = 0.2$. Average difference (favours PT/OT): 0.02 points (0.00007 to 0.03 points), $p = 0.04$.

Subgroup analyses

Planned subgroup analyses for the NEADL total score found no evidence of a difference in treatment effect at 3 months according to baseline NEADL total score, disease severity or age (*Figure 3*).

Carer data

In total, 473 (62%) patients stated that they had a carer and 406 (86%) carers agreed to take part in the trial. Carer mean age was 67 years and 76% were female. The relationship between patient and carer was partner or spouse in the majority (72%). Although there was no difference in the carer SF-12 physical component summary score at 3 months, there was less decline in the carer SF-12 mental component summary score (difference –2.1, 95% CI –3.9 to –0.3; $p = 0.02$) (*Table 13*), although this was not maintained with longer follow-up.

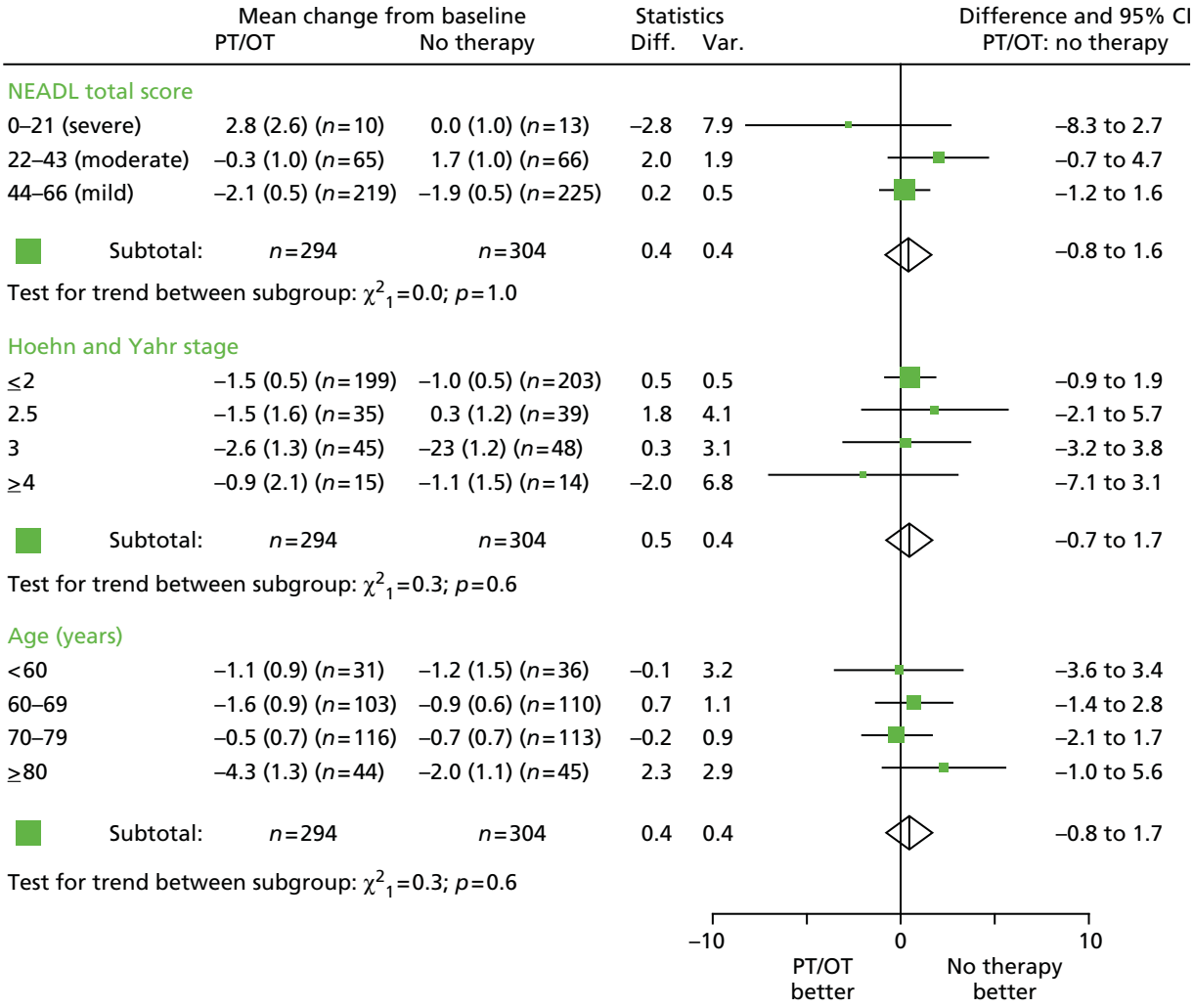

FIGURE 3 Subgroup analyses for NEADL total score at 3 months. NEADL total score: ranges from 0 to 66 where higher scores are better and a positive change is an improvement in score. Diff., difference; var., variance.

TABLE 13 Carer SF-12 QoL scores at 3 months

	Baseline		3 months		Mean change from baseline			
Subscale	PT/OT	No therapy	PT/OT	No therapy	PT/OT	No therapy	Mean difference (95% CI)[a]	*p*-value
Physical functioning								
n	171	181	169	181	151	156	–5.6 (–11.0 to –0.2)	0.04
Score	70.3 (35.4)	76.0 (30.5)	68.6 (35.8)	70.3 (30.0)	–0.7 (24.8)	–6.3 (23.0)		
Role physical								
n	173	183	169	185	155	163	–0.5 (–5.3 to 4.3)	0.8
Score	75.4 (28.5)	76.7 (26.8)	69.8 (28.8)	71.0 (27.1)	–5.4 (19.6)	–5.9 (23.8)		
Role emotional								
n	172	182	170	183	155	162	–4.4 (–9.0 to 0.2)	0.06
Score	83.6 (23.1)	81.9 (22.9)	80.4 (24.2)	76.4 (24.9)	–1.7 (20.0)	–6.1 (21.5)		
Social functioning								
n	175	186	171	189	157	169	–3.8 (–8.9 to 1.3)	0.1
Score	84.9 (22.9)	83.3 (23.6)	81.0 (24.5)	78.3 (26.9)	–2.9 (21.9)	–6.7 (24.5)		
Mental health								
n	174	183	170	188	156	167	–4.3 (–8.2 to –0.4)	0.03
Score	68.8 (21.1)	68.6 (18.5)	67.6 (20.2)	64.6 (21.9)	–0.2 (16.7)	–4.5 (18.9)		
Vitality								
n	175	184	170	188	156	167	–4.6 (–9.2 to 0.05)	0.05
Score	57.4 (25.6)	61.8 (22.6)	53.8 (25.9)	53.2 (24.5)	–3.5 (21.0)	–8.1 (21.1)		
Bodily pain								
n	173	184	170	189	156	168	2.9 (–2.2 to 7.9)	0.3
Score	77.7 (29.3)	76.4 (28.7)	74.1 (28.8)	74.2 (28.5)	–4.6 (25.0)	–1.8 (21.1)		

	Baseline		3 months		Mean change from baseline			
Subscale	PT/OT	No therapy	PT/OT	No therapy	PT/OT	No therapy	Mean difference (95% CI)[a]	*p*-value
General health								
n	174	186	170	190	155	170	–0.9 (–5.0 to 3.3)	0.7
Score	64.2 (25.3)	65.6 (26.1)	58.9 (26.0)	61.0 (25.3)	–4.4 (18.6)	–5.3 (19.5)		
Physical component summary								
n	166	171	165	174	146	144	–0.6 (–2.3 to 1.2)	0.5
Score	47.1 (12.5)	48.2 (11.4)	45.1 (13.3)	46.4 (11.6)	–1.6 (7.5)	–2.1 (7.5)		
Mental component summary								
n	166	171	165	174	146	144	–2.1 (–3.9 to –0.3)	0.02
Score	51.1 (10.2)	50.1 (8.9)	49.7 (10.2)	48.0 (10.5)	–0.5 (7.6)	–2.6 (7.9)		

a To aid interpretation, regardless of scale, a positive mean difference favours no therapy group and a negative mean difference favours PT/OT group.
SF-12: ranges from 0–100 where higher scores are better and a positive change is an improvement in score.

Safety

By 3 months in the therapy group, falls had occurred in 10 patients (some patients reported multiple fall episodes), resulting in 17 GP, one ambulance and three hospital visits (accident and emergency, outpatient). In the no therapy group, falls were reported in nine patients, resulting in 11 GP, two ambulance and eight hospital visits. There were also six falls in another six patients that resulted in an overnight stay in hospital or prolongation of hospitalisation (four patients in the therapy group and two in the no therapy group). Duration of hospital stay ranged from 1 to 31 days. Injuries using equipment were reported by two patients (one in each group), both when the patient was using a rollator or frame.

Over the 15-month duration of the trial, 43 patients in the therapy group reported having had a fall (some patients reported multiple fall episodes), resulting in 68 GP, 17 ambulance and 34 hospital visits (accident and emergency, outpatient). In the no therapy group, 49 patients reported falls, resulting in 69 GP, 21 ambulance and 37 hospital visits. There were also in total 27 falls that resulted in an overnight stay in hospital or prolongation of hospitalisation (13 falls in 10 patients in the therapy group and 14 falls in 12 patients in the no therapy group). Duration of hospital stay ranged from 1 to 72 days.

Economic evaluation

Table 14 presents data on resource use by type of contact for each arm of the trial. Data are presented for all participants after randomisation using intention-to-treat analysis. *Table 15* presents data on the associated costs by category of resource use for each arm of the trial. Aggregation of the categories of all costs identified in *Table 15* result in mean costs per patient of £1708 (95% CI £1379 to £2072) and £1541 (95% CI £1329 to £1752; *Table 14*) for the PT/OT and control arms, respectively.

The mean number of QALYs gained per patient was 0.791 (95% CI 0.765 to 0.818) in the therapy arm and 0.764 (95% CI 0.737 to 0.791) in the control arm (*Table 16*). Compared with the control group, therapy resulted in an incremental cost per patient of £164 (95% CI –£141 to £468) and an incremental QALY gain of 0.027 (95% CI –0.010 to 0.065). Combining incremental costs and consequences into a single summary score resulted in an incremental cost per QALY gained (ICER) of £3493 (95% CI –£169,371 to £176,358).

Figure 4 presents the scatterplot of incremental costs and incremental QALYs with 95% confidence ellipse on the cost-effectiveness plane. *Figure 5* presents the CEAC at different values as the threshold value of the ICER is raised. At a willingness-to-pay threshold of £20,000 per QALY, the probability of PT/OT being more cost-effective at £20,000 was 50.5%.

TABLE 14 Health and social care resource utilisation

Contact type	PT/OT ($n = 381$)	Control ($n = 381$)
PT/OT service		
PT appointment number, mean (SD)	3.52 (4.02)	1.31 (2.79)
OT appointment number, mean (SD)	1.73 (2.23)	0.43 (1.13)
Primary care		
GP appointment number, mean (SD)	4.49 (4.53)	4.76 (4.42)
GP home visit number, mean (SD)	0.47 (1.61)	0.38 (1.24)
Practice nurse appointment number, mean (SD)	2.19 (3.86)	2.05 (4.08)
Nurse home visit number, mean (SD)	0.50 (2.28)	0.56 (2.37)
Private GP appointment number, mean (SD)	0.38 (1.79)	0.52 (2.70)
Speech/language appointment number, mean (SD)	0.60 (2.04)	0.85 (3.30)
Secondary care		
Outpatient bed-days, mean (SD)	0.14 (0.67)	0.08 (0.47)
Inpatient bed-days, mean (SD)	0.19 (0.58)	0.20 (0.58)
Outpatient appointment numbers, mean (SD)	3.71 (3.95)	3.29 (4.26)
Accident and emergency attendance, mean (SD)	0.06 (0.34)	0.07 (0.48)
PD nurse appointment number, mean (SD)	1.88 (2.09)	1.69 (1.78)
Social care		
Health visitor contact number, mean (SD)	0.26 (1.00)	0.12 (0.55)
Social worker contact number, mean (SD)	0.36 (2.15)	0.16 (0.75)

TABLE 15 Costs associated with therapy and control group

	Mean cost (£) per patient		
Cost category	PT/OT, $n = 381$	Control, $n = 381$	Mean difference (95% CI)
PT/OT	136	62	74 (61 to 88)
Primary care	322	336	–15 (–54 to 25)
Secondary care	1150	1084	65 (–163 to 308)
Aid or adaptation	18	22	–5 (–15 to 7)
Social care	82	36	44 (9 to 92)
Total NHS and Personal Social Services	1708 (1379 to 2072)	1541 (1329 to 1752)	164 (–141 to 468)

TABLE 16 Total costs, QALYs and ICER (95% CI)

Allocation	Total cost (£)	Incremental cost (£)	QALYs	Incremental QALYs	ICER (£)
Control	1541 (1329 to 1752)	–	0.764 (0.737 to 0.791)	–	–
PT/OT	1708 (1379 to 2072)	164 (–141 to 468)	0.791 (0.765 to 0.818)	0.027 (–0.010 to 0.065)	3493 (–169,371 to 176,358)

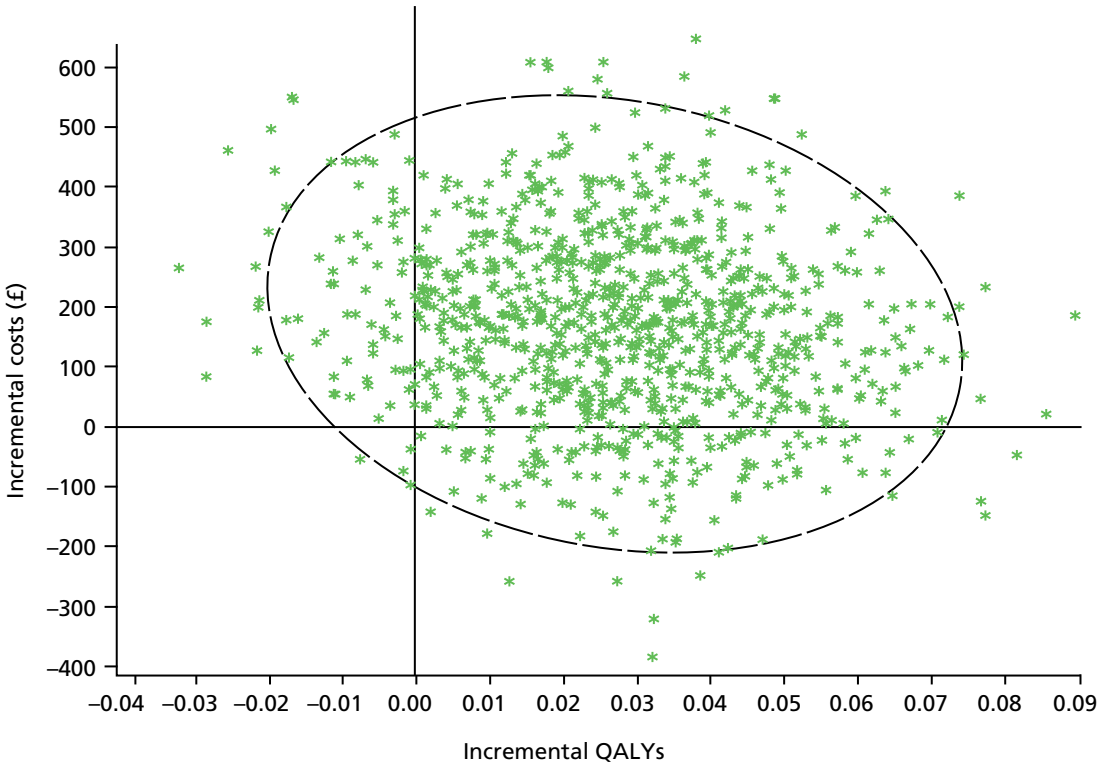

FIGURE 4 Incremental costs and QALYs for therapy compared with control: cost-effectiveness plane.

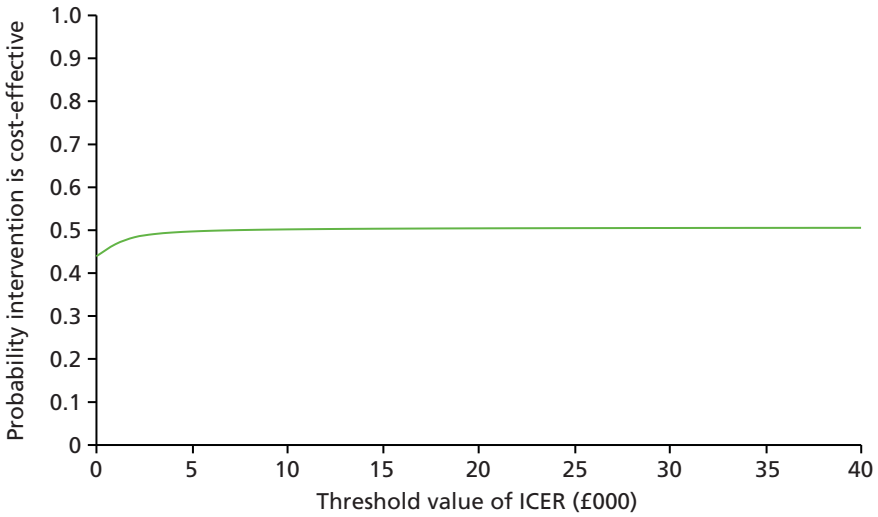

FIGURE 5 Cost-effectiveness acceptability curve.

Chapter 4 Discussion

Key findings

Effectiveness analysis

The PD REHAB trial showed that NHS PT and OT produced no immediate beneficial effects on ADL or QoL in patients with mild to moderate PD. At 3 months, there was no difference in NEADL total score (difference 0.5 points, 95% CI –0.7 to 1.7; $p = 0.4$) or PDQ-39 summary index (difference 0.007 points, 95% CI –1.5 to 1.5 points; $p = 1.0$) between groups. EQ-5D quotient was of borderline significance in favour of therapy (–0.03, 95% CI –0.07 to –0.002; $p = 0.04$).

Using repeated measures analysis, the NEADL primary outcome measure failed to show any effect 9 and 15 months after randomisation (NEADL total score 0.07 higher in the therapy arm, 95% CI –0.64 to 0.77; $p = 0.9$). In contrast, the PDQ-39 summary index (curves diverging at 1.55 points per annum, 95% CI 0.47 to 2.62 points; $p = 0.005$) and EQ-5D quotient (0.02, 95% CI 0.00007 to 0.03; $p = 0.04$) showed significant differences in favour of the therapy arm with long-term follow-up. Crucially, however, the absolute size of the long-term difference in PDQ-39 summary index was small (15-month difference 2.2 points, 95% CI 0.5 to 3.9 points; $p = 0.01$) and not at a clinically significant level, which we had previously set at twice the MCIC value (1.6×2 points),[23] so it is unlikely to be clinically significant to patients. The small difference in PDQ-39 summary index was driven by differences in the PDQ-39 domains of ADL (curves diverging at 2.29 points per annum, 95% CI 0.58 to 4.01; $p = 0.009$), emotional well-being (curves diverging at 2.66 points per annum, 95% CI 1.0 to 4.31; $p = 0.002$) and social support (curves diverging at 1.92 points per annum, 95% CI 0.33 to 3.51 points; $p = 0.02$) in favour of therapy. Importantly, these differences do not reach the individual MCIC levels for these domains either (4.4, 4.2 and 11.4, respectively).[23]

The PD REHAB trial clearly shows that PT and OT, as currently practised in the NHS, do not produce immediate or long-term clinically meaningful improvements in ADL or QoL in patients with mild to moderate PD.

Health economics analysis

The PD REHAB trial found no statistically significant differences in its primary outcome. While PT/OT was associated with a small gain in QALYs at a small incremental cost, the difference was not statistically significant. These QALY and cost results are unsurprising given that any difference was premised on a change in the primary outcome.

The protocol required expressing these results in terms of a CEAC. This approach employs differences in both cost and QALYs regardless of statistical significance. The intervention led to a small incremental QALY gain at a small incremental cost. The incremental cost per QALY was just under £4000 but had wide CIs (*Table 16*).

The CEAC put the probability of the intervention being cost-effective for a willingness-to-pay threshold of both £20,000 and £30,000 at 50.5%.

More robust findings might be expected from a meta-analysis of other relevant studies. However, as reported previously, only one other trial that included evidence on cost-effectiveness was identified.[27] It, too, showed no statistically significant difference in either costs or outcomes, so its inclusion would make little difference to the overall outcome.

The cost-effectiveness analysis depended on the assumption that change in PD medication in the short term was unlikely. There was a possibility that the effect of PT/OT could be beneficial, leading to a reduction in medication in the intervention group. However, there was no difference in levodopa dose equivalents in either arm between baseline and 15-month follow-up, so this will not have affected the cost-effectiveness analysis.

On reflection, we consider that CEAC analysis should proceed only if the results show a difference in outcome that is considered clinically meaningful. This seems unlikely in the case of PD rehabilitation.

Adverse events

Following a risk assessment, only targeted adverse events were recorded in PD REHAB. These included therapy-related adverse events and serious adverse events, such as falls or equipment failure leading to injury requiring a hospital, GP or ambulance visit. Falls occurred in a similar number of patients in the therapy and control arms over the first 3 months and the whole 15 months of the trial. Injuries using a rollator or frame were reported by one patient in each arm of the trial.

Subgroup analyses

Planned subgroup analyses were performed to examine whether the NEADL score response at 3 months was dependent on initial disability with the NEADL total score (severe, 0–21; moderate, 22–43; and mild, 44–66), age (< 60 years, 60–69 years, 70–79 years and ≥ 80 years), or disease severity using the Hoehn and Yahr stage (≤ 2, 2.5, 3 and ≥ 4). As detailed in *Figure 3*, no trends in response were found with any of these variables.

We hypothesised that patients with more severe disease would show a better response, but the subgroup analyses examining the response according to the baseline NEADL score and Hoehn and Yahr stage do not support this. Similarly, older patients might respond better to the therapies because of greater levels of frailty and comorbidities, but there was no evidence of this in the subgroup analysis.

Lack of response

Our Cochrane review of PT versus no intervention in PD showed that all forms of PT produced small benefits in motor function and ADL but no change in QoL.[8,9] The Cochrane review of OT found insufficient evidence about effectiveness.[7] The absence of any motor effect (PDQ-39 mobility domain) or response in ADL in PD REHAB is likely to be multifactorial because of the early disease stage of most of the patients, the low dose of intervention, and the lack of consistency in therapy assessment and intervention approaches.

Trial population

Traditionally, PT and OT have been used in the more advanced stages of PD, often once balance problems and falls have developed (Hoehn and Yahr stage 3 and above).[2] Most patients in PD REHAB had Hoehn and Yahr scores less than 3 at randomisation, so less severe disease may not respond to therapies as delivered in the NHS, whereas more severe disease may respond, although this remains to be established.

Therapy dose

The median therapy dose was four sessions of 58 minutes over 8 weeks for both therapies combined, including assessments. This is low in comparison with the previous five PT trials in the Cochrane review (5–52 weeks' therapy).[8] A recent Dutch trial of PT in Parkinson's disease (ParkNet)[29] also showed no evidence in favour of therapy.[40] Total contact time between patients and physiotherapists over 6 months in ParkNet was 15 sessions of 30 minutes, nearly double that in PD REHAB.[29] Importantly, however, the dose delivered in PD REHAB reflects what therapists routinely deliver in NHS practice.

Lack of consistency in therapy assessment and intervention approaches

Therapy expert groups recommended an individual goal-setting approach for the PD REHAB interventions, as this is recognised as gold standard practice and addresses the personalised needs and wishes of the individual receiving rehabilitation. The content of both types of therapy (see *Tables 9* and *10*) was in keeping with UK NHS PT and OT and European guidelines.[3–6] However, an individualised goal-setting approach with this content may not be directly transferable to patients with mild disease, particularly when no treatment protocol exists for early PD. Expert groups were very supportive of early referral. Indeed, we were unable to run the study in some sites as all patients were automatically referred at their first PD clinic appointment, so the team was not in equipoise about the value of the therapies.

The lack of task-related practice was also of particular concern, as this activity is a logical 'practice makes perfect' intervention when struggling with specific ADL and, more importantly, has been shown to be a significant factor in functional recovery in stroke rehabilitation trials.[41]

We were also very concerned by the low and unstructured prescription of exercise in the PD REHAB trial, in addition to the low dose of exercise, which we would have expected to see administered as routine practice in the early stages of the disease.

Carer quality of life

The small difference in favour of therapy in the carer SF-12 mental component summary score at 3 months disappeared with long-term follow-up. This might have been a result of a short-term effect on carer stress but, given the large number of comparisons performed in the trial, this may be a chance finding.

Limitations

Issues concerning low intervention dose, mild disease stage and lack of consistency in therapy assessment and intervention approaches are considered in the preceding sections.

We believe the fidelity of the intervention was reasonable in both arms of this pragmatic real-world trial. In the PT and OT arm, 93% of patients received the therapies within 3 months of randomisation (CONSORT diagram; see *Figure 1*), whereas only 2% of the no therapy arm crossed over to receive treatment within 3 months, mainly a result of progression of motor problems. It is unlikely that these small proportions of crossovers led to the lack of effect seen in the trial.

In spite of all of the patients suffering from self-reported problems with ADL, many had mild disease with near normal NEADL scores. This may have led to a floor effect, as the NEADL score could not improve much from such a good baseline score. However, this emphasises still further our conclusion that existing NHS PT and OT in this well-functioning population is ineffective.

Implications for trial design

Size and duration

The PD REHAB ($n = 762$), the Dutch ParkFit[42] ($n = 540$) and the ParkNet[29] ($n = 699$) trials show that large pragmatic rehabilitation trials are feasible in PD and that long-term follow-up is mandatory and achievable. Previous PT trials in PD have been relatively small (range 6–153) and with follow-up of less than 3 months.[8] It is now clear that larger and longer trials can be done in PD, and these will provide more reliable answers.

The successful pragmatic design of PD REHAB shows that patients will complete questionnaires and post them back long after therapy has been completed. This positive experience is in keeping with our previous pragmatic trials of medical interventions (PD MED) and surgery (PD SURG) in PD.[36,43,44]

Therapy content

The PD REHAB trial adopted an individualised goal setting approach to PT and OT which may not be directly transferable to patients with mild PD. This resulted in a relatively low dose of therapy intervention, with a lack of task-related practice and surprisingly low levels of exercise prescribed. The content of OT was as expected in terms of provision of equipment (e.g. bed levers, etc.) and onward referral to other services. However, we would have expected to have observed evidence of more practice of specific ADL tasks. In future trials of physical therapies in PD, more formalised and intensive intervention programmes should be adopted with more task-related practice, as this may be more effective.

Patient and public involvement

Trial design

A representative from Parkinson's UK (Mrs Ramilla Patel, Regional Manager, Parkinson's UK) was a co-applicant on the grant. She was involved in the design of the study and was a member of the trial management group. Specific participant-oriented responsibilities were also discussed in the Patient Advisory Group, namely participant and carer information sheets.

Improved communication

One of the main roles of the Patient Advisory Group was to ensure that the language used in all trial documentation, newsletters and other communications with participants were comprehensible by a non-expert audience. Specifically, the group:

1. reviewed and edited the participant information sheets and consent forms
2. wrote articles in the newsletters reflecting their experiences of PD. These newsletters were sent to our whole trial community including doctors, nurses, therapists, participants and carers
3. were involved in the dissemination of results to participants and carers mainly through the Parkinson's UK newsletter.

The patient as the expert

Throughout the PD REHAB trial, annual meetings were held to provide support and education, and to share best practice for physiotherapists and occupational therapists. A key part of the ongoing training was the inclusion of panel sessions where the patient was the expert. The three annual patient panel sessions were a popular and insightful opportunity for patients to describe and reflect on their experiences of PT or OT. This reversal of the usual patient/therapist roles provided a forum for the patients to candidly discuss their view of therapy and answer therapists' questions in a neutral environment.

Oversight

In line with the HTA guidelines, two members of the Patient Advisory Group were also members of the trial steering committee.

Patient Advisory Group support

Members of the Patient Advisory Group were supported by Mrs Ramilla Patel and the person leading the group. The latter changed over the course of the trial, commencing with Dr Sandy Herron-Marx, then Sunil Shah and finally Dr Caroline Rick. Patient Advisory Group communication was primarily by e-mail. This reduced travel burden on people with a movement disorder and enabled people who lived further from Birmingham to participate. It also allowed people to review documents at their own convenience. The group membership was flexible, so people could opt out of reviewing/writing documents or leave the group if they were no longer able or willing to participate.

Non-viable objectives

Part of the Patient Advisory Group's remit was to develop recommendations for practice and patient information leaflets (top-tip leaflet) about therapy choices based on the results of the trial. However, the null result of the trial precluded any such involvement.

Dissemination

Members of the Patient Advisory Group were invited to the final Collaborators' Meeting to hear the first trial results at the same time as the other collaborators. The group were involved in writing the lay summary of the trial findings for the participants, which was disseminated at the same time as the results were published in a peer-reviewed journal.

Lessons learned from Patient Advisory Group

The role of patient and public involvement in clinical research is a constantly evolving process. Since the completion of the PD REHAB trial, we have developed a generic Parkinson's Patient Advisory Group with the support of Parkinson's UK. This group will work across all of the PD trials in the BCTU portfolio. This will include the design of new trials and the interpretation and dissemination of the long-term results of the older trials. Individual members have the option to opt in or out of any project depending on their personal experience and interest. Feedback from the PD REHAB Patient Advisory Group has informed this new group's objectives and code of conduct.

Conclusions

What the study found

The NHS-provided PT and OT did not produce immediate or long-term clinically meaningful improvements in ADL or QoL in mild to moderate PD. This evidence does not support the use of low-dose, patient-centred, goal-directed PT and OT in patients in the early stages of PD.

Implications for research

More formalised and intensive physical therapy programmes should be developed for different stages of PD. These should then be tested in large-scale RCTs at all stages of PD. Such trials should include QoL measures and follow-up should continue for at least 1 year after the therapy to look for any long-term or carry-over effects of therapy.

Acknowledgements

We thank all the patients who agreed to enter the study, the investigators who contributed to the trial and the Dementia and Neurodegenerative Disease (DeNDRoN) Clinical Research Network for their support with recruitment. We also thank the Service Users Group for their help in designing the trial. The PDQ-39 questionnaire was developed by Crispin Jenkinson, Ray Fitzpatrick and Viv Peto in 1993, who have asserted their moral rights in it, and the copyright, which is owned by Isis Innovation Limited. The questionnaire was first published in 1995 in the journal *Quality of Life Research*. No part of this questionnaire may be reproduced without the prior written consent of Isis Innovation Limited.

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Carl E Clarke (Chief Investigator), **Catherine M Sackley**, **Marion F Walker**, **Natalie Ives** and **Keith Wheatley** designed the trial.

Carl E Clarke, **Catherine M Sackley**, **Natalie Ives**, **Keith Wheatley**, **Smitaa Patel** and **Caroline E Rick** ran the trial and **Carl E Clarke** recruited patients.

Natalie Ives, **Smitaa Patel** and **Rebecca Woolley** performed the interim and final data analyses.

Shihua Zhu, **Rebecca Kandiyali** and **Guiqing Yao** performed the health economics analysis.

Carl E Clarke, **Catherine M Sackley**, **Marion F Walker**, **Natalie Ives**, **Smitaa Patel**, **Caroline E Rick**, **Keith Wheatley** and **Guiqing Yao** interpreted the data and wrote the paper. The authors assume responsibility for the accuracy and completeness of the data and for the overall content and integrity of the paper.

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Publications from PD REHAB

Clarke CE, Patel S, Ives N, Rick CE, Dowling F, Woolley R, *et al.* Physiotherapy and occupational therapy vs no therapy in mild to moderate Parkinson disease: a randomized clinical trial. *JAMA Neurol* 2016;**73**:291–9.

Clarke CE, Patel S, Woolley R, Ives N, Rick CE, Wheatley K, Walker MF, Sackley CM, on behalf of the PD REHAB Collaborative Group. PD REHAB RCT of physio- and occupational therapy in Parkinson's disease. Association of British Neurologists Annual Conference, Cardiff, UK, May 2014.

Clarke CE, Patel S, Woolley R, Ives N, Rick CE, Wheatley K, Walker MF, Sackley CM, on behalf of the PD REHAB Collaborative Group. PD REHAB: A large pragmatic randomised controlled trial of physiotherapy and occupational therapy versus no therapy in mild to moderate Parkinson's disease. 18th International Congress of Parkinson's Disease and Movement Disorders, Stockholm, Sweden, 8–12 June 2014.

Dowling FP, Rick C, Sackley C, Walker M, Ives N, Patel S, *et al.* Parkinson's disease REHAB: Randomised controlled trial to study the effectiveness and cost-effectiveness of physiotherapy and occupational therapy for people with PD. 16th International Congress of Parkinson's Disease and Movement Disorders, Dublin, Ireland, 17–21 June 2012. *Mov Disord* 2012;**27**:S115, meeting abstract: 360.

Rick C, Clarke C, Sackley C, Walker M, Ives N, Patel S, *et al.* on behalf of the PD REHAB Collaborative Group. PD REHAB: randomised controlled trial to study the effectiveness and cost-effectiveness of physiotherapy and occupational therapy for people with PD. *Mov Disord* 2010;**25**:S717.

Dowling FP, Rick CE, Clarke CE, Walker M, Ives N, Patel S, *et al.* PD REHAB: randomised controlled trial to study the effectiveness and cost-effectiveness of physiotherapy and occupational therapy for people with PD. Parkinson's UK conference, York, 2010.

References

1. de Lau LM, Breteler MM. Epidemiology of Parkinson's disease. *Lancet Neurol* 2006;**5**:525–35. http://dx.doi.org/10.1016/S1474-4422(06)70471-9
2. National Collaborating Centre for Chronic Conditions. *National Institute for Health and Clinical Excellence (NICE) Guidelines – Parkinson's Disease: Diagnosis and Management in Primary and Secondary Care*. London: Royal College of Physicians; 2006.
3. Plant RP, Jones D, Ashburn A, Lovgreen B, Kinnear E, Handford F. *Evaluation of Physiotherapy in Parkinson's Disease: Project Update. The Science and Practice of Multidisciplinary Care in Parkinson's Disease and Parkinsonism.* London: British Geriatric Society; 1999.
4. Keus S, Hendriks H, Bloem B, Bredero-Cohen A, de Goede C, van Haaren M, *et al. KNGF Guidelines for Physical Therapy in Patients with Parkinson's Disease*. Amersfoort: Royal Dutch Society for Physical Therapy; 2004.
5. Deane K, Ellis-Hill C, Dekker K, Davies P, Clarke CE. A survey of current occupational therapy practice for Parkinson's disease in the United Kingdom. *Br J Occup Ther* 2003;**66**:193–200. http://dx.doi.org/10.1177/030802260306600503
6. Deane K, Ellis-Hill C, Dekker K, Davies P, Clarke CE. A Delphi survey of best practice occupational therapy practice for Parkinson's disease in the United Kingdom. *Br J Occup Ther* 2003;**66**:247–54. http://dx.doi.org/10.1177/030802260306600603
7. Dixon L, Duncan D, Johnson P, Kirkby L, O'Connell H, Taylor H, *et al.* Occupational therapy for patients with Parkinson's disease. *Cochrane Database Syst Rev* 2007;**3**:CD002813. http://dx.doi.org/10.1002/14651858.CD002813.pub2
8. Tomlinson CL, Patel S, Meek C, Clarke CE, Stowe R, Shah L, *et al.* Physiotherapy versus placebo or no intervention in Parkinson's disease. *Cochrane Database Syst Rev* 2012;**8**:CD002817. http://dx.doi.org/10.1002/14651858.CD002817.pub2
9. Tomlinson CL, Patel S, Meek C, Herd CP, Clarke CE, Stowe R, *et al.* Physiotherapy intervention in Parkinson's disease: systematic review and meta-analysis. *BMJ* 2012;**345**:e5004. http://dx.doi.org/10.1136/bmj.e5004
10. Clarke CE, Furmston A, Morgan E, Patel S, Sackley C, Walker M, *et al.* Pilot randomised controlled trial of occupational therapy to optimise independence in Parkinson's disease: the PD OT trial. *J Neurol Neurosurg Psychiatry* 2009;**80**:976–8. http://dx.doi.org/10.1136/jnnp.2007.138586
11. Tomlinson CL, Herd CP, Clarke CE, Meek C, Patel S, Stowe R, *et al.* Physiotherapy for Parkinson's disease: a comparison of techniques. *Cochrane Database Syst Rev* 2014;**6**:CD002815. http://dx.doi.org/10.1002/14651858.CD002815.pub2
12. Gibb WRG, Lees AJ. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1988;**51**:745–52. http://dx.doi.org/10.1136/jnnp.51.6.745
13. Sackley C, Atkinson J, Walker M. Occupational therapy in nursing and residential care settings: a description of a randomised controlled trial intervention. *Br J Occup Ther* 2004;**67**:104–10. http://dx.doi.org/10.1177/030802260406700302
14. Paterson M, Higgs J, Wilcox S. The artistry of judgement: a model for occupational therapy practice. *Br J Occ Ther* 2005;**68**:409–11. http://dx.doi.org/10.1177/030802260506800905
15. Ebrahim S, Nouri F, Barer D. Measuring disability after a stroke. *J Epidemiol Commun Health* 1985;**39**:86–9. http://dx.doi.org/10.1136/jech.39.1.86

16. Legg L, Drummond A, Leonardi-Bee J, Gladman JR, Corr S, Donkervoort M, *et al.* Occupational therapy for patients with problems in personal activities of daily living after stroke: systematic review of randomised trials. *BMJ* 2007;**335**:922. http://dx.doi.org/10.1136/bmj.39343.466863.55

17. Sackley C, Wade DT, Mant D, Atkinson JC, Yudkin P, Cardoso K, *et al.* Cluster randomized pilot controlled trial of an occupational therapy intervention for residents with stroke in UK care homes. *Stroke* 2006;**37**:2336–41. http://dx.doi.org/10.1161/01.STR.0000237124.20596.92

18. Clark F, Azen SP, Zemke R, Jackson J, Carlson M, Mandel D, *et al.* Occupational therapy for independent-living older adults. A randomized controlled trial. *JAMA* 1997;**278**:1321–6. http://dx.doi.org/10.1001/jama.1997.03550160041036

19. Walker M, Gladman J, Lincoln N, Siemonsma P, Whiteley T. A randomised controlled trial of occupational therapy for stroke patients not admitted to hospital. *Lancet* 1999;**354**:278–80. http://dx.doi.org/10.1016/S0140-6736(98)11128-5

20. Gilbertson L, Langhorne P, Walker A, Allen A, Murray G. Domiciliary occupational therapy for patients with stroke discharged from hospital: randomised controlled trial. *BMJ* 2000;**320**:603–6. http://dx.doi.org/10.1136/bmj.320.7235.603

21. Ashburn A, Fazakarley L, Ballinger C, Pickering R, McLellan LD, Fitton C. A randomised controlled trial of a home based exercise programme to reduce the risk of falling among people with Parkinson's disease. *J Neurol Neurosurg Psychiatry* 2007;**78**:678–84. http://dx.doi.org/10.1136/jnnp.2006.099333

22. Wade DT, Gage H, Owen C, Trend P, Grossmith C, Kaye J. Multidisciplinary rehabilitation for people with Parkinson's disease: a randomised controlled study. *J Neurol Neurosurg Psychiatry* 2003;**74**:158–62. http://dx.doi.org/10.1136/jnnp.74.2.158

23. Peto V, Jenkinson C, Fitzpatrick R. Determining minimally important differences for the PDQ-39 Parkinson's disease questionnaire. *Age Ageing* 2001;**30**:299–302. http://dx.doi.org/10.1093/ageing/30.4.299

24. Meek C, Morgan E, Walker M, Furmston A, Aragon A, Birleson A, *et al.* Occupational therapy to optimise independence in Parkinson's disease: the designing and recording of a randomised controlled trial intervention. *Br J Occ Ther* 2010;**73**:178–85. http://dx.doi.org/10.4276/030802210X12706313444027

25. Bhatia K, Brooks DJ, Burn DJ, Clarke CE, Grosset DG, MacMahon DG, *et al.* Updated guidelines for the management of Parkinson's disease. *Hosp Med* 2001;**62**:456–70. http://dx.doi.org/10.12968/hosp.2001.62.8.1621

26. Parkinson's Disease Society. *Parkinson's Aware in Primary Care*. London: Parkinson's Disease Society; 2003.

27. Fletcher E, Goodwin V, Richards S, Campbell J, Taylor R. An exercise intervention to prevent falls in Parkinson's: an economic evaluation. *BMC Health Serv Res* 2012;**12**:426. http://dx.doi.org/10.1186/1472-6963-12-426

28. Gage H, Kaye J, Owen C, Trend P, Wade D. Evaluating rehabilitation using cost–consequences analysis: an example in Parkinson's disease. *Clin Rehab* 2006;**20**:232–8. http://dx.doi.org/10.1191/0269215506cr936oa

29. Munneke M, Nijkrake MJ, Keus SH, Kwakkel G, Berendse HW, Roos RA, *et al.* Efficacy of community-based physiotherapy networks for patients with Parkinson's disease: a cluster-randomised trial. *Lancet Neurol* 2010;**9**:46–54. http://dx.doi.org/10.1016/S1474-4422(09)70327-8

30. Clarke CE, Patel S, Ives N, Rick CE, Dowling F, Woolley R, *et al*. Physiotherapy and occupational therapy vs no therapy in mild to moderate Parkinson disease: a randomized clinical trial. *JAMA Neurol* 2016;**73**:291–9.

31. Jenkinson C, Fitzpatrick R, Peto V, Greenhall R, Hyman N. The Parkinson's Disease Questionnaire (PDQ-39): development and validation of a Parkinson's disease summary index score. *Age Ageing* 1997;**26**:353–7. http://dx.doi.org/10.1093/ageing/26.5.353

32. Tomlinson CL, Stowe R, Patel S, Rick C, Gray R, Clarke CE. Systematic review of levodopa dose equivalency reporting in Parkinson's disease. *Mov Disord* 2010;**25**:2649–53. http://dx.doi.org/10.1002/mds.23429

33. Schafer J. *Analysis of Incomplete Multivariate Data*. London: Chapman & Hall; 1999.

34. Jenkinson C, Heffernan C, Doll H, Fitzpatrick R. The Parkinson's Disease Questionnaire (PDQ-39): evidence for a method of imputing missing data. *Age Ageing* 2006;**35**:497–502. http://dx.doi.org/10.1093/ageing/afl055

35. PD MED Collaborative Group. Long-term effectiveness of dopamine agonists and monoamine oxidase B inhibitors compared with levodopa as initial treatment for Parkinson's disease (PD MED): a large, open-label, pragmatic randomised trial. *Lancet* 2014;**384**:1196–205. http://dx.doi.org/10.1016/S0140-6736(14)60683-8

36. Williams A, Gill S, Varma T, Jenkinson C, Quinn N, Mitchell R, *et al.* Deep brain stimulation plus best medical therapy versus best medical therapy alone for advanced Parkinson's disease (PD SURG trial): a randomised, open-label trial. *Lancet Neurol* 2010;**9**:581–91. http://dx.doi.org/10.1016/S1474-4422(10)70093-4

37. Curtis L. *Unit Costs of Health and Social Care 2012*. Canterbury: PSSRU, University of Kent; 2012.

38. Department of Health. *Reference Costs 2011–12*. London: Department of Health; 2012.

39. Department of Health. *National Tariff 2011–12.* London: Department of Health; 2012. URL: http://webarchive.nationalarchives.gov.uk/20130507170152/https:/www.gov.uk/government/publications/confirmation-of-payment-by-results-pbr-arrangements-for-2011-12 (accessed 4 April 2013).

40. Rochester L, Nieuwboer A, Lord S. Physiotherapy for Parkinson's disease: defining evidence within a framework for intervention. *Neurodegener Dis Manag* 2011;**1**:57–65. http://dx.doi.org/10.2217/nmt.11.1

41. Walker MF. Stroke rehabilitation: evidence-based or evidence-tinged? *J Rehabil Med* 2007;**39**:193–7. http://dx.doi.org/10.2340/16501977-0063

42. van Nimwegen M, Speelman AD, Overeem S, van de Warrenburg BP, Smulders K, Dontje ML, *et al.* Promotion of physical activity and fitness in sedentary patients with Parkinson's disease: randomised controlled trial. *BMJ* 2013;**346**:f576. http://dx.doi.org/10.1136/bmj.f576

43. Clarke C, Patel S, Ives N, Rick C, Jenkinson C, Wheatley K, *et al.* A large randomised trial assessing quality of life in patients with later PD: results from PD MED LATER. *Parkinsonism Relat Disord* 2012;**18**:S33. http://dx.doi.org/10.1016/S1353-8020(11)70206-1

44. Gray R, Patel S, Ives N, Rick C, Jenkinson C, Wheatley K, *et al.* A large randomised trial assessing quality of life in patients with early Parkinson's disease: results from PD MED EARLY. *Parkinsonism Relat Disord* 2012;**18**:S32. http://dx.doi.org/10.1016/S1353-8020(11)70205-X

Appendix 1 UK Parkinson's Disease Society Brain Bank Diagnostic Criteria

STEP 1. Diagnosis of Parkinsonian syndrome

Bradykinesia (slowness of initiation of voluntary movement with progressive reduction in speed and amplitude of repetitive actions).

And at least one of the following:

(a) muscular rigidity
(b) 4–6 Hz rest tremor
(c) postural instability not caused by primary visual, vestibular, cerebellar or proprioceptive dysfunction.

STEP 2. Exclusion criteria for Parkinson's disease

History of repeated strokes with stepwise progression of Parkinsonian features.

History of repeated head injury.

History of definite encephalitis.

Oculogyric crises.

Neuroleptic treatment at onset of symptoms.

More than one affected relative.

Sustained remission.

Strictly unilateral features after three years.

Supranuclear gaze palsy.

Cerebellar signs.

Early severe autonomic involvement.

Early severe dementia with disturbances of memory, language and praxis.

Babinski sign.

Presence of a cerebral tumour or communicating hydrocephalus on CT scan.

Negative response to large doses of levodopa (if malabsorption excluded).

MPTP exposure.

STEP 3. Supportive prospective positive criteria for Parkinson's disease. Three or more required for diagnosis of definite Parkinson's disease

Unilateral onset.

Rest tremor present.

Progressive disorder.

Persistent asymmetry affecting the side of onset most.

Excellent response (70–100%) to levodopa.

Severe levodopa-induced chorea.

Levodopa response for 5 years or more.

Clinical course of 10 years or more.

MPTP, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine.

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Appendix 2 Patient information sheet

Patient Information Sheet – Front Sheet

Insert Local NHS Trust Logo

RANDOMISED CONTROLLED TRIAL TO ASSESS THE CLINICAL- AND COST-EFFECTIVENESS OF PHYSIOTHERAPY AND OCCUPATIONAL THERAPY IN PARKINSON'S DISEASE (PD REHAB)

Patient Information Sheet

PD REHAB logo – To be inserted

Local PI Contact details here

Local Nurse Contact details here

Local PALS Group Contact detail here

BCTU Contact details

Version 9, 11th June 2010

PATIENT INFORMATION SHEET

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

What is the purpose of the study?

We want to know whether occupational therapy and physiotherapy help people with Parkinson's disease. Occupational therapy mainly aims to improve physical function and independence. It involves a qualified therapist assessing a patient's problems with their disease, often at home, then devising practical ways to help them such as providing aids and adaptations (e.g. walking aids, hand rails, raised seating etc). Physiotherapy focuses on working with the patient, carer and family to improve their understanding of the condition, maintain general fitness and independence in mobility, both inside and outside the home.

Currently there is no good evidence whether occupational therapy and physiotherapy benefit patients with Parkinson's disease. This study aims to answer the question: do patients benefit from therapy and does any benefit persist after they have finished their occupational therapy and physiotherapy? This information will be used to help optimise treatment for future Parkinson's disease patients.

Why have I been asked?

The study will include 750 patients with Parkinson's disease at about 40 centres throughout the United Kingdom. We are asking you to take part in the study because you have Parkinson's disease and you may potentially benefit from occupational therapy and/or physiotherapy.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason though it would be very helpful if you would agree to continue to provide information. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

This is a randomised study. Sometimes, because we do not know which way of treating patients is best, we need to make comparisons. People will be put into two groups. The groups are selected by a computer at random, like flipping a coin. Patients in each group then have a different treatment and these are compared. If you decide to take part, you will be allocated at random to receive occupational therapy and physiotherapy immediately or to

have the therapies deferred until the end of the study after 15 months. You will have a 50:50 chance of getting therapy immediately.

If you decide to take part, the research staff at your site will answer any questions you have then ask you to sign a consent form. They will then ask you to complete the study questionnaires. There are 4 brief questionnaires for you (and one for your carer if they chose to join the trial) at baseline, 3 9 and 15 months. These are easy to do and have been used in Parkinson's disease studies and other conditions for many years. It will take around 20 minutes for you to complete all of these questionnaires.

If you are allocated to immediate therapy, then the trial occupational therapist and physiotherapist at your site will visit you at home to assess what help can be offered. They will then arrange this help and, if necessary, visit you again.

If you are allocated to delayed therapy, we will ask your general practitioner or hospital specialist to defer arranging any occupational therapy or physiotherapy until the study finishes 15 months after you join the trial. You will also get some 'Top-tip' leaflets which will have been developed by the patient/carer group who are part of the study team.

We will send you the same questionnaires to fill in at home 3, 9 and 15 months after you enter the study. You will be asked to complete these, then post them back to us in the freepost envelope we will send you.

What are the possible disadvantages and risks of taking part?

We do not anticipate any disadvantages or risks in taking part. There may be a small increased risk of falls during therapy as participants may become more mobile, but your therapists will minimise this risk by carefully training you. The risk of falls will further be minimised by the specific training of therapists in handling patients with Parkinson's disease.

What are the possible benefits of taking part?

Although you may not benefit directly from taking part, the information we get from this study may help us to look after future patients with Parkinson's Disease better. The top-tip leaflets developed at the end of the study will also be shared with the wider Parkinson's disease community.

What if something goes wrong?

If you are harmed by taking part in this research, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you: ask to speak to the complaints manager of the hospital.

If you have a concern about any aspect of this study you should ask to speak to the researcher who will do their best to answer your questions (Local PI contact details here). If you remain unhappy and wish to complain formally you can contact your local PALS group (contact details here)

Will my taking part in this study be kept confidential?

All information collected in the study will remain strictly confidential in the same way as your other medical records. The information will be put into a computer and analysed, but you will not be identified when the results are reported.

We would also like your permission to tell your GP that you are taking part in the study. You may still take part in the study, if you do not wish us to contact your GP

What will happen to the results of the research study?

The results of the study will be published in a medical journal after the study has been completed but you will not be identified in any report or publication. Carers and patients with Parkinson's disease are part of the study team. They will lead on using the findings from the study to develop 'Top-Tip' leaflets and other lay summaries and share this information with the wider Parkinson's disease community.

What happens if I become incapacitated during the trial?

If you become incapacitated during the trial, you will be withdrawn from the study and we will not send you any further questionnaires. We will keep the information you gave us before you became incapacitated and it will be used in the results of the study.

Who is organising and funding the research?

The study is being funded by the Health Technology Assessment Programme which is part of the UK National Institute for Health Research. No payments will be made to the patients, therapists, nurses, or doctors taking part in the study.

Who has looked at the research?

All research in the NHS is looked at by a independent group of people called a Research Ethics Committee to protect your safety, rights, well being and dignity. This study has been reviewed and approved by *Warwick* Research Ethics Committee *insert date*

Contact for Further Information

Should you want further information about the study please contact: *<Insert details of local PI>*

If you decide to take part in this study, you will be given a copy of this information sheet and a signed consent form to keep.

Thank you for taking the time to read this information sheet.

Version 9, 11th June 2010

Appendix 3 Carer information sheet

Carer Information Sheet – Front Sheet

Insert Local NHS Trust Logo

RANDOMISED CONTROLLED TRIAL TO ASSESS THE CLINICAL- AND COST-EFFECTIVENESS OF PHYSIOTHERAPY AND OCCUPATIONAL THERAPY IN PARKINSON'S DISEASE (PD REHAB)

Carer Information Sheet

PD REHAB logo – To be inserted

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BCTU Contact details

Version 9, 11th June 2010

CARER INFORMATION SHEET

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Thank you for reading this.

What is the purpose of the study?

We want to know whether occupational therapy and physiotherapy help people with Parkinson's disease. Occupational therapy mainly aims to improve physical function and independence. It involves a qualified therapist assessing a patient's problems with their disease, often at home, then devising practical ways to help them such as providing aids and adaptations (e.g. walking aids, hand rails, raised seating etc). Physiotherapy focuses on working with the patient, carer and family to improve their understanding of the condition, maintain general fitness and independence in mobility, both inside and outside the home.

Currently there is no good evidence whether occupational therapy and physiotherapy benefit patients with Parkinson's disease. This study aims to answer the question do patients benefit from therapy, and does any benefit persist after they have finished their occupational therapy and physiotherapy. This information will be used to help optimise treatment for future Parkinson's disease patients.

Why have I been asked?

The trial will include 750 patients with Parkinson's disease and their carers at over 40 centres throughout the United Kingdom.

We are asking you to take part in the study because you are the main carer for someone with Parkinson's disease who has been asked to take part in the PD REHAB trial.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care the person you care for will receive.

What will happen to me if I take part?

We want to find out whether giving the patient you care for occupational therapy and physiotherapy affects your own quality of life. We will do this by asking you to fill in a quality of life questionnaire before the trial begins, then we will post the same questionnaire to you to fill in at home 3, 9 and 15 months after you enter the study.

You will be asked to complete these, then post them back to us in the freepost envelope we will send the participant.

What are the possible disadvantages and risks of taking part?

We do not anticipate any disadvantages or risks in taking part.

What are the possible benefits of taking part?

Although you may not benefit directly from taking part, the information we get from this study may help us to look after future patients with PD better.

Will my taking part in this study be kept confidential?

All information collected in the study will remain strictly confidential in the same way as your other medical records. The information will be put into a computer and analysed, but you will not be identified when the results are reported.

What will happen to the results of the research study?

The results of the study will be published in a medical journal after the study has been completed, but you will not be identified in any report or publication.

Who is organising and funding the research?

The study is being funded by the Health Technology Assessment Programme which is part of the UK National Institute for Health Research. No payments will be made to the patients, therapists, nurses, or doctors taking part in the study.

The study has been approved by National and Local Research Ethics Committees.

Contact for Further Information

Should you want further information about the study please contact: *<Insert details of local PI>*

If you decide to take part in this study, you will be given a copy of this information sheet and a signed consent form to keep.

Thank you for taking the time to read this information sheet

Version 9, 11th June 2010

Appendix 4 Patient consent form

Patient Consent Form

RANDOMISED CONTROLLED TRIAL TO ASSESS THE CLINICAL- AND COST EFFECTIVENESS OF PHYSIOTHERAPY AND OCCUPATIONAL THERAPY IN PARKINSON'S DISEASE (PD Rehab)

Please initial box

1. I confirm that I have read and understand the information sheet dated11th June 2010(Version 9) for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without the quality of my medical care or legal rights being affected. ☐
3. I understand that sections of any of my medical notes may be looked at by responsible individuals running the trial or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐
4. I agree to take part in the above study. ☐
5. I give consent to my GP being informed about my participation in this study. (optional) ☐

_____	_____	_____
Name of patient	Date	Signature
_____	_____	_____
Name of person informing patient	Date	Signature

For further information about the study please contact: *<Insert details of local PI>*

1 for patient; 1 for BCTU; 1 to be kept with hospital notes; 1 for site file

Version 9, 11th June2010

Appendix 5 Carer consent form

Carer Consent Form
RANDOMISED CONTROLLED TRIAL TO ASSESS THE CLINICAL- AND COST EFFECTIVENESS OF PHYSIOTHERAPY AND OCCUPATIONAL THERAPY IN PARKINSON'S DISEASE

Please initial box

1. I confirm that I have read and understand the information sheet dated 11th June 2010 (Version 9) for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected. ☐
3. I agree to take part in the above study. ☐

_____	_____	_____
Name of Carer	Date	Signature
_____	_____	_____
Name of person informing Carer	Date	Signature

For further information about the study please contact: *<Insert details of local PI>*

1 for Carer; 1 for BCTU; 1 to be kept with hospital notes; 1 for site file

Version 9, 11th June2010

Appendix 6 General practitioner letter

Doctor

Practice
Street

City
Postcode

PATIENT NAME	*DATE RANDOMISED*
DATE OF BIRTH	*TRIAL NUMBER*
HOSPITAL NUMBER	*ALLOCATED TREATMENT*

Dear Dr *GP*

Re: Randomised controlled trial to assess the clinical and cost-effectiveness of physiotherapy and occupational therapy in Parkinson's disease (PD REHAB trial)

Your patient, named above, has agreed to take part in the PD REHABtrial. This is a large nationwide pragmatic randomised controlled trial to assess whether occupational therapy and physiotherapy are effective and safe in Parkinson's disease.

In this study, we will examine the effects of occupational therapy and physiotherapy provided in the patient's home compared with no therapy in 750 patients with PD who have significant problems with activities of daily living. Patients who are allocated at random to receive therapy immediately will be visited at home by qualified occupational therapists and physiotherapists who will assess their needs and arrange for treatments, aids and adaptations, etc as necessary. Patients allocated to no therapy will receive standard NHS care.

We would be grateful if you would defer the arrangement of occupational therapy and physiotherapy until after the end of the trial (15 months from randomisation) for this patient. At the end of this period, if this patient was allocated to no therapy, we will contact you in order that the patient can receive physiotherapy and occupational therapy per your usual practice.

We will monitor all patients'mobility, disability (activities of daily living), health-related quality of life and health care costs. These will be assessed by questionnaires before entry to the trial and, by post, at 3, 9 and 15 months after entry to the study. With the data from this trial, we will have sufficient statistical power to show whether combined occupational therapy and physiotherapy are effective and safe in Parkinson's disease and whether they are cost-effective.

The trial is designed to fit in with routine practice as far as possible and to impose minimal additional workload, especially on general practitioners.

PD REHAB is being run by the University of Birmingham Clinical Trials Unit and is co-ordinated by Professor Clarke (neurologist), Professor Sackley (physiotherapist), and Ms Natalie Ives (statistician).

The local co-ordinator for the trial is [*insert name and hospital*]. The trial has been reviewed by the National Research Ethics Committee.

If you require any further information about the study, it can be obtained from: *<Insert details of local PI>*

Please file this letter in the patient's notes. I would appreciate being notified if he/she is no longer one of your patients.

Yours sincerely

Local co-ordinator

University of Birmingham Clinical Trials Unit contact details

Version 9, 11th June2010

Appendix 7 Flow diagram of randomisation process

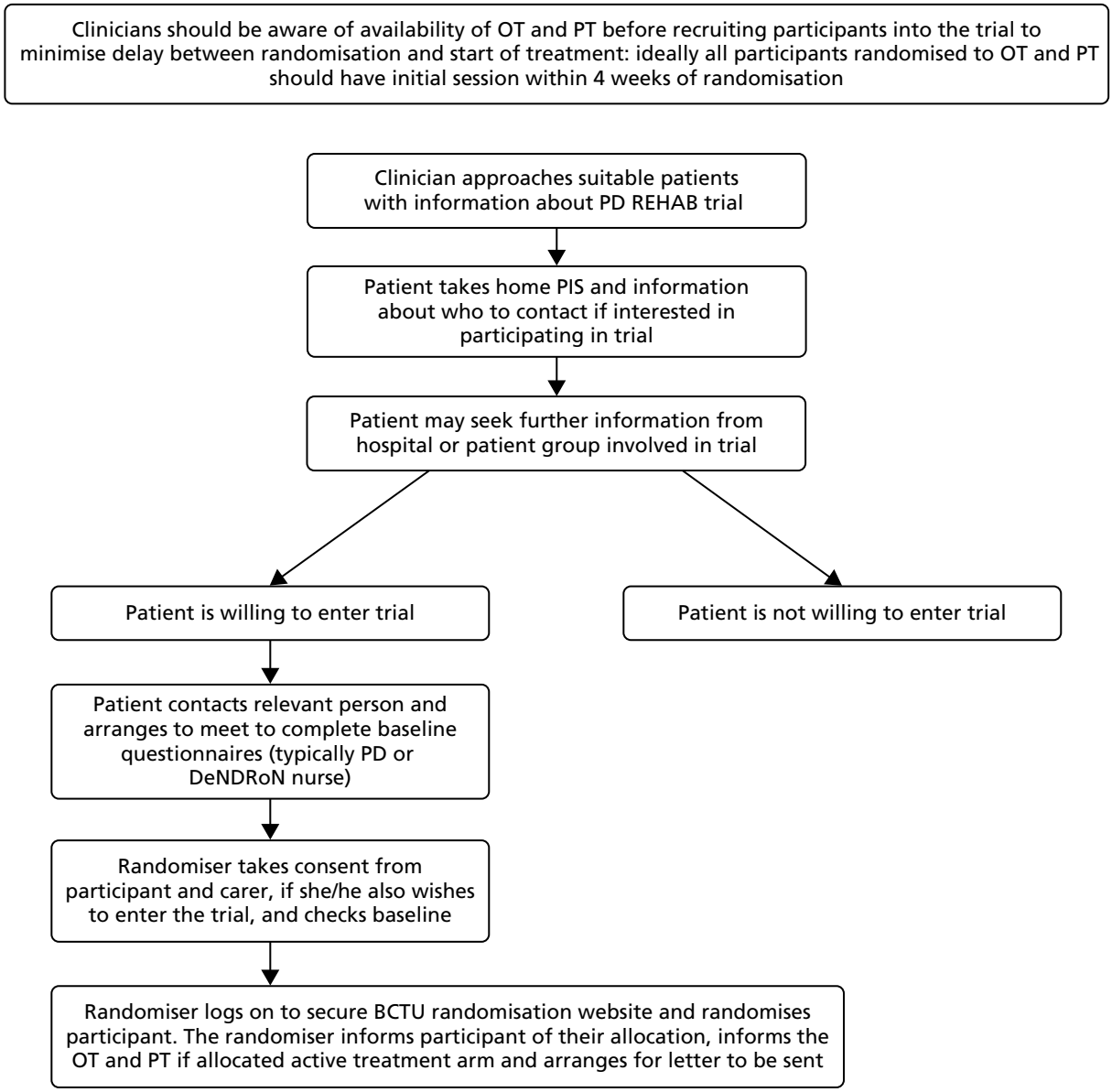


FIGURE 6 Flow diagram. PIS, patient information sheet.

Appendix 8 Hoehn and Yahr stages

Stage 1.0: Unilateral involvement only.

Stage 1.5: Unilateral and axial involvement.

Stage 2.0: Bilateral involvement without impairment of balance.

Stage 2.5: Mild bilateral involvement with recovery on retropulsion (pull) test.

Stage 3.0: Mild to moderate bilateral involvement, some postural instability but physically independent.

Stage 4.0: Severe disability, still able to walk and to stand unassisted.

Stage 5.0: Wheelchair bound or bedridden unless aided.

Appendix 9 Patient baseline data at randomisation

PD REHAB PATIENT Randomisation FORM

Part A: Identifying Details

Patient's full name:	Sex: Male ☐ Female ☐
Date of birth: / /	Hospital number:
Responsible clinician:	Hospital:
Patient's address:	NHS number
	Patient's telephone number:

Part B: Inclusion/Exclusion Criteria

Patient has idiopathic Parkinson's disease: Yes ☐ No ■	Patient reports limitations in activities of daily living: Yes ☐ No ■
Patient has dementia: Yes ■ No ☐	Patient has had occupational therapy in last 1 year: Yes ■ No ☐
Patient has had physiotherapy in last 1 year: Yes ■ No ☐	Patient can be assessed and treated within 1 month: Yes ☐ No ■
Consent has been taken: Yes ☐ No ■	Baseline forms have been completed: Yes ☐ No ■

If any shaded boxes are ticked, the patient is not eligible for randomisation.

Part C: Carer Information

Does the patient have a carer: Yes ☐ No ☐

If carer has consented to join PD REHAB

Name of Carer

Date of birth: / /

Has the carer consented to join PD REHAB: Yes ☐ No ☐

If carer has consented to join PD REHAB

Relationship to Participant

Sex: Male ☐ Female ☐

Part D: NEADL Total

Nottingham Extended ADL Index total:

Now log on to:PD REHAB randomisation Website URL

Part E: Trial Details

Date of Randomisation: ...../..... /..... ..... PD REHAB trial number: .....

Treatment Allocation .....

Version 9, 11th June2010

Appendix 10 Entry form

Identifying Details

Patient's full name:	Patient Trial Number:
Date of birth: / /	Hospital number:

Medical Details

Date of PD Diagnosis: Month: ..... Year:	
Weight:	Unit of Measure: Kg/St (delete as appropriate)
Height:	Unit of Measure: Ft/M (delete as appropriate)
Current Medication Levodopa? No☐ Yes☐ **If yes**, which? ..... Daily dose (mg)? ..... Eg 1 Sinemet 125 tablet = 100mg daily dose (levodopa)	
Dopamine Agonist? No☐ Yes☐ **If yes**, which? ..... Daily dose (mg)?	
MAOB inhibitor? No☐ Yes☐ **If yes**, which? ..... Daily dose (mg)?	
COMT inhibitor? No☐ Yes☐ **If yes**, which? ..... Daily dose (mg)?	
Amantadine? No☐ Yes☐ **If yes** Daily dose (mg)?	
Apomorphine? No☐ Yes☐ **If yes** Daily dose (mg)?	

Duodopa? No ☐ Yes ☐ **If yes**Daily dose (mg)? .....
Other PD Medication? No ☐ Yes ☐ **If yes** What medication? Daily dose (mg)? .....

Form completed by (print name):

Signed: ..... Date: .....

Appendix 11 Occupational therapy initial interview log

PD REHAB Trial Participant	Name:	Trial No:
	DOB:	Date of Interview:

1) INDOOR MOBILITY Prompts: *Turning* *Freezing* *Initiation* *Carrying items / Multi Tasking* *Stairs*	
2) OUTDOOR MOBILITY & TRAVEL Prompts: *Freezing* *Confidence* *Frequency & Destination* *Driving* *Car Transfers* *Public transport*	
3) FALLS Prompts: *When (Time of Day)* *What (Doing)* *Where* Strategies Alarm systems	
4) TRANSFERS Prompts: *Sit to Stand* *Bed Mobility* *Bathing/Showering* *Toilet (Day & Night)*	
5) DRESSING / GROOMING Prompts: *Timing* *Location/Position* *Buttons & fastenings*	
6)EATING / DRINKING Prompts: *Use of Cutlery* *Drinking* *Positioning* *Eating Out*	

7) ENVIRONMENTAL ISSUES Prompts: *Handrails* *Steps* *Banisters* *Organisation of furniture*	
8) HOUSEHOLD TASKS Prompts: *Shopping* *Handling Money* *Cooking* *House Work* *Paperwork & home management*	
9) COGNITIVE/EMOTIONAL Prompts: *Executive Functions* *Visuospatial* *Decision Making* *Depression* *Memory* *Anxiety* *Apathy* *Mood*	
10) COMMUNICATION Prompts: *Speech* *Handwriting* *Phone* Computer	
11)SOCIAL ACTIVITIES Prompts: *Frequency & Location*	
12) SUPPORT Prompts: *Carers* *Allowances / Benefits* *Contact with PDS*	
13) SLEEPING & FATIGUE Prompts: *Routine* *Daytime Sleeping* *Energy Levels*	
14) EMPLOYMENT Prompts: *Contract Hours* *Difficulties*	

Form Completed By: _____

Signed: _____ Date: _____

Appendix 12 Occupational therapy treatment record form

PD REHAB Trial Participant	Name:	Trial No:
	DOB:	Date of Assessment:

Purpose of session – record time in minutes

One to one or group session……

INITIAL INTERVIEW

Location of Intervention……(DESCRIBE - for example - Pt's home / Out-patient Clinic / Pt's local shopping area / Pt's work place / Other)

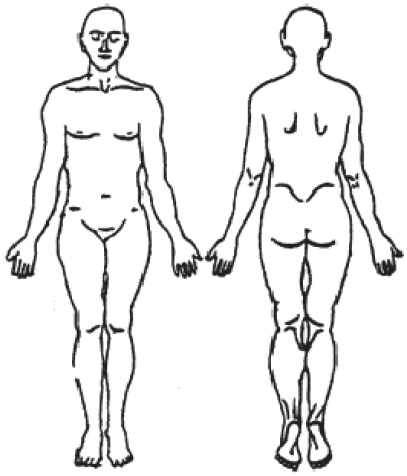
	1. INDOOR MOBILITY	2. OUTDOOR MOBILITY	3. FALLS	4. TRANSFERS	5. DRESSING GROOMING	6. EATING DRINKING	7 ENVIRONMENTAL ISSUES	8 HOUSEHOLD TASKS	9. COGNITIVE EMOTIONAL	10. COMMUNICATION	11. SOCIAL ACTIVITIES	12. SUPPORT	13. SLEEPING & FATIGUE	14. EMPLOYMENT
ASSESSMENT														
GOAL SETTING														
EDUCATION														
REFERRAL														
LIAISON														
EQUIPMENT PRESCRIPTION														
ADAPTATION PRESCRIPTION														
PRACTICE / TRAINING														
SPECIFIC TECHNIQUES														

Form Completed By: _____

Signed: _____ Date: _____

Appendix 13 Initial interview log

PD REHAB Trial Participant	Name:	Trial No:
	DOB:	Date of Interview:
	Time of Interview:	On/ Off Medication:



PRESENTING PROBLEM

HISTORY OF PRESENTING CONDITION

COURSE OF DISEASE AND CURRENT STATUS

IMPAIRMENTS IN FUNCTIONS AND ACTIVITY LIMITATIONS BODY POSTURE, TRANSFERS, BALANCE, GAIT, UPPER LIMB	
PROBLEMS WITH PARTICIPATION	
PHYSICAL ACTIVITY LEVELS	
FALLS AND RISK OF FALLS	
PD TREATMENT MEDICAL, SURGICAL, AHP	
CO-MORBIDITIES	**CO-MORBIDITIES TREATMENT**
SOCIAL AND FAMILY HISTORY	**OTHER**
EXPECTATIONS OF TREATMENT	

PHYSICAL EXAMINATION

BODY POSTURE OBSERVATION, MEASUREMENT
PHYSICAL CAPACITY OBSERVATION, MEASUREMENT
TRANSFERS OBSERVATION, MEASUREMENT
BALANCE OBSERVATION, MEASUREMENT
GAIT OBSERVATION, MEASUREMENT
UPPER LIMB OBSERVATION, MEASUREMENT
OTHER **e.g. OTHER OUTCOME MEASURES**

GOAL SETTING AND TREATMENT PLANNING

Form Completed By: _____

Signed: _____ Date: _____

Appendix 14 Physiotherapy treatment record form

PD REHAB Trial Participant	Name:	Trial No: ☐☐☐☐
	DOB:	Date of Assessment:

Purpose of session – record time in minutes

INITIAL INTERVIEW **One to one or group session……**

Location of Intervention……(DESCRIBE - for example - Pt's home / Out-patient Clinic / Pt's local shopping area / Pt's work place / Other)

	1. Gait and indoor mobility	2. Outdoor mobility	3. Balance and falls	4. Transfers	5. Posture	6. Physical Conditioning	7. Upper-Limb Function	8. Self-Care	9. Domestic ADL	10. Leisure-related activities	11. Work-related (paid and non-paid) activities	12. Other
Initial assessment												
Goal setting												
Ongoing assessment and review												
Compensatory strategies												
Cueing and cognitive strategies												
Visual, auditory (including verbal), and sensory feedback												
Strength training												
Flexibility training												
Coordination and movement control training												
Aerobic/ endurance training												
Balance training												
Functional, task-specific training												
Education, advice and information												
Provision of aids and equipment												
Training of caregiver(s)												
Liaison												
Referral												
Other												

Assessment completed by…… Date ……/……../……..

Signed……..……

Appendix 15 Health-care usage questionnaire

We would like to know how much use you have made of the health and social services over the last 3/6 *deleted as appropriate* months. If you are not exactly sure, we would rather have your best guess than no information at all.

Please answer every question, even if the answer is 'No'.

1 Over the last 3/ 6 *deleted as appropriate* months, if, and how many times, have you used the services of any of the following:

Type of service	**No**	**Yes**	**If yes: Number of visits**
a. A GP?			
At home?			
In the surgery?			
b. A practice nurse?			
At home?			
In the surgery?			
c. A Parkinson's Disease Nurse Specialist?			
d. A health visitor?			
e. A social worker?			
f. A physiotherapist?			
g. An occupational therapist?			
h. A speech or language therapist?			
i. A private practitioner such as an acupuncturist			
j. Other (please specify)			

2. Over the last 3 / 6 months, have you suffered from a fall that resulted in injury and/or medical attention?

☐ No, please go to question 3

☐ Yes, please give details:

a) Did you see your GP? No ☐ Yes ☐ How many times _____

Dates of fall (day/month/year):

1st fall _____; please give details: _____

2nd fall _____;please give details: _____

3rd fall _____ ;please give details: _____

b) Were you seen by Ambulance Staff? No ☐ Yes ☐ How many times _____

Dates of fall (day/month/year):

1st fall _____ ; please give details: _____

2nd fall _____ ;please give details: _____

3rd fall _____ ;please give details: _____

3. Over the last 3 / 6 months have you been to hospital for any reason (include falls)?

☐ No

☐ Yes, please give details:

Outpatient visit (please go to 3a) or A & E (please go to 3b);In patient (please go to 3c)

3a. Hospital outpatients

Episode*	**Name of Hospital**	**Reason for the Appointment**	**Speciality of Department**	**Number of appointments***
1st				
2nd				
3rd				

*episode means a visit or group of visits related to a particular problem. Please write down how many appointments you have had for each episode.

3b. Accident & emergency (or A&E please include visits which took place immediately before any admissions to hospital).

Episode	**Name of Hospital**	**Reason for visits**	**Is this because of a fall?**
1st			
2nd			
3rd			

3c. Hospital Inpatient

Episode	**Name of hospital**	**Ward Speciality**	**Reasons for Admission**	**No. of nights***

1st				
2nd				
3rd				

**If you were treated as a day patient (day case), then please write 0 under "number of nights" Being a day patient means needing a hospital bed for tests or surgery for a half day or full day, but not needing to stay overnight.*

4a. Are you currently in paid employment?

No ☐ (please go to question 4c) Yes ☐ (please go to question 4b)

4b If yes, due to your Parkinson's disease have you had to reduce the number of hours per week you work due to your Parkinson's disease over the last 3/6 *deleted as appropriate*months? (*Please tick only one*).

☐ No, I work the same hours. Please state how many hours this is ☐

☐ Yes, I have had to reduce my working hours by ☐ working hours per- week.

4c If you are not employed:,

In the last 3/6 *deleted as appropriate*months have you had to stop work completelydue to your Parkinson's disease

☐ No ☐ Yes

In the last 3/6 *deleted as appropriate*months have you had to reduce the number of hours per week you spend carrying out your normal daily activities?

☐ No

☐ Yes I have had to reduce them by ☐ hours per week. (eg gardening, housework, social activity).

5 Over the last 3/6 *deleted as appropriate* months has a relative or friend taken time off work to look after you?

☐ No

☐ Yes, how many hours ☐

☐ Yes, had to stop work completely

6 In the last 3/6 *deleted as appropriate* months did you make regular use of the following?

Name of service	**No**	**Yes**	**If yes:** **Number of times on average per week?**
a. Home care/home help			How many home visits?
b. Meals on wheels			How many meals?
c. Day centre			How many days?
d. Luncheon Club			How many meals?
e. Sitting Service			How many days?
f. Other (please specify)			

7. Have you moved into institutional care (i.e. a residential or nursing home)?

☐ No

☐ Yes, date admitted (month/ year):_____

Type of home: ☐ Nursing ☐ Residential

Address of Home _____

_____

8 In the last 3/6 *deleted as appropriate* months did you buy any aid or adaptation paid by yourself or by a friends or relative? Eg, walking frames, grab bars, stair lift, wheel chair

Type of aid or adaptations	**No**	**Yes**	**Cost to you (£'s)**
a			
b			
c			
d			

9. In the last 3/6 *deleted as appropriate*months, approximately how much additional money have you spent on travel (taxis car park fees and public transport because of your Parkinson's disease

☐ None

☐ Yes,I have spent £ _____

10. Do you have to pay for your Parkinson's disease medication?

☐ No

☐ Yes,I have spent £ _____ per month

11. Do you receive benefits?

☐ No

☐ Yes,

Low ☐ Medium ☐ High ☐

12. If you would like to tell us about any other costs incurred because of your Parkinson's disease over the last 3/6 *deleted as appropriate*months, please write them here.

☐ No

☐ Yes, please give details: .....

Thank you for your help.

Version 9, 11th June2010

Appendix 16 Adverse event/serious adverse event form

The only adverse events being recorded in this trial are 'falls or equipment failure leading to injury requiring a hospital or GP visit'. If such an event should occur, please report this by fax to the trial office as soon as possible using the form below.

Patient Details:

Patient's full name: Sex: Male ☐ Female ☐

Date of birth: / / Hospital number:

Responsible clinician: Hospital:

PD REHAB trial number:

AE Description:

Date event started: ...../...../..... Date event ceased: ...../...../.....

Outcome: Fatal ☐ Recovered ☐ Continuing ☐

Details of adverse event: .....

.....

.....

.....

.....

Did the event require hospitalisation? No ☐ Yes ☐ No of days ☐

Reason why you consider event to be intervention related: .....

.....

.....

.....

Name of person reporting: .....

Telephone Number: .....

Date: ...../...../.....

Version 9, 11th June 2010

Appendix 17 Trial exit form

PD REHAB Trial Participant Number	Participant name
Exited PD REHAB Trial on	*insert date*

Has the patient died? No ☐ Yes ☐

If Yes, When did they die, ...

What was the cause of death .....

Weight on exiting the trial .....

Medication on exiting trial

Levodopa? No ☐ Yes ☐

If yes, which? ..... Daily dose (mg)? .....

Eg 1 Sinemet 125 tablet = 100mg daily dose (levodopa)

Dopamine Agonist? No ☐ Yes ☐

If yes, which? ..... Daily dose (mg)? .....

MAOB inhibitor? No ☐ Yes ☐

If yes, which? ..... Daily dose (mg)? .....

COMT inhibitor? No ☐ Yes ☐

If yes, which? ..... Daily dose (mg)? .....

Amantadine? No ☐ Yes ☐

If yes Daily dose (mg)? .....

Apomorphine? No ☐ Yes ☐

If yes Daily dose (mg)? .....

Duodopa? No☐ Yes☐ **If yes** Daily dose (mg)? .....
Other PD Medication? No☐ Yes☐ **If yes** What medication? Daily dose (mg)? .....

Your patient was randomised to the *Physiotherapy and Occupational therapy* / *Control*group. If randomised to the control group, did you prescribe Occupational or Physiotherapy in the last 15 months?

Occupational therapy No☐ Yes☐ if yes, please give details .....

Physiotherapy No☐ Yes☐ if yes, please give details .....

Control group patients may now be referred for PT or OT through your normal mechanisms
Please return this questionnaire in the freepost envelope provided.

Version 9, 11th June2010

Appendix 18 Patient invitation letter

<<Hospital Logo>>

INVITATION

PD REHAB - Randomised Controlled Trial to Assess the Clinical- and Cost-Effectiveness of Physiotherapy and Occupational Therapy in Parkinson's Disease

Dear Patient,

We are carrying out a clinical trial that is managed by the University of Birmingham to examine the effectiveness of Occupational therapy and Physiotherapy for people with Parkinson's disease funded by the National Institute for Health Research. We understand that you have Parkinson's disease (PD) and *have expressed an interest / joined a register indicating that you might be interested<delete as appropriate>* in taking part in Parkinson's disease research.

If you have Parkinson's disease and have difficulties with some activities of daily living and have not had Physiotherapy or Occupational therapy in the last 12 months, you could be eligible to join the trial. The trial has to compare groups of people who are receiving therapy and those who are not. So joining the trial would give you a 50:50 chance of receiving Occupational therapy and Physiotherapy.

For those joining the trial we will use questionnaires to follow the progress of your quality of life at the start, and at 3, 9 and 15 months into the trial. We would also like to ask your own doctor about your health and will need to know about any medications you are taking for your Parkinson's disease. Of course if you were deemed by your doctor to be in urgent need of either or both services you would be referred in the normal way.

We enclose a patient information sheet (version 9) for you which describes the trial.

Would you like to take part in this trial?

Would you like to learn more about this clinical trial?

Do you have any other questions?

Then please contact us at the address above or complete the attached reply slip and we will be in touch with you.

Yours sincerely,

<local PI>

Reply Slip

Please complete this reply slip and send to:

<Local PI>
Address
Address
Address

I am:

- ☐ Interested in taking part in the study
- ☐ Would like to learn more about the study
- ☐ Do not wish to take part in the study

Name ……

Address ……
……
……
……
……

Tel: ……

Email: ……

Any other questions or comments

Thank you.

EME
HS&DR
HTA
PGfAR
PHR

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