Physiotherapy and occupational therapy vs no therapy in mild to moderate Parkinson disease

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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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Abstract

IMPORTANCE It is unclear whether physiotherapy and occupational therapy are clinically and cost-effective in Parkinson's disease.

OBJECTIVE To perform a large pragmatic randomised trial to evaluate the clinical and cost-effectiveness of individualised physiotherapy and occupational therapy in Parkinson's disease.

DESIGN, SETTING, AND PATIENTS PD REHAB was a multicenter, open label, parallel group, controlled efficacy trial. 762 patients with mild-moderate Parkinson's disease were recruited from 38 sites across the United Kingdom. Recruitment took place between October 2009 and June 2012.

INTERVENTIONS Participants with limitations in activities of daily living (ADL) were randomised to physiotherapy and occupational therapy or no therapy.

MAIN OUTCOMES AND MEASURES The primary outcome was the Nottingham Extended Activities of Daily Living (NEADL) scale at 3 months post-randomisation. Secondary outcomes were: health-related quality of life (QoL; Parkinson's Disease Questionnaire-39, PDQ-39; EuroQol-EQ-5D); adverse events; carer QoL. Outcomes were assessed before, 3, 9, and 15 months post-randomisation.

RESULTS At 3 months, there was no difference between groups in NEADL total score (difference 0·5 points, 95% 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). EuroQol-EQ-5D quotient was of borderline significance in favour of therapy (-0·03, 95% CI -0·07 to -0·002; p=0·04). Median therapist contact time was four visits of 58 minutes over 8 weeks. Repeated measures analysis showed no difference in NEADL total score, but PDQ-39 summary index (diverging 1.6 points per annum, 95% CI 0.47 to 2.62; p=0.005) and EuroQol-EQ-5D (0.02, 95% CI 0.00007 to 0.03; p=0.04) showed small differences in favour of therapy. There was no difference in adverse events.

CONCLUSIONS AND RELEVANCE Physiotherapy and occupational therapy did not produce immediate or medium term clinically meaningful improvements in ADL or QoL in

mild-moderate Parkinson’s disease. This evidence does not support the use of low dose, patient-centered, goal-directed physiotherapy and occupational therapy in patients in the early stages of Parkinson's disease. Future research should explore the development and testing of more structured and intensive physical and occupational therapy programmes in patients with all stages of Parkinson's disease.

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Introduction

Parkinson's disease causes 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 including falls, with mental health problems and other non-motor symptoms. Physiotherapy and occupational therapy are traditionally used later in the disease.[1] However, service provision varies widely, with some centers involving physiotherapists and occupational therapists from diagnosis, while other areas have no specialist services.

Cochrane reviews of physiotherapy for Parkinson's disease found small but significant effects on motor function, but not quality of life.[2,3] A Cochrane review of occupational therapy found insufficient evidence of effectiveness.[4] Previous trials with both therapies were small with short-term follow-up.[2-4] Despite this lack of evidence, the UK National Institute for Health and Care Effectiveness guidelines, although recognising these shortcomings and recommending further trials, stated that all patients should have access to both therapies.[1] The PD REHAB trial was designed to evaluate the clinical and cost-effectiveness of individualised physiotherapy and occupational therapy in patients with Parkinson's disease. The current trial design was informed by our pilot study of occupational therapy in Parkinson's disease (PD OT).[5]

Methods

PD REHAB was a large-scale pragmatic multicenter randomised controlled trial to evaluate the effects of individualised physiotherapy and occupational therapy on ADL and quality of life (QOL) in patients with Parkinson's disease. The trial protocol (last accessed 5th November 2015) is available at: http://www.birmingham.ac.uk/pdrehab-docs.

Study participants

Recruitment took place between October 2009 and June 2012. Patients from 38 neurology or geriatric medicine outpatient centers across the UK were invited to take part. Eligibility criteria were: idiopathic Parkinson's disease defined by UK Parkinson's Disease Society

Brain Bank Criteria;[6] self or carer reported limitations in ADL; and the investigator was uncertain that they would require physiotherapy and/or occupational therapy during the 15 months of the trial, i.e. equipoise about the need for therapy existed Exclusion criteria were: dementia as locally defined; receipt of physiotherapy or occupational therapy for Parkinson's disease in the last 12 months. All patients gave written informed consent before randomisation. Ethical approval was granted by the West Midlands Research Ethics Committee (08/H1211/168) and local approval was obtained at each participating center.

Randomisation and Therapy Allocation

Patients were randomised (1:1) between combined physiotherapy and occupational therapy (therapies group) or no therapy (control group) using an on-line randomisation service at the University of Birmingham Clinical Trials Unit. Randomisation used a computer-based algorithm with minimisation by baseline Nottingham Extended Activities of Daily Living (NEADL) total score (severe 0 to 21; moderate 22 to 43; mild limitations in ADL 44 to 66), Hoehn and Yahr stage (H&Y)[7] (≤2; 2.5; 3;≥4) and age (<60; 60 to 69; 70 to 79; ≥80 years).

Intervention

Physiotherapy and occupational therapy were delivered in the community and/or outpatients by qualified therapists working within the National Health Service (NHS) per local practice. Before the trial, a framework for therapy content was developed and agreed by expert therapist groups based on previous work on standards of NHS physiotherapy and occupational therapy and European guidelines.[8-11] This framework was based on usual NHS practice and not an innovative intervention. Following initial assessments by both therapists, therapy was tailored to individual patient's requirements using a patient-centered joint goal setting approach. Interactions between therapists and patients were described and quantified using pre-defined recording forms and included administration time (e.g. ordering equipment). Controls consented to have therapies deferred until the end of the 15 month trial, unless pressing reasons for therapy developed. Since therapies may have been arranged outside the trial, controls were asked whether they had received any therapy at each assessment point.

Primary outcome measure

Total NEADL score at 3 months post-randomisation was the primary outcome measure.[12] NEADL measures instrumental ADL which are specifically addressed by physiotherapy and occupational therapy and includes more complex ADL issues such as making a meal, cleaning and travelling on public transport. The NEADL scale was developed for stroke, but is used widely as a generic outcome measure in rehabilitation trials of older people. It is sensitive to change in occupational therapy trials,[13] and was successfully used in our pilot study of occupational therapy for Parkinson's disease, with good correlation with the Unified Parkinson's Disease Rating Scale and the Parkinson's Disease Questionnaire (PDQ-39) ADL domains.[5]

Secondary outcome measures were patient-rated QOL using the 39-item PDQ-39,[14] comprised of eight domains and the most widely used disease-specific QOL rating scale for Parkinson's disease, and EuroQol-5D (EQ-5D; 3 level version), a generic QOL scale; adverse events; and carer well-being using Short Form-12 (SF-12; version 2). Following a risk assessment, only therapy-related adverse events and serious adverse events were recorded. These were defined as falls or equipment failure leading to injury requiring a hospital, general practitioner (GP), ambulance visit, or death. A health economics analysis was conducted alongside PD REHAB and will be reported separately. Outcomes were collected in person at baseline before randomisation, then by post at 3, 9, and 15 months after randomisation. Anti-parkinsonian medication dosage was converted into levodopa dose equivalents using a standard formula.[15]

Statistical analysis

A minimally clinically important change (MCIC) in NEADL score in stroke patients is 1 to 2 points.[16] However, such a small change may be of little benefit to patients; a clinically meaningful change in NEADL for patients is likely to be around double this at 2·5 points. A 2 point change in NEADL score represents becoming independent in one item (e.g. stair climbing, crossing roads) or improvement in two items (e.g. 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 standard deviation (SD) from the PD OT pilot trial[5] 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 drop-out.

The primary analysis was change in NEADL total score in the therapies group between baseline and the 3 month assessment compared with that in the no therapy group. An independent two-sample t-test was used to compare changes between baseline and 3 months in the NEADL score between the two groups. Results are presented as mean difference between groups with 95% confidence interval (CI). This analysis was repeated for individual NEADL domains and secondary outcome measures. The medium term effect or whether any benefit of treatment persisted beyond the initial intervention period was evaluated at 9 and 15 months post-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. Missing data in PDQ-39 domain scores were imputed using an expectation maximisation algorithm.[17 18] There is no established imputation method for the NEADL scale, therefore 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 employed a test of interaction to explore the effect of the therapies at different levels of ADL, disease stage, and age at 3 months. All subgroup analyses were interpreted cautiously.

Analyses were performed using SAS version 9·2 (Cary, NC, USA). Interim analyses of un-blinded efficacy and safety data were reviewed annually by an independent Data Monitoring Committee which reported to an independent Trial Steering Committee.

Results

Study Population

762 people with Parkinson's disease were randomised to either combined physiotherapy and occupational therapy or no therapy (381 per group; CONSORT diagram, Figure 1).

Baseline characteristics were similar between groups (Table 1). Mean age was 70 years, 65% were male and median disease duration was 3·1 years (mean 4·6 years). Most patients had mild to moderate disease, with 67% in H&Y ≤2 and median NEADL total score 54 (mean 51).

At 3 months, 92% of patients in each arm had completed the NEADL (Figure 1). By 15 months, 311 (82% of 381 patients randomised) in the therapies arm had completed the NEADL compared with 322 (85% of 381 patients randomised) in the control arm.

25 patients (6%) allocated to the therapies arm did not receive therapy by 3 months post-randomisation (12 started physiotherapy and/or occupational therapy after 3 months and 13 never received any therapy; Figure 1). Nine patients (2%) allocated to no therapy received therapy for Parkinson's disease-related problems within 3 months, mainly worsening Parkinson's disease symptoms including falls and imbalance (Figure 1).

Therapy content

In the therapies group, the median total number of therapy sessions was four (range 1-21), with a mean time per session of 58 minutes. Mean duration of therapy was 8 weeks. Mean total dose of both therapies was 263 minutes (range 38-1198). Most physiotherapy was performed in outpatients (53%) rather than the community (39%), or other (8%), whereas occupational therapy was more commonly performed in the community (69%) rather than outpatients (29%), or other (2%).

Physiotherapy logs showed the most frequent interventions were for gait (96% of patients), posture (93%), balance (90%), physical conditioning (81%), and transfers (78%).

Occupational therapy logs showed 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%).

Validation of therapy logs was undertaken by comparing logs with full-text therapy notes for 38 patients chosen at random from 10 geographically diverse centers. Interventions were grouped into: assessment, equipment/adaptation prescription, exercise recommendations, referral to other specialists, and 'other advice'. Physiotherapists prescribed a range of

exercise programmes tailored to their assessment of patient mobility and activity levels. Only three physiotherapists provided specific Parkinson's disease exercise advice accompanied by a booklet, and there was no evidence of a formal exercise progression protocol for any patient. Occupational therapy assessed the full range of ADL, but predominant interventions were equipment provision, onward referral, and 'other advice' (e.g. management of sleep disorders, applying for benefits). There was little task-related practice.

Outcome measures

Mean NEADL total score deteriorated from baseline to 3 months by 1·5 points in the therapies group compared with 1·0 point in the no therapy group (difference 0·5 points, 95% CI -0·7-+1·7, p=0·4; Table 2). No difference was seen in any of the individual categories of the NEADL scale (Table 2). Repeated measures analysis of the NEADL across all time points showed no difference between the treatment arms (Figure 2; eTable 1).

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-+1·5, p=1·0; Table 2). No difference was seen in any of the eight domains of the PDQ-39 (Table 2). The slight improvement of 0·002 points in the EuroQol EQ-5D quotient in the therapies 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--0·002, p=0·04; Table 2). There was no difference in the EuroQol EQ-5D visual analogue score (difference -0·2, 95% CI -2·6-+2·2, p=0·9; Table 2).

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

Sensitivity analysis with imputation of missing NEADL values did not change the results. Repeating the PDQ-39 analysis without imputation of missing values using the expectation

maximisation algorithm also did not affect the results. We analysed the primary outcome of mean change between baseline and 3 months for NEADL total score data using analysis of covariance adjusting for baseline NEADL score and the other minimisation variables, but this made no difference to the result.

Planned subgroup analyses for NEADL total score found no evidence of difference in therapy effect at 3 months according to baseline total NEADL score, age, or disease severity (eFigure 1).

Four hundred and seventy three (62%) patients had a carer and 406 (86%) carers agreed to take part in the trial (mean age 67 years; 76% female). The relationship between patient and carer was most often partner or spouse (72%). Although there was no difference in carer SF-12 physical component score at 3 months, there was less decline in carer SF-12 mental component score (difference -2·1, 95 CI -3·9--0·3, p=0·02; Table 3) although this was not maintained with longer follow-up (eTables 3 and 4).

Adverse Events

Targeted adverse events are detailed in eTable 5. There were no differences in adverse events between trial arms at 3 or 15 months.

Discussion

PD REHAB showed that physiotherapy and occupational therapy produced no clinically meaningful immediate or medium term beneficial effects on ADL or QOL in mild to moderate Parkinson's disease. The medium term significant differences in QOL measured by PDQ-39 summary index and EuroQol EQ-5D quotient in favour of therapy were small and did not reach clinically significant levels which we defined as twice MCIC levels.

Our Cochrane review of physiotherapy versus no intervention in Parkinson's disease showed that all forms of physical therapy produced small benefits in motor function and ADL, but no change in QOL.[19] The Cochrane review of occupational therapy found insufficient evidence about effectiveness in two small trials,[4] although a recent large (n=191) Dutch trial found that occupational therapy improved self-perceived performance, but not QOL.[20] The

absence of any motor effect (PDQ-39 mobility domain) or response in ADL in PD REHAB is likely to be multifactorial, due to early disease stage of most patients, low 'dose' of intervention, and lack of consistency in therapy assessment and intervention.

Traditionally, physiotherapy and occupational therapy have been used in the more advanced stages of Parkinson's disease, once imbalance and falls have developed (H&Y ≥3).[1] As a result of using the uncertainty principle for recruitment, most patients in PD REHAB had H&Y less than three at randomisation. It is possible that such mild to moderate disease may not respond to the therapies, whereas more severe disease may respond, although this remains to be established. As a consequence, the results of PD REHAB can only be generalised to patients with mild to moderate disease.

Median therapy 'dose' was four sessions of 58 minutes over 8 weeks for both therapies combined. This is low in comparison with the previous five physiotherapy trials in the Cochrane review (5 to 52 weeks therapy).[3] A Dutch trial of physiotherapy in Parkinson's disease (ParkNet)[21] also showed no evidence in favour of therapy. Total contact time between patients and physiotherapists over 6 months in ParkNet was 15 sessions of 30 minutes, nearly double that in PD REHAB.[21] Importantly though, the dose delivered in PD REHAB reflects routine NHS practice.

Therapy expert groups recommended an individual 'goal setting' approach for PD REHAB interventions, as this is the gold standard and addresses the personalised needs and wishes of the individual. Therapy content was in keeping with NHS and European guidelines on physiotherapy and occupational therapy.[8-11] However, an individualised goal setting approach with this content may not be transferable to patients with mild disease. The lack of task-related practice is of particular concern as this has been shown to be a significant factor in stroke rehabilitation trials.[2] We were also concerned by the low prescription and dose of exercise in PD REHAB.

The possibility that patients with more severe disease might show a better response was examined in a planned subgroup analysis examining response according to baseline NEADL score and Hoehn and Yahr stage. Whilst the data did not support this hypothesis, the

numbers with severe disease were small, so this is likely to be under-powered. Similarly, older patients might respond better to the therapies because of greater levels of frailty and co-morbidities, but there was no evidence of this in the subgroup analysis.

The fidelity of the intervention was reasonable in both arms of this pragmatic 'real-world' trial. In the therapies arm, 93% of patients received therapies within 3 months of randomisation. Whereas, only 2% of the no therapy arm crossed-over to receive treatment within 3 months, mainly due to motor progression. It is unlikely that these small proportions of cross-overs led to the lack of effect seen in the trial.

In spite of all patients reporting ADL problems at baseline, many had mild disease. 29% had a NEADL score at baseline of >61 and 14% had a score of ≥65 (mean baseline score 51/66). This may have led to a floor effect, since the NEADL score could not improve much from a good baseline score. However, planned subgroup analysis showed that there was still no response in patients with more severe baseline NEADL scores. It should also be noted that the NEADL results are supported by the lack of a clinically meaningful effect on PDQ-39 ADL domain.

Conclusions

Physiotherapy and occupational therapy using an individual goal setting approach produced no clinically meaningful short or medium term benefits in ADL or QOL in patients with mild to moderate Parkinson's disease. This evidence does not support the use of low dose, goal-directed physiotherapy and occupational therapy in patients in the early stages of Parkinson's disease. Future research should explore the development and testing of more structured and intensive physical therapy programmes in patients with all stages of Parkinson's disease.

ARTICLE INFORMATION

Author Contributions: CEC (chief investigator), CS, MW, NI, and KW designed the trial. CEC, CS, NI, KW, SP, and CR ran the trial and CEC recruited patients. NI, SP, Versha Cheed and RW performed the interim and final data analyses. CEC, CS, MW, NI, SP, CR, KW interpreted the data and wrote the paper.

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Table 1 Demographics and baseline characteristics

		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%)
Gender	Male (N, %)	240 (63%)	258 (68%)
Body Mass Index (kg/m^2)	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 & 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%)
Drug dose			
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
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

NEADL=Nottingham Extended Activities of Daily Living (total score ranges from 0 to 66, where higher scores are better); PDQ-39=Parkinson's Disease Questionnaire-39 (summary index ranges from 0 to 100, where lower scores are better); SD=Standard Deviation; IQR=Interquartile Range. Age, Hoehn & Yahr stage and NEADL total score were minimisation variables in the randomisation algorithm.

Table 2 Patient activities of daily living and quality of life scores at 3 months

	Baseline		3 months		Mean change from baseline		Mean difference (95% CI)†	p-value
	PT/OT	No therapy	PT/OT	No therapy	PT/OT	No therapy		
NEADL								
Total score	N=381	N=381	N=294	N=304	N=294	N=304	0.5 (-0.7 to 1.7)	0.4
	50.5 (12.9)	50.9 (13.3)	49.6 (14.0)	50.3 (14.5)	-1.5 (7.8)	-1.0 (7.4)		
Mobility	N=376	N=372	N=338	N=338	N=334	N=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	N=379	N=373	N=337	N=337	N=335	N=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	N=374	N=370	N=330	N=332	N=325	N=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	N=376	N=365	N=318	N=329	N=316	N=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	N=377	N=349	N=351	N=348	N=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
Activities of Daily Living	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
EQ-5D								
Quotient Score	N=378	N=374	N=345	N=345	N=342	N=338	-0.03 (-0.07 to -0.002)	0.04
	0.64 (0.27)	0.66 (0.25)	0.65 (0.25)	0.63 (0.26)	0.002 (0.23)	-0.03 (0.21)		
Visual Analogue Score	N=376	N=376	N=346	N=347	N=341	N=342	-0.2 (-2.6 to 2.2)	0.9
	68.5 (17.5)	68.6 (17.0)	67.4 (18.2)	66.8 (17.8)	-1.8 (17.1)	-1.9 (14.3)		

Data is 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 VAS: ranges from 0 to 100 where higher scores are better and a positive change is an improvement in score.

† To aid interpretation, regardless of scale, a positive mean difference favours no therapy group and a negative mean difference favours PT/OT group.

Table 3 Carer quality of life scores

	Baseline		3 months		Mean change from baseline		Mean difference (95% CI)†	p-value
	PT/OT	No therapy	PT/OT	No therapy	PT/OT	No therapy		
SF-12								
Physical functioning	N=171	N=181	N=169	N=181	N=151	N=156	-5.6 (-11.0 to -0.2)	0.04
	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	N=183	N=169	N=185	N=155	N=163	-0.5 (-5.3 to 4.3)	0.8
	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	N=182	N=170	N=183	N=155	N=162	-4.4 (-9.0 to 0.2)	0.06
	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	N=186	N=171	N=189	N=157	N=169	-3.8 (-8.9 to 1.3)	0.1
	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	N=183	N=170	N=188	N=156	N=167	-4.3 (-8.2 to -0.4)	0.03
	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	N=184	N=170	N=188	N=156	N=167	-4.6 (-9.2 to 0.05)	0.05
	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	N=184	N=170	N=189	N=156	N=168	2.9 (-2.2 to 7.9)	0.3
	77.7 (29.3)	76.4 (28.7)	74.1 (28.8)	74.2 (28.5)	-4.6 (25.0)	-1.8 (21.1)		
General health	N=174	N=186	N=170	N=190	N=155	N=170	-0.9 (-5.0 to 3.3)	0.7
	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 score	N=166	N=171	N=165	N=174	N=146	N=144	-0.6 (-2.3 to 1.2)	0.5
	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 score	N=166	N=171	N=165	N=174	N=146	N=144	-2.1 (-3.9 to -0.3)	0.02
	51.1 (10.2)	50.1 (8.9)	49.7 (10.2)	48.0 (10.5)	-0.5 (7.6)	-2.6 (7.9)		

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

Figure legends

Figure 1 CONSORT diagram for PD REHAB. Patient recruitment and follow-up

Figure 2 Medium term scores in activities of daily living and quality of life

eFigure 1 Subgroup analyses for NEADL total score at 3 months