Research Paper

Phase II randomised controlled trial of a 6-month self-managed community exercise programme for people with Parkinson’s disease

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ABSTRACT

Background Evidence for longer term exercise delivery for people with Parkinson’s disease (PwP) is deficient. Aim Evaluate safety and adherence to a minimally supported community exercise intervention and estimate effect sizes (ES).

Methods 2-arm parallel phase II randomised controlled trial with blind assessment. PwP able to walk ≥100 m and with no contraindication to exercise were recruited from the Thames valley, UK, and randomised (1:1) to intervention (exercise) or control (handwriting) groups, via a concealed computer-generated list. Groups received a 6-month, twice weekly programme. Exercise was undertaken in community facilities (30 min aerobic and 30 min resistance) and handwriting at home, both were delivered through workbooks with monthly support visits. Primary outcome was a 2 min walk, twice weekly programme. Exercise was delivered through workbooks with monthly support visits. Primary outcome was a 2 min walk, with motor symptoms (Movement Disorder Society Unified Parkinson’s Disease Rating Scale, MDS-UPDRS III), fitness, health and well-being measured.

Results Between December 2011 and August 2013, n=53 (n=54 analysed) were allocated to exercise and n=53 (n=54 analysed) were allocated to handwriting. N=37 adhered to the exercise, most attending ≥1 session/week. Aerobic exercise was performed in 99% of attended sessions and resistance in 95%. Attrition and adverse events (AEs) were similar between groups, no serious AEs (n=2) were observed in exercise, but 3 serious AEs (n=1) were observed in handwriting. The randomisation list used was supported community exercise intervention and estimate effects sizes on fitness, motor and non-motor symptoms (Movement Disorder Society Unified Parkinson’s Disease Rating Scale, MDS-UPDRS III), fitness, health and well-being measures.

Conclusions PwP exercised safely and the possible long-term benefits observed supported a substantive evaluation of this community programme. Trial registration number NCT01439022.

INTRODUCTION

Short-term exercise has been shown to benefit or stop deterioration in symptoms offering potential personal, societal and economic benefits for the management of Parkinson’s disease (PD), but many people with Parkinson’s disease (PwP) undertake less exercise than other age-matched people, and less than recommended to maintain good health. While exercise may improve health and well-being and reduce motor and non-motor symptoms in PwP, there is a lack of evidence for the long-term benefits. This is in part due to the difficulties of effectively delivering exercise over the longer term; existing researched interventions are predominantly not cost-effective or sustainable. Thus, there is a need for more evidence on how to best deliver a solution that is effective long term.

Exercise referral schemes run throughout the UK are standardised, widely commissioned and have been shown to be effective for cardiac conditions and older people offering a pragmatic solution for PwP. However, PwP are under-represented within standard UK exercise referral schemes and report significant barriers.

With the help of fitness professionals, PwP and clinicians, a supported self-managed community exercise programme for people with long-term neurological conditions was developed to fit within existing community fitness centres delivered in gyms by professional with expertise in clinical exercise. The intervention was guided by behaviour change theory that considered an individual’s capability, opportunity and motivation and incorporated appropriate evidence for safe effective exercise and self-determination theory. In this phase II exploratory trial, we evaluated the programme’s utility focusing on the extent to which people safely participated and adhered to the 6-month exercise programme. We also sought to estimate effects sizes on fitness, motor and non-motor symptoms, and health and well-being measures.

METHODS

Design A two-arm parallel single-blind phase II randomised controlled trial of community-delivered exercise for PwP. Participants recruited to the study were allocated the next available study number by the blinded assessor. The study number related to a computer-generated randomisation list drawn up by the Oxford Primary Care Clinical Trials Unit (Nuffield Department of Primary Care Health Sciences) that randomised individuals (1:1) into either intervention (exercise) or control groups (handwriting). The randomisation list used...
minimisation to balance groups for gender and whether or not individuals used medication for PD at baseline. The list was held by the principal investigator who informed those supporting the intervention of group allocation. Group allocation was concealed from the assessor until the end of the study.

Setting
Participants were recruited from Oxfordshire, Berkshire and Buckinghamshire, UK, and assessments were carried out at the Movement Science Laboratory, Oxford Brookes University, Oxford, UK.

Participants
The study received National Health Service (NHS) ethical approval (National Research Ethics Service (NRES) Committee South Central—Southampton A: 11/SC/0267), was registered with ClinicalTrials.Gov (NCT01439022) and was conducted in accordance with the Declaration of Helsinki.

People with idiopathic PD were recruited from neurology clinics at the John Radcliffe, Royal Berkshire and Heatherwood and Wexham Park hospitals (via the dementias and neurodegeneration research network), general practitioner (GP) practices (via Thames Valley Primary Care Research Network) and through local Parkinson’s UK meetings.

Inclusion criteria were: (1) diagnosis of idiopathic PD (as defined by the UK PD Society Brain Bank criteria);20 (2) able to walk ≥100 m (with or without walking aid), Exclusion criteria were: (1) a diagnosis of dementia; (2) history of additional prior neurological condition; (3) severe depression or psychosis or a mental state that would preclude consistent active involvement with the study over its duration; (4) cardiac precautions that would prevent the participant from participating in the intervention; (5) any known contraindication to exercise; (6) reduced cognitive function of any cause (Mini–Mental State Examination <23); (7) an orthopaedic condition that limited independent walking. Participants’ medication was continued as normal and was recorded.

Intervention
Online supplementary 1 contains details of the intervention according to the Template for Intervention Description and Replication (TIDier) guidelines.21 Briefly, both the intervention (exercise) and control groups (handwriting) were prescribed activity sessions lasting 60 min twice a week over a period of 6 months. After the 6-month assessment no further instruction for exercise (or handwriting practice) was given.

Exercise group
The exercise sessions took place at community leisure facilities in Oxfordshire and Berkshire and were supported by monthly visits from a professional experienced in clinical exercise. The exercise programme was delivered through an exercise booklet and consisted of 30 min of aerobic training (55–85% age-predicted heart rate maximum (220-age)) followed by 30 min of resistance training.

Handwriting group
The handwriting sessions took place in the participant’s home and were supported by monthly visits by the same staff that supported exercise sessions. The programme was delivered through handwriting workbooks and consisted of ‘warm-up’ hand exercises followed by a variety of writing exercises, finishing with hand exercises.

Assessment
Demographic information, medical history relating to PD, including current medication use and cognition (Mini–Mental State Examination) were ascertained at the baseline assessment.

All outcome measures were performed at baseline (entry), 3 months (halfway intervention), 6 months and (end intervention) and 12 months. Measurements were made by the same assessor blinded to intervention allocation and trained in the Movement Disorder Society Unified Parkinson’s Disease Rating Scale (MDS-UPDRS).22 If a patient had ON and OFF periods, assessments were carried out during ON state. Participants followed their usual Parkinson’s medication regime, but were asked to refrain from consumption of alcohol, cigarettes, food and caffeine and to avoid exercise for a period of 3 hours prior to the assessment.

Outcome measures
A detailed description of outcome measures can be found in the online supplementary 1.

Motor: The primary outcome measure was the 2 min walk test.23 Mobility was also measured using the timed up and go test,23 and dexterity using the nine-hole peg test.24 Global motor function was assessed using the motor examination of the MDS-UPDRS (III).25

Fitness: Aerobic fitness was determined using a stepwise incremental exercise test. The work rate protocol consisted of 2 min steps starting with unloaded cycling, then increasing to 50 W and thereafter by 25 W. Participants were verbally encouraged to carry on for as long as they could and the test was terminated when the participant reached volitional exhaustion. Rate of oxygen consumption was calculated as the average oxygen consumed over the past 30 s of the test (maximal oxygen consumption, \( V_{O2}\max \) L/min).26 Leg power was measured using a ‘power meter’,27 the maximum power achieved from each leg separately was recorded and reported as an average. Grip strength was measured using a hand-held dynamometer, the maximum force of each hand was recorded and reported as the average.28

Health and well-being: Health-related quality of life was measured using the Euro-QOL (EQ5D-5L)29 and Short Form Health Survey (SF-36).30 scores are reported for the EQ5D-5L index score and SF-36 physical and mental scores. Non-motor symptoms were assessed using the PD’s non-motor symptom questionnaire31 and self-reported fatigue using the Fatigue Severity Scale (FSS).32 Health status was measured using body mass index and resting blood pressure and physical activity using the Physical Activity Scale for the Elderly.33

Intervention fidelity
Adherence and fidelity was obtained from the exercise booklets. For aerobic exercise, time (in minutes) and exercise equipment used was reported, along with rating of perceived exhaustion and heart rate at the end of the exercise. Resistance training was recorded as the weight (kg) used for the exercise and the number of the repetitions for each exercise, with training volume calculated (weight (kg)×number of repetitions). Engagement with the control intervention was determined by number of handwriting sessions attempted.

Data analysis
While this was a phase II trial and not designed to determine efficacy, the sample size was based on the estimated effect on 2 min walk distance. To detect a clinically meaningful change of 12 m in the 2 min walk would require an effect size of 0.55, with a power of 80% and α of 0.05, 80 participants (40 in each
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group) would be required. Allowing for attrition, we aimed to recruit a total of 100 participants.

Data were analysed based on the intention-to-treat principle. Descriptive statistics were calculated for demographic characteristics and compliance data. Independent samples t-test or χ² test was used to assess differences between group mean and frequencies at baseline. Progression in training volume was investigated using linear regression in SPSS (V.19). For outcome data the linear mixed models (LMM) procedure of SAS V.9.4 was used to determine the mean changes in measures, as response variables, according to two intervention regimes (exercise and handwriting) and three repeated measurements, using baseline as a covariate. Further and based on the differences of least square (marginal) means between two groups (exercise vs handwriting) provided by LMM analysis, powers, effect sizes (Cohen’s d) and their 95% non-central confidence limits were calculated.

RESULTS

Recruitment, randomisation and participant flow

Between December 2011 and August 2013, the trial recruited 105 participants within the proposed time line. We could not record the number of people screened in the eight GP surgeries and PD clinics (John Radcliffe, Royal Berkshire and Heatherwood and Wexham Park Hospitals) or the total number of people informed of the study via either presentation at group meetings or newsletter articles at seven local Parkinson’s UK groups (Oxford, Newbury, Bracknell, Wokingham, Reading, Hazlemere and High Wycombe). The study was also promoted on Parkinson’s UK and Michael J Fox websites.

In total, 170 people, contacted through one or more of these routes, expressed interest in the study; 107 were assessed for eligibility with only 2 not meeting criteria, leaving 105 people. Table 1 shows preintervention assessment data, while there was no statistical difference between groups, scores for 2 min walk and MDS-UPDRS III tended to be better in the exercise group. Only one person, in the exercise group, used a walking aid. VO₂ data were unavailable on 11 people from each group due to contraindications. One participant did not receive the allocated intervention, allocated to handwriting group but received exercise, and was included in analysis as part of exercise group. The allocations error was due to a misunderstanding of the allocation by the staff delivering intervention. The error was discovered after the completion of the intervention.

Attrition after randomisation was similar between groups, and participant flow can be found in figure 1. Two people were excluded after randomisation (one from each group) for no longer meeting eligibility criteria due to a revised/additional diagnosis (Lewy body dementia, multiple system atrophy). Retention was similar between groups with ≥80% retention for both groups at the 3 and 6 months dropping to 67% in the exercise group and 63% in handwriting group at 12 months. Unrelated medical reasons were the main cause of lost to follow-up at the primary (6-month) assessment point. Most of these occurred prior to the 3-month appointment resulting in participants dropping out of the trial. Five participants experienced serious adverse events (n=2 exercise group, n=3 handwriting group) during the trial, these were deemed unrelated to either intervention (fall resulting in hospitalisation n=2, acute pancreatitis n=1, death n=2).

Intervention fidelity

Exercise group: In total, 17 individuals discontinued intervention (figure 1), 8 individuals due to medical reasons and 1 individual was excluded due to additional diagnosis of Lewy body dementia. Participants were deemed to have discontinued intervention if they attended none or only the initial session (n=9), reasons can be found in figure 1. There were two related adverse events; these were an abnormal heart rate response to exercise and orthostatic hypotension, both participants continued with the intervention following medical clearance. All discontinued intervention occurred within the first 3 months.

Intervention fidelity was further investigated in the 37 participants that did not discontinue the exercise programme. Most people (n=32) attended 1 or more sessions a week on average and the median number of session attended was 40 out of the 48 prescribed sessions.

In 1341 out of the 1350 sessions attended (99%), the aerobic component was performed for a mean (SD) time of 30.2 (±3.6) minutes per session. The exercise bike was the most popular mode of aerobic exercise (676 sessions), followed by treadmill (353 sessions) and mixed modes (309 sessions), cross trainer or rowing machine made up ~1% of sessions. The mean (SD) heart rate during the aerobic component was 116±20 bpm with 93% of aerobic sessions performed with in the target zone.

Considering the resistance component, in 95% of attended sessions the two-arm pull down exercise was performed, 93% arm raises, 91% leg press, 85% sit-to-stands, 80% ‘wood chop’ and 25% leg extensions. Linear regression revealed a significant increase (≤0.05) in resistance training volume (resistance weight×number of repetitions) during the exercise programme for all exercises except arm raises. The β coefficient indicated two arm pull down resistance training volume increased by 3.0 (SE 0.7) kg per session (R² 0.12, p≤0.0001), leg press volume 10.0 (SE 1.1) kg per session (R² 0.24, p≤0.0001), sit-to-stand 2.7 (SE 0.3) kg per session (R² 0.20, p≤0.0001), ‘wood chop’ 2.3 (SE 0.66) kg per session (R² 0.10, p≤0.0001) and leg extension volume 1.7 (SE 0.6) kg per session (R² 0.08, p=0.04).

Handwriting group: In total, 11 individuals had discontinued intervention by the 6-month follow-up, most did not give a reason (n=6) and there were three discontinued intervention due to medical reasons (figure 1). Two serious adverse events were recorded that did not result in discontinue intervention; a fall that occurred during the intervention and a death which occurred after the intervention in the follow-up period. There were no related adverse events in the handwriting group. The median number of handwriting sessions performed was 40 out of the 48 prescribed sessions and most people (n=36) did more than one session a week on average.

Outcome

Follow-up assessments were completed in September 2014. Outcome data are reported in table 2, small-to-moderate effect sizes (0.1–0.3) were found for a number of outcomes. Effect sizes are between group and considered all three follow-up assessments; the largest effect was found on MDS-UPDRS III −0.30 (95% CI 0.07 to 0.54) which was significantly lower at the primary end point (end intervention) in the exercise group (p<0.05) indicating an improvement in motor symptoms. Two-minute walk distance, the primary outcome measure, produced the second largest effect 0.20 (95% CI −0.44 to 0.45), in favour of the intervention group, with the largest difference found between groups at 12 months (p=0.063). Small effects were found for improvement in leg power and aerobic capacity fitness parameters and in perceived health-related quality of life health (EQ5D-5L visual analogue scale and SF-36 physical sub-scale). Effects that favoured the control group were found for non-motor symptoms and fatigue. For the above measures, the direction of effect was consistent over all three assessment points.
DISCUSSION

People with PD will use community leisure facilities to undertake exercise delivered through an exercise booklet supported by a professional with expertise in clinical exercise. Furthermore, our data are encouraging that 6-month intervention seems to lead to improvements in mobility and motor symptoms that are sustained over a year. Although the exercise programme was not fully adhered to by all, most patients became engaged with the exercise programme, and these potential long-term benefits were observed with intention-to-treat analysis. There were no serious adverse events related to the exercise and, after investigation, all individuals that had related adverse event were able to continue with the intervention. Essentially most patients, after receiving instructions to initiate the programme, were able to largely self-manage their exercise, achieving the prescribed exercise and progressing, with minimal support. As such our study establishes that the use of community exercise facilities is feasible to achieve long-term gains for PwP.

The effects we observed compare favourably to those reported in systematic reviews. A meta-analysis of aerobic training, primarily driven by studies with short interventions and follow-ups (<16 weeks), found a pooled mean difference in MDS-UPDRS III of −0.57 (95% CI −0.95 to 0.19) in favour of aerobic exercise.\(^1\) we found a difference of −3.0±1.5, −4.0±1.4 and −1.5±1.6 at 3, 6 and 12 months, respectively. Uhrbrand et al\(^2\) found in their review that improvements in the MSD-UPDRS III were more associated with resistance than aerobic exercise modes. Our exercise programme incorporated both aerobic and resistance exercise and combining training modalities may be important to optimise benefits.\(^2\) However, while individuals progressed, we did not observe the improvements in aerobic and resistance fitness measures that might be expected.\(^1\)\(^2\) It is therefore plausible that the improvements in motor symptoms observed might be to some extent attributable to exercise-induced neuroplasticity identified in animal models of the disease,\(^3\)\(^4\) rather than just improved physical capacity. This supports the need for studies designed to distinguish improvements in physical capacity from any possible neuroplasticity effects.

These findings should be interpreted considering limitations. It should be recognised that the study was not designed to determine efficacy and the number of patients was not large, reducing the precision of estimating the size of any benefit. We also used a control group that received a handwriting intervention in order to engage people through the study period, participant flow indicates that this was successfully achieved and indicates a desire for interventions to address handwriting problem in this

<table>
<thead>
<tr>
<th>Table 1 Baseline characteristic and pre intervention assessment data</th>
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<tr>
<td>Exercise</td>
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<tr>
<td>Demographics</td>
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<tr>
<td>n=54</td>
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<tr>
<td>Age (years)</td>
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<td>Gender (M:F)</td>
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<td>MMSE</td>
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<td>Time since diagnosis</td>
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<td>MOA-B inhibitors</td>
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<td>COMT inhibitors</td>
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<tr>
<td>Motor symptoms</td>
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<tr>
<td>Two-minute walk test (m)</td>
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<tr>
<td>UPDRS part III</td>
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<tr>
<td>Nine-hole peg test (s)</td>
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<td>TUG (s)</td>
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<tr>
<td>Fitness</td>
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<td>VO₂ (L/min)</td>
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<td>Leg power (W)</td>
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<td>Grip strength (W)</td>
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<tr>
<td>EQOD-SL</td>
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<tr>
<td>SF-36—physical</td>
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<tr>
<td>SF-36—mental</td>
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<td>N-MSQ</td>
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<tr>
<td>FSS</td>
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<tr>
<td>BMI</td>
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<tr>
<td>MAP BP (mm Hg)</td>
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<td>PASE</td>
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Mean±SD, delta, between group difference (exercise—handwriting)±SE of difference reported with p value of independent samples t-test, for nominal data p value for χ² statistic reported.

BMI, body mass index (weight (kg)/[height (m)]²); COMT, catechol-O-methyl transferase; EQOD-SL (VAS) index score of the Euro-QOL EQ5D-5L; F, female; FSS, Fatigue Severity Scale; M, male; MAP BP, mean arterial blood pressure ((systolic blood pressure (mm Hg)+2×diastolic blood pressure (mm Hg))/3); MDS-UPDRS III, Movement Disorder Society Unified Parkinson’s Disease Rating Scale part III; MMSE, Mini-Mental State Examination; MOA-B, monoamine oxidase type B; N, no; N-MSQ, Parkinson’s disease non-motor symptom questionnaire; PASE, Physical Activity Scale for the Elderly; PD, Parkinson’s disease; SF-36, Short Form (36 item) Health Survey, physical and mental subscores; TUG, timed up and go test; VAS, visual analogue scale; VO₂, oxygen consumption; Y, yes.
group. However, the engagement of the control group may have diluted the effects found. Overall physical activity levels did not differ between groups and both groups increased physical activity levels from baseline. This may have particularly impacted on health and well-being measures that reflect multiple factors, indeed, effects for non-motor symptoms and fatigue favoured the control group. In multiple sclerosis, the effect of exercise on fatigue has received considerable research attention and while individuals may have to balance rest and activity to participate in exercise, exercise is recommended to benefit this symptom.6 However, we did observe, albeit small, potential positive effects on quality of life. This is encouraging as systematic reviews have not established improvements in this construct despite the improvements in motor symptoms.1 2 Certainly, while systematic reviews support that exercise interventions can benefit PwP and are safe,3 4 7 38 they also confirm that the longer term effects have not been established and that pragmatic delivery models are largely untested.3 –6 We propose that the intervention provides evidence for effectively supporting PwP to engage with an exercise programme for 6 months through standard community resources. The adherence to the programme compares favourably to adherence to standard UK exercise referral,41 with 69% of our participants adhering to the exercise programme and 86% of these individuals attending more than one session a week on average compared with a pooled rate of 37% (95% CI 20% to 54%) for exercise referral. There was also excellent

Figure 1 CONSORT flow diagram.


Movement disorders
<table>
<thead>
<tr>
<th>Table 2</th>
<th>Outcome</th>
<th>3-month</th>
<th>6-month</th>
<th>12-month</th>
<th>Effect size d (95% CI)</th>
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<td></td>
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<td>Exercise</td>
<td>Handwriting</td>
<td>Delta</td>
<td>Exercise</td>
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<tr>
<td>Motor symptoms</td>
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<td>Two-minute walk test (m)</td>
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<td>Nine-hole peg test (s)</td>
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<td>9.8±0.3</td>
<td>9.8±0.3</td>
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<td>TUG (s)</td>
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<td>Fitness</td>
<td>71.2±0.4</td>
<td>71.2±0.4</td>
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<td>Aerobic (VO2max to L/min)</td>
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<td>3.3±0.1</td>
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<td>Leg power (watts)</td>
<td>26.5±0.1</td>
<td>26.4±0.1</td>
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<td>Grip strength (kg)</td>
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<td>SF-36—physical</td>
<td>64.2±2</td>
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<td>SF-36—mental</td>
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<td>FSS</td>
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<td>8.2±0.4</td>
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<td>BMI</td>
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<td>MAP BP (mm Hg)</td>
<td>79.7±0.2</td>
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<td>5.1±11</td>
<td>77.6±0.8</td>
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Least squares means±SE estimates. Delta, between group difference (exercise−handwriting); effect size, Cohen’s d based on least squares (marginal) means differences over all assessments with non-central 95% CIs.

BMI, body mass index (weight (kg) / height (m)²); EQ5D-5L (VAS) index score of the Euro-QOL EQ5D-5L; FSS, Fatigue Severity Scale; MAP BP, mean arterial blood pressure (systolic blood pressure (mmHg)+2×diastolic blood pressure(mmHg)/3); MDS-UPDRS III, Movement Disorder Society Unified Parkinson’s Disease Rating Scale part III; N-MSQ, Parkinson’s disease non-motor symptom questionnaire; PASE, Physical Activity Scale for the Elderly; SF-36, Short Form (36 item) Health Survey, physical and mental subscores; VO2max, maximal oxygen consumption; TUG, timed up and go test; VAS, visual analogue scale.

compliance to the exercise programme content and there was good evidence demonstrating that individuals progressed through the programme, in terms of increasing training volume.

Considering our intervention, individuals participated safely in the community-supported exercise programme. The eligibility criteria and participant screening and monitoring were effective in selecting people suitable for the intervention. However, this group may present or develop coexisting pathology that can affect their ability to exercise and medical reasons were the predominant reasons to discontinue intervention. We found that most issues effecting exercise participation could be safely managed either directly by the practitioner supporting the intervention or through advice from or referral to appropriate medical professionals, highlighting the role of appropriately trained professionals to support and guild self-managed community exercise programmes. Importantly a National Occupational Standards, for supporting exercise in people with neurological conditions are available for professional education.

It should be considered that, while we used a wide range of recruitment routes and methods reducing the risk of recruitment bias, participants were recruited from Oxfordshire, Berkshire and Buckinghamshire, which are affluent areas of the UK. Acknowledging this limitation, we nevertheless propose the findings are largely generalisable to relatively healthy PwP. Therefore, the intervention represents a sustainable viable exercise programme for supporting PwP in community leisure venues across the UK, which could be implemented through existing exercise referral systems. The fundamental components of the intervention and delivery model could also be applied or adapted to other healthcare systems and conditions. PwP in England have higher rates of emergency admissions with longer hospital stays, higher costs (£907 million over 4 years) and in-hospital mortality; with many of the issues secondary to inactivity. Thus, PD is a good model for developing community clinical exercise programmes suitable for other neurological-degenerative conditions and, as such, the study has application to another three million individuals. The information gained from this research remain highly relevant and important to the needs of the public health services to adapt both to the ageing demographic and to people living longer with long-term neurological conditions.

In summary, at present, the evidence indicates that patients can be informed that attending a leisure centre to undertake this programme carries minimal risk and may improve or maintain motor symptoms. A substantive evaluation including wider geography, longer follow-up and cost-effectiveness is now indicated in order to determine whether this technology should be taken up by the NHS and would significantly add to the scientific knowledge of the cost-effectiveness of longer term exercise for this group. This technology has the potential to be implemented in the UK and worldwide.

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REFERENCES

3 Cruickshank TM, Reyes AR, Ziman MR. A systematic review and meta-analysis of strength training in individuals with multiple sclerosis or Parkinson disease. Medicine (Baltimore) 2015;94:411.
15 Oxfordshire Exercise on Referral data 2015;Unpublished internal document, Oxfordshire Sport and Physical Activity (requests info@oxspa.co.uk).

Movement disorders

Phase II randomised controlled trial of a 6-month self-managed community exercise programme for people with Parkinson’s disease

Johnny Collett, Marloes Franssen, Andy Meaney, Derick Wade, Hooshang Izadi, Martin Tims, Charlotte Winward, Marko Bogdanovic, Andrew Farmer and Helen Dawes

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