High-Cadence Cycling for Parkinson Disease: A Single-Arm Hybrid Implementation and Effectiveness Clinical Trial in the Community Setting

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Abstract

BACKGROUND

Efficacy of exercise to improve motor symptoms in Parkinson Disease (PD) has been established in multiple clinical trials. The Pedaling for Parkinson's™ (PFP) program is an existing community-based cycling intervention for individuals with PD. Although the program design was informed by efficacy studies, the implementation and effectiveness of the program have not been studied. We used a hybrid trial, which blends the study of implementation and effectiveness, to study the implementation of PFP in community gyms in the greater Boston area.

METHODS

This was a single-arm open-label pragmatic hybrid type 3 clinical trial designed to test implementation and observe clinical effectiveness. The implementation strategy consisted of enhanced multi-modal training and support for community-based gyms to implement the PFP protocol. Individuals with Hoehn and Yahr stage I-III idiopathic PD were recruited to participate. Primary implementation outcomes included adoption, gym fidelity, participant adherence, implementation cost, sustainability, acceptability, and safety. Secondary effectiveness outcomes included disease and quality of life measures.

RESULTS

34 gyms were invited to participate. 4 gyms agreed to participate and implemented the PFP protocol. 24 individuals with idiopathic PD agreed to participate in the study and started classes. The program was implemented safely and sustainably across all sites but with high fidelity at only one of four gyms. 58% of individuals who started classes completed at least 80% of classes. 96% of participants who started classes enjoyed the program and 87% wished to continue. No effectiveness outcomes demonstrated a significant change from pre to post.

CONCLUSION

Our implementation strategy of additional multi-modal training and support in starting a PFP class was insufficient to achieve wide adoption of and high fidelity and adherence to the PFP protocol. However, participating gyms' modifications of the PFP protocol in this study suggests such protocol modification may be necessary for effective implementation in the community setting. Future studies should first establish effectiveness of a revised PFP protocol. Implementation could then be achieved through a participatory approach in which barriers to gym participation are identified and mitigated early in the implementation process.

Contributions To The Literature

- Exercise therapy for Parkinson Disease (PD) improves motor symptoms and may be disease-modifying. Numerous studies have demonstrated the efficacy of exercise, but few have examined

implementation and effectiveness in the community.

- This trial examined the impact of a multi-modal strategy to enhance implementation of a community-based cycling program for PD, and observed effectiveness of the intervention.
- Despite the enhanced implementation strategy, very few gyms agreed to implement the program, gym fidelity to the protocol was poor, and effectiveness was not observed. Insights gained from participating gyms' modification to the protocol suggest changes to the protocol that could improve effectiveness. Further research is needed to better identify barriers to implementation.

Background

Parkinson Disease (PD) is a common neurodegenerative disorder. Progressive rigidity, tremor, slowness, and falls, along with myriad non-motor symptoms rob patients of quality of life.¹ Pharmacologic therapy can mitigate symptoms but has not been shown to protect the brain from further damage and degeneration.^{2,3} Non-pharmacologic therapy—in particular exercise—can also improve symptoms. There is speculation that exercise may even slow disease progression and protect neurons.^{4–6} While many exercises such as dance,⁷ tai-chi,^{8,9} running,⁶ boxing,^{10–12} Nordic walking,^{13,14} qigong,¹⁵ and aquatic exercise^{16,17} have demonstrated efficacy in small clinical trials, few studies¹¹ have examined the implementation and effectiveness of these interventions in the real-world setting. Lack of evidence regarding feasibility and effectiveness of exercise may be one barrier to its routine prescription for individuals with PD.

Hybrid trials blending implementation and effectiveness research may shorten the time gap between research discovery and routine uptake. Based on the framework proposed by Curran et al. in their 2012 paper¹⁸ detailing methods for blending clinical effectiveness and implementation research, we designed a type 3 hybrid trial to test implementation and observe effectiveness of the Pedaling for Parkinson's™ (PFP) program¹⁹—a community-based high-cadence cycling intervention.

We chose to study the PFP cycling program for two reasons. First, cycling may be especially beneficial because it is often inexplicably but remarkably preserved in individuals with advanced PD who would never be able to run or complete many of the other exercise interventions available.^{20,21} Second, PFP was designed based on the results of several clinical trials examining forced high cadence cycling (FHCC), which have been found to be effective at improving Parkinson's symptoms. While PFP does not utilize FHCC as part of its program, the PFP protocol employs (non-forced) high cadence cycling (HCC). However, this methodology has never been studied in a clinical trial.

Multiple small controlled trials have demonstrated that FHCC can ameliorate motor symptoms in individuals with PD as measured by the Unified Parkinson's Disease Rating Scale-Part III and Timed up and Go.^{22–31} In FHCC, individuals with PD pedal with either a tandem co-rider or a motor providing external augmentation at a cadence of 80–90 revolutions per minute (rpm)—which is faster than most

individuals would pedal on their own. Although the rate is augmented, cycling on either device is an active, not passive, activity. In comparing FHCC versus cycling at a self-selected cadence on a stationary indoor bicycle, most of the published literature has found that, despite similar cardiovascular exertion in the two modes, improved motor symptoms are only observed in the forced-cadence modality.^{26,29-31} One recent study did demonstrate gains in both forced and voluntary groups, but it was noted that the voluntary group self-selected to pedal at a cadence near the target achieved by the forced group.²⁵

Despite the noted benefit of FHCC, the tandem or motor-augmented bicycle equipment required to implement this protocol in the community is not readily available or affordable. Based on his research of FHCC at The Cleveland Clinic, Jay Alberts, PhD along with Cathy Frazier, a person with Parkinson's, launched The Pedaling for Parkinson's™ (PFP) program,¹⁹ as an accessible and affordable alternative to FHCC. In PFP, individuals with PD are verbally coached to achieve moderate-exertion, high-cadence cycling (HCC) on solo-rider "spin" bikes. This differs from FHCC because there is no physical augmentation, only auditory and social cues encouraging participants to pedal at a high rate.

Although anecdotal evidence suggests participants in existing PFP programs enjoy the classes, dissemination of the intervention remains limited and the effectiveness of the program has not been established. Even though written instructions on how to run the PFP program are available, informal discussion with gyms that had already implemented a Parkinson's cycling program revealed they had sought out additional instruction in starting their program. This additional support was obtained either directly from the volunteer coordinator running PFP, from a class participant who had taken part in a PFP elsewhere, or from a for-profit company not affiliated with PFP that charged a fee to support setting up a PD cycling program. Based on this information, we hypothesized that community gyms might be more willing to implement the program with additional support that would empower them to realize that they could implement the program without specialized knowledge of Parkinson's Disease and within their existing infrastructure. We therefore developed an implementation strategy of enhanced multi-modal training coupled with ongoing local support to supplement the existing written PFP start-up materials.

We designed a type 3 hybrid trial to test our implementation strategy while gathering observational effectiveness data. Hybrid type 3 trials are best suited to interventions supported by strong "indirect" efficacy or effectiveness data whose rapid implementation is being encouraged by prevailing policy or culture.¹⁸ In the case of the PFP program, FHCC provides strong indirect evidence that HCC may be effective. Additionally, clinical guidelines already strongly recommend exercise for Parkinson's and the PFP program has already been implemented at over 100 sites around the country.¹⁹

Consistent with the type 3 hybrid trial design, our primary outcomes were implementation measures and our secondary outcomes were exploratory effectiveness measures. We hypothesized that with our enhanced implementation strategy, PFP HCC could be implemented with high gym fidelity and participant adherence in a community-based setting and would be safe, affordable, and sustainable. If such implementation was achieved, we hypothesized HCC would be effective – ie would lead to motor, cognitive, and quality of life gains similar to those observed in controlled trials utilizing FHCC.

Methods:

Study Design: We designed a single-arm open-label pragmatic hybrid type 3 clinical trial to test implementation and observe effectiveness of an eight-week PFP intervention in community-based gyms. The trial was prospectively registered on ClinicalTrials.gov, Identifier: NCT03675932. The study is reported according to the Standards for Reporting Implementation Studies (StaRI) checklist. Primary implementation outcomes were protocol adoption, gym fidelity, participant adherence, implementation cost, sustainability, acceptability, and safety. Secondary effectiveness outcomes included measures of motor severity, cognition, and quality of life.

Implementation outcomes were evaluated based on data gathered in class and questionnaires completed by instructors/participants. Participants were evaluated for effectiveness outcomes within two weeks pre- and one week post-participation in the classes. The protocol and consent forms were approved by the Partners Human Research Committee. All procedures followed were in accordance with the ethical standards of the responsible institutional or regional committee on human experimentation or in accordance with the Helsinki Declaration of 1975, as revised in 1983. All participants provided written informed consent. Study data were collected and managed using REDCap electronic data capture tools hosted at Partners Healthcare.³²

Implementation Strategy: We recruited gyms in the greater Boston area to implement PFP classes based on their geographic diversity and access to participants with PD. As per PFP protocol, gyms were required to read and sign the PFP licensing agreement. This agreement details general instructions for implementation of the program along with legal requirements for participation. In order to encourage the adoption of the program, we designed an augmented implementation strategy which included the following components: First, staff at each site underwent an in person or by phone 45-minute protocol training. Second, staff attested to viewing a 60-minute video produced by study investigators (KEM) that 1) introduced the clinical features of PD 2) summarized the research behind FHCC 3) detailed how to set up a PFP class.³³ Third, gyms were provided with pre-made handouts detailing the structure of the classes, highlighting exertion targets, and how to record participant bike settings. Fourth, gyms received ongoing study staff support with the opportunity to ask questions regarding implementation.

Intervention

Similar to several FHCC studies,^{24,25,30} the duration of the intervention was 24 one-hour spin classes over eight to nine weeks. The PFP protocol consists of a 10-minute warm-up, 40-minute main set during which participants target a cadence of 80–90 rpm and an exertion level at either 60–80% of their maximum heart rate or Borg rating of perceived exertion (RPE) between 4–7/10,^{34,35} and a 10-minute cool-down. If participants cannot achieve the full protocol, instructors encourage rest breaks to allow safe maximal participation. After the intervention concluded, gyms and participants decided independently if they would continue offering/taking classes.

Study Participants

Participants were recruited through flyers, referral, PD support groups, websites, and a targeted approach whereby participants were identified by zip codes proximal to gym locations. Full eligibility criteria are detailed in **Supplementary Appendix 1**. Participants had a clinically confirmed diagnosis of Hoehn and Yahr stage I-III idiopathic PD while ON anti-parkinsonian medication, and stable medication regimen. Participants agreed not to initiate a new structured exercise plan or new course of physical therapy for the duration of the intervention but could continue any pre-existing exercise routine (including group classes).

At the first visit, participants were asked to provide demographic data, medical history, a list of their PD medications, frequency of falls in the week prior, and information about prior exercise experience. They also underwent measures of physical activity and cognition via International Physical Activity Questionnaire-Short Form³⁶ and the Montreal Cognitive Assessment.³⁷ These instruments were not used as outcome measures but rather to help characterize the population who chose to participate in the intervention.

Primary Endpoints: Implementation Outcomes

Adoption of the PFP program was measured by the number of potential participating gyms with spin bikes who ultimately implemented the program. *Fidelity* of gyms to PFP protocol was measured via direct observation of classes by KEM, as well as each gym's subjective report of whether they could implement the class as per protocol. Additionally, in-class cadence and RPE data was collected by spin instructors to determine whether gyms were generally meeting cadence and exertion targets with their participants. Instructors had participants rate their exertion using the Borg RPE scale at 1, 20, and 39-minutes into the main set. Average cadence and exertion were measured in this way because community-based classes often lack access to continuous cadence and heart rate monitoring. Participant *adherence* to the intervention was measured through record of attendance over the 24 offered sessions. We considered those who started the classes, did not withdraw from the study, were not lost to follow up, and completed at least 80% of the sessions to have adhered to the intervention.

Cost was estimated based on 1) study staff record of implementation strategy cost and 2) a post study survey querying gyms and participants about intervention costs they incurred. *Sustainability* was measured via telephone eight weeks after conclusion of the intervention to determine if gyms continued to offer PFP classes and participants continued HCC. *Acceptability* of the program was measured through Likert scale⁷ and free-text questions designed to capture participant and gym subjective experience. *Safety* was monitored through tracking of adverse events (AE) as reported by instructors. Participants were queried by phone regarding interval AE between weeks 3–6, and eight weeks after the intervention. Serious AE were defined as life-threatening, requiring hospitalization, or leading to a persistent disruption of baseline function.

Secondary Endpoints: Effectiveness Outcomes

Participants were evaluated within two weeks before (pre-test) and one week after (post-test) the intervention. Participants were tested "ON" medications at the same time of day (within one hour) to

reduce medication-related performance fluctuation. Post-test evaluations were not conducted on the last day of class due to previously documented motor and cognitive improvements immediately following a single session of FHCC.²⁸ A modified version of the Unified Parkinson's Disease Rating Scale (UPDRS)³⁸ (excluding rigidity and retropulsion) was used so that it could be videotaped and rated remotely by a movement disorders neurologist blinded to whether the visit was pre- or post-intervention. This modified version has been shown to be reliable and valid, both at cross-sectional time points and longitudinally.³⁹ Timed Up and Go (TUG)⁴⁰ and Trail Making Test (TMT) A & B^{41,42} were tested. Quality of life was assessed via PROMIS-Global Health v1.1: A 10-item questionnaire that assesses participant reported outcomes regarding their overall (global) health.^{43,44} This instrument produces physical and mental health T-scores, the distributions of which are standardized such that a 50 represents the mean for the US general population and the standard deviation around that mean is 10 points. This instrument was chosen as a more global assessment than the PD specific Parkinson Disease Questionnaire-39 (PDQ-39).

Statistical Analysis

Implementation outcomes are reported descriptively. To determine independent baseline predictors of adherence, comparison of covariates across adherence was carried out using a Wilcoxon rank-sum test for continuous variables and a Fisher exact test for categorical variables. Effectiveness outcomes were analyzed on an intention to treat basis and tested against the null hypothesis of no change using a mixed effects linear model with a fixed effect for time (pre-test or post-test) random effects for site and participant. Effectiveness outcomes aside from PROMIS global health are reported as estimated mean change in scores.

If the true adherence proportion is 80% we calculated that a sample of 30 participants would provide an estimate of the true adherence with a confidence interval of 0.31 (0.61–0.92). We also calculated that a sample size of 30 participants would provide 80% power to reject the null hypothesis of no change in UPDRS scores compared to an alternative hypothesis of 3.3 points mean change using a significance level of 5% (two-tailed) and a standard deviation of 6.0. Previously reported data in exercise studies for PD indicate that UPDRS scores will have a standard deviation of 6.0 for the change from baseline to week eight when measured OFF medication.³⁰ We expected a smaller standard deviation since we utilized a modified version of the UPDRS and tested participants ON medication. Comparison to a hypothesized value of no change was based on previous studies that have shown no improvement in UPDRS scores for those participating in voluntary exercise.^{29,30}

Results

Baseline characteristics of gyms

Figure 1 describes gym recruitment and participation. 34 gyms were considered potential participants of the study, of which only 6 agreed to participate and completed the implementation training. Ultimately, only four gyms (including three Young Men's Christian Association (YMCA) gyms) completed the study.

The largest barrier to gym recruitment (10 gyms) was inability of the gyms to obtain permission of a governing association (needed to sign the licensing contract for PFP). The majority of the rest of the gyms who declined to participate (8 gyms) did not provide us with a reason for their unwillingness. Two important structural barriers we identified were lack of spin bikes and lack of a handicap accessible gym entrance.

Baseline characteristics of participants

48 participants were pre-screened for eligibility. 19 of those participants declined to participate, most commonly due to inconvenient class time or location. Figure 2 depicts participant participation as well as adherence. Baseline characteristics of the 27 enrolled participants are listed in Table 1. Participants were older, highly educated white adults with moderate disease severity. At baseline this cohort already had a high level of physical activity measured using the IPAQ-sf. Four participants had fallen one or more times in the week prior to the baseline assessment. 93% (n = 25) of participants had prior experience on a road or stationary bike with 78% (n = 21) endorsing comfort cycling outdoors on a road or bike path. Only 17% (n = 4) had ever previously participated in a spin class and only one of those individuals for a frequency of three times a week or more.

Table 1
Participant Characteristics

Characteristic	All Participants (n = 27)	Tolerated Intervention (n = 14)	Did Not Tolerate Intervention (n = 10)	<i>p</i>
Age (years)	68.1 (8.05)	69.4 (8.53)	65.0 (7.62)	0.259
Sex (% female)	30% (8)	14% (2)	50% (5)	0.085
White race, non-Hispanic ethnicity	100% (27)	100% (14)	100% (10)	1.000
Bachelor's degree or higher	78% (21)	64.3% (9)	90% (9)	0.341
Body mass index (kg/m ²)	26.1 (4.45)	27.5 (3.91)	24.8 (4.89)	0.122
Hoehn and Yahr stage	19% (5)	14% (2)	30% (3)	0.250
I	67% (18)	64% (9)	60% (6)	
II	14% (4)	21% (3)	10% (1)	
III				
Time since PD diagnosis (years)	5.8 (5.51)	5.6 (5.54)	6.2(6.51)	0.703
Duration of symptoms (years)	7.4 (5.58)	7.6 (6.19)	7.8 (5.63)	0.664
Implanted deep brain stimulator	7% (2)	7% (1)	0.0% (0)	1.000
Levodopa equivalent daily dose (LEDD) (mg)	487.9 (439.30)	469.8 (458.49)	465.1 (271.36)	0.618
Baseline Montreal Cognitive Assessment Score (/30)	25.63 (3.40)	26.0 (3.51)	24.9 (3.75)	0.237

IPAQ-sf: International Physical Activity Questionnaire – short form. PROMIS: Participant-Reported

Outcomes Measurement Information System. All measures reported as Percent (n) or Mean (SD)

except PROMIS is reported as T-scores. PROMIS scores of 48.7 and 51.1 can be interpreted to

mean physical and mental health of this cohort fell near the national average. P values reflect comparison between characteristics of those who tolerated the intervention as compared to those who did not. Three participants enrolled in the trial but were not able to undertake the intervention as their gym dropped out. Their data is not reflected in the adherence comparison but is reflected in the second column detailing baseline characteristics of all participants.

Characteristic	All Participants (n = 27)	Tolerated Intervention (n = 14)	Did Not Tolerate Intervention (n = 10)	p
Baseline IPAQ-sf Level of Physical Activity	56% (15)	57.1% (8)	50.0% (5)	0.715
High	33% (9)	35.7% (5)	20.0% (2)	
Moderate	11% (3)	7.1% (1)	30.0% (3)	
Low				
Baseline PROMIS global health	48.7 (7.21)	49.3 (7.41)	46.6 (4.83)	0.575
Physical T-score	51.1 (8.39)	50.0 (7.60)	51.4 (10.14)	0.368
Mental T-score				
IPAQ-sf: International Physical Activity Questionnaire – short form. PROMIS: Participant-Reported				
Outcomes Measurement Information System. All measures reported as Percent (n) or Mean (SD)				
except PROMIS is reported as T-scores. PROMIS scores of 48.7 and 51.1 can be interpreted to				
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Protocol violations

Six participants violated the protocol eight times including increasing anti-parkinsonian medication (n = 3), starting a new round of physical therapy (n = 4), and starting a new exercise program (n = 1). These participants were included in the safety, adherence, and effectiveness analyses.

Primary endpoints: Implementation Outcomes

Adoption

Only Gym A elected to start the PFP program from scratch. Gyms B and D converted their current PD cycling classes to PFP protocol; Gym C was already executing the PFP program per protocol and agreed to participate in the study with novel participants. Staff at all four participating gyms completed protocol training and attested to watching the training video. Gym staff reported the video was helpful and motivating, but too long.

Fidelity. Gym B implemented the PFP protocol as prescribed (ie: participants were coached to complete 10 minute warm up, 40 minute main set at average cadence of 80–90 rpm *for the entire time*, and 10 minute cool down). The other three gyms found the protocol too difficult for most participants to achieve

and adapted the protocol to include interval training (eg: 1-minute on, 1-minute off). Average cadences are shown in Figs. 3 and 4. Participants in gyms C and A were below cadence targets in early classes, but by the last week of the study, all four gyms achieved an average between 75–85 rpm, just shy of the 80–90 rpm target. On average, across all four sites participants achieved the target RPE at 1-minute into the main set only 3% of the time. Half way through the main set the target was achieved 78% of the time. One-minute before the end of the main set the target was achieved 93% of the time and exceeded 15% percent of the time.

Adherence

14 of the 24 participants (58% ; 95% CI = 39–78%) who started classes completed at least 80% of the classes (our pre-specified definition of adherence). Baseline participant characteristics did not differ significantly between those who adhered to the study and those who did not (Table 1). The most common reasons for non-adherence were medical conditions that arose over the course of the study and schedule conflicts (Fig. 2).

Nearly all participants travelled to class by car: 83% driving themselves and 13% driven by someone else. Average one-way transit distance was 10.8 miles (SD 9.31) and time 21.9 minutes (SD 11.62). Classes were offered starting mid-morning through early afternoon; 78% of participants found these times convenient.

Implementation Cost. The cost of the implementation strategy included: cost of video production (~\$5000), time required to develop the video and additional training materials (~ 40 hours of investigator time) and time required for ongoing support of the gyms in their initial implementation (~ 1 hr investigator time per gym per week for the three weeks surrounding first class date). *Intervention cost.* All YMCAs chose to offer the program as an included benefit of membership. One YMCA opted to offer the program for free for the 8 weeks of the research study and thereafter charge gym membership fees to continue participation. One YMCA allowed non-members to participate for a fee of \$100 for the 8 week session. The non-YMCA charged \$11 per class; participants there estimated they spent on average \$238.75 in tuition for the 8 week program. At the conclusion of the study participants were asked via written exit-survey how much they would consider to be a reasonable and sustainable amount to pay for this type of program. 18 participants chose to answer and considered an average of \$5.50 per class (range \$0–30) to be a reasonable and sustainable amount to pay for this type of program. Gyms estimated that cost to produce an 8 week class session ranged from \$1500 - \$2,200, with the majority allocated to cover salary for the instructor. Other cost components were bike lease fees, cleaning supplies, heart rate monitors, and marketing.

Sustainability

All four gyms opted to continue offering the program and were still offering it at eight weeks post. 18 of 23 (78%) participants who completed the post-survey evaluation continued to practice HCC after the end

of the intervention (89% of those individuals riding at their study-site). 13 of 23 (56%) participants were cycling at least once during the eighth week post.

Acceptability. All four gyms ‘strongly agreed’ that they enjoyed offering the PFP program and that it was easy to implement. Gyms agreed (‘somewhat agreed’ to ‘strongly agreed’) that participants achieved target cadence and experienced motor and cardiovascular gains. Of the 23 participants who completed the post-survey: 96% agreed they enjoyed participating in the program and 87% agreed they would continue participating if they could. 70% agreed their mood improved; 83% agreed their endurance improved. **Supplementary Appendix 2** further details participant responses.

In free text response, 43% of participants listed camaraderie as something they liked best about the program while 26% cited the instructor and 22% cited the structure as favorite parts of the program. Other likes included: access, the challenge, the facility, motor benefit, music, participating in research, and ‘everything.’ The most common dislike was saddle soreness cited by 35% of participants. 30% of participants said there was ‘nothing’ they disliked about the program. 17% disliked traveling to participate. Selected comments made by participants during AE check-ins are listed in **Supplementary Appendix 3**.

Safety/Adverse Events

62% of the 24 participants who started classes reported an AE between date of consent and eight weeks-post (Table 2). Most of these AE’s were mild and not considered related to the study intervention. Pneumonia requiring hospitalization and post-operative internal bleeding after elective knee surgery were the only two serious AEs; neither was considered related to study interventions. Musculoskeletal and connective tissue disorders (primarily saddle soreness and knee pain) were the most common AEs related to the study interventions and did not affect compliance. Back pain and a broken foot after the end of the study did prevent two participants from continuing cycling after the end of the intervention. No falls occurred during or immediately before or after class, but falls outside of class did limit some participants’ ability to fully participate in subsequent classes. Dyspnea and palpitations required two participants to end a single session early but did not prevent subsequent return to class.

Table 2
Frequency List of Reported Adverse Events

Event according to system organ class or preferred term	Total Events n	Participants n (%)
Cardiac disorders	2	2 (7%)
Dyspnea (1)		
Palpitations (1)		
Eye disorders	1	1 (4%)
Eye hemorrhage (1)		
General disorders and administration site conditions	1	1 (4%)
Fatigue (1)		
Infections and infestations	1	1 (4%)
Pneumonia requiring hospitalization (1)		
Injury, poisoning and procedural complication	4	3 (11%)
Fall (4)		
Musculoskeletal and connective tissue disorders	15	12 (44%)
Back pain (2)		
Broken foot (1)		
Knee pain (3)		
Leg cramps (1)		
Saddle soreness (5)		
Swollen quadriceps (1)		
Shoulder pain (1)		
Plantar fasciitis (1)		
Nervous system disorders	3	3 (11%)
Hand numbness (1)		
Listing to one side on bicycle (1)		
Loss of consciousness associated with fall (1)		
Psychiatric disorders	1	1 (4%)
Depressed mood (1)		

Event according to system organ class or preferred term	Total Events n	Participants n (%)
Respiratory, thoracic and mediastinal disorders	4	4 (15%)
Common cold (1)		
Sinus infection (2)		
Vascular disorders	1	1 (4%)
Post-operative internal bleeding (1)		
Parenthetical numbers in the first column indicate absolute number of events. Events were deemed related		
to study intervention if they occurred during a cycling class or appeared to be temporally related to a class		
(eg: leg cramps at night but only on the nights after class). The following events were not thought to be		
related to cycling classes: eye hemorrhage, pneumonia, all falls, broken foot, back pain (1/2), knee pain (1/3), shoulder pain, loss of consciousness, all psychiatric/respiratory/vascular disorders. Listing to one side on the		
bicycle may be caused by dystonia associated with PD. This phenomenon had been previously witnessed		
by spin instructors in another individual with PD prior to start of the study.		

Secondary endpoints: Effectiveness Outcomes

Estimates and standard errors of change in effectiveness outcomes from longitudinal regression models are shown in Table 3. There was no significant improvement in any of the effectiveness outcomes.

Table 3
Exploratory Effectiveness Outcomes

Outcome	Pre-Intervention	Estimated Change (95% CI)	SE	p value
PROMIS-global health	48.15	-1.81 (-4.87–1.26)	1.53 1.49	0.25
physical t-score	50.60	-1.97 (-4.96–1.01)		0.20
mental t-score				
Modified UPDRS (/ 84)	13.55	0.3 (-1.12–1.67)	0.69	0.67
TUG (sec)	10.86	0.45 (-0.22–1.11)	0.33	0.19
TMT A (sec)	41.65 85.44	1.86 (-1.45–5.11)	1.63 6.62	0.27
TMT B (sec)		-8.18 (-22.08–4.87)		0.23
Pre-intervention values are reported as mean estimates.				

Discussion

In this implementation study, adoption, fidelity and adherence to the PFP cycling classes was poor. Three out of the four gyms modified the PFP protocol over the course of the trial suggesting that modification of the existing PFP program may be needed for successful translation to a community setting. The program was generally safe, enjoyable, and sustainable, however the intervention failed to demonstrate improvement in effectiveness outcomes. This may have been due to low recruitment of gyms and participants, poor fidelity to the PFP program, poor adherence by participants, or it may suggest that the PFP program is not as effective as the FHCC program.

Out of 34 potential participating gyms, only four gyms completed the study. Three out of these four gyms already offered some form of cycling for patients with Parkinson's prior to the study; only one gym initiated the program from scratch. Failure to obtain permission from a central governing body resulted in 10 gyms' inability to participate in the needed time frame. Barriers related to cost, equipment, and personnel were observed in a few of the gyms but further research is needed to determine additional barriers to gym participation. Future implementation of novel exercise programming for individuals with PD may benefit from a participatory design approach which would allow earlier identification of barriers to implementation.

Our implementation strategy of enhanced training had poor yield in improving fidelity to the PFP protocol. A wide variety of cadences within and between sites were recorded. Only Gym B implemented the protocol as specified. We suspect Gym B was able to offer the program per protocol from the beginning because a higher proportion of their participants had prior spin class experience. The other three gyms adapted the intervention into an interval program to allow participants structured rest between attempts to achieve target cadence and exertion. Although this was in violation of the PFP protocol, these adapted

interval programs resulted in most participants achieving cadence goals by the end of the eight-week intervention.

Based on data collected from the gyms about their adaptations, Gym C developed the most robust interval program. This gym also produced the most tightly grouped participant cadences, which suggests high-reliability of their program design. Future studies could examine a revised PFP protocol that closely mirrors the real-world adaptations made by these gyms. As it took nearly the entire eight weeks to achieve cadence goals with this adapted design, future studies should consider assessing participants and gyms after a longer intervention period.

Participant adherence was low (58%) due to adverse events (mostly unrelated to study intervention), scheduling logistics, transportation, and cost (Fig. 2). It is unclear how this compares with other studies due to inconsistent or lack of reported adherence data.⁴⁵ Future implementation attempts should focus on reducing barriers to adherence by increasing the number of participating gyms or other options for accessing the intervention, and reducing costs. Remote classes using internet connected spin bikes in participant homes could be compared to in-person classes to see whether this will improve adherence (or worsen adherence due to the lack of camaraderie). Cost could be addressed through partnering with philanthropic and community-focused organizations. We found participating YMCAs were more willing to undertake the cost of setting up the programs in part because of their mission to serve the community, experience working with other chronic health conditions, and ability to subsidize programs through fundraising.

Limitations

Due to poor adoption as discussed above, only 4 gyms participated in our study; as a result, target enrollment of 30 participants was not achieved. Such a small sample of gyms and participants may not have allowed adequate assessment of the program. This study was also limited by the lack of a control group; however, we did not feel that a randomized trial was justified without further pilot data on PFP program implementation. The demographics of the entirely white, highly educated, and baseline-fit cohort also limit generalizability, especially to underserved communities. Finally, although much of the FHCC literature has tested participants OFF medication, we chose to test ON medication because we believed the discomfort to participants in testing OFF medication was not justified for exploratory outcomes.

Conclusions

The implementation strategy of additional multi-modal training and support in starting a PFP class was insufficient to achieve wide adoption of and high fidelity and adherence to the PFP protocol. Failure to obtain governing organization permission along with unknown barriers prevented broader gym participation. Based on the protocol adaptations made by three of four gyms in this study, modification of the existing PFP protocol to an interval-training format may be necessary. However, a decrease in sustained cadence speed and cardiovascular intensity may lower program efficacy. More research is

needed to first establish effectiveness of a revised community-based protocol. This could be accomplished through an iterative participatory design approach with participants and gyms that first identifies a feasible protocol through qualitative methods and then tests effectiveness of this protocol. Once effectiveness is established, implementation of the program should be further studied in partnership with a broad sample of community gyms.

Abbreviations

AE – Adverse Event

FHCC – Forced High Cadence Cycling

HCC – High Cadence Cycling

H&Y – Hoehn and Yahr Staging of Parkinson Disease

IPAQ-sf – International Physical Activity Questionnaire – short form

MoCA – Montreal Cognitive Assessment

PD – Parkinson Disease

PROMIS—Participant-Reported Outcomes Measurement Information System

PFP – Pedaling for Parkinson's[™]

RPE – Rating of Perceived Exertion

TMT – Trail Making Test

TUG – Timed Up and Go

UPDRS – Unified Parkinson's Disease Rating Scale

YMCA – Young Men's Christian Association

Declarations

Ethics approval and consent to participate: The protocol and consent forms were approved by the Partners Human Research Committee. All procedures followed were in accordance with the ethical standards of the responsible institutional or regional committee on human experimentation or in accordance with the Helsinki Declaration of 1975, as revised in 1983. All participants provided written informed consent.

Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions

KEM: Conception, organization, execution of research project; design, review and critique of statistical analysis; writing of first draft of manuscript

RKJ: Organization and execution of the research project; review and critique of the manuscript

JC: Design and execution of statistical analysis; review and critique of the manuscript

AW: Conception, organization, execution of research project; design, review and critique of statistical analysis; review and critique of manuscript

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Figures

Figure 1

Gym Recruitment and Participation. Recruitment, retention, and participation of community-based gyms is depicted in this diagram. 34 gyms were contacted regarding participation in the study. Four gyms (including three YMCAs) ultimately completed the study.

Figure 2

Participant Participation and Adherence. All participants who enrolled were analyzed with intention to treat (ITT) analysis. Medical reasons for inability to tolerate the class included arthritis, back pain, and complication from elective surgery.

Figure 3

Individual Average Cadence per Class. Each individuals' average cadence per class is graphed along with participants from the same study site.

Figure 4

Average Cadence per Class per Site. Average cadence per class is compared across sites.

Supplementary Files

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