



Exhibit 2 – Standards

Pedaling for Parkinson's

Indoor Stationary Cycling for People with Parkinson's

The standards are set forth below following information on the purpose, background and nature of a forced exercise cycling program. The standards identified as requirements are mandatory while those marked as guidelines are advisory.

Purpose

The goal of this Pedaling For Parkinson's program is to provide a means of applying recent data related to the benefits of assisted or forced exercise in human Parkinson's disease (PD) patients.

Background

Studies of parkinsonian animals indicate forced-exercise is beneficial for the treatment of PD as symptoms are relieved and motor function is improved. These animal studies suggest exercising at higher, i.e., "forced", rates may be necessary for symptom relief and improved motor function. To date, most human exercise studies have not reported substantial global improvements in PD patients' overall motor performance following voluntary exercise.

The discrepancy between the results of animal and human studies may be due to differences in exercise mode or rate. Human interventions have largely used paradigms or exercises that are voluntarily controlled by the patient while animal studies used forced-exercise interventions that required the animals to exercise at rates greater than their preferred voluntary rate.

A consequence of PD is reduced motor cortical activity. This may prevent PD patients from exercising at a rate that is sufficient to produce the beneficial effects of exercise on global motor function. An exercise paradigm that augments PD patients' voluntary efforts may be necessary to produce global improvements in motor functions, i.e., in motor functions that are not directly involved in the exercise. Assisted or forced exercise embodies this concept by augmenting the voluntary efforts of PD patients so that they can exercise on a stationary cycle at a higher rate (80-90 revolutions per minute or RPMs) than they could voluntarily on their own (typically 50-60 RPMs).

This concept is being researched in studies underway at the Cleveland Clinic. One of the completed studies found that, following a forced exercise cycling program, a group of PD patients showed on average a 35% improvement in a common measure of motor function whereas a second group of PD patients, cycling voluntarily in the same study, did not exhibit any improvement. See, Ridgel AL, Vitek JL, Alberts JL. (2009) Forced, Not Voluntary, Exercise Improves Motor Function in Parkinson's Disease Patients. *Neurorehabilitation & Neural Repair*. 23(6):600-8. The forced exercise group pedaled at a cadence 30% greater than their preferred voluntary rate and both groups exercised within the same range of aerobic intensity (60% to 80% of their individualized training heart rate).

Assisted/Forced Exercise

Assisted or forced exercise is operationally defined as a mode of aerobic exercise in which the voluntary efforts of an individual are augmented so that the individual can exercise at rates faster than they could achieve voluntarily. Assistance typically takes the form of another individual riding a tandem cycle with the patient; this rider is known as the “captain” even though they may not be located in the front position of the tandem. The captain is responsible for monitoring the performance of the PD patient and pedaling at a pace and resistance (gear) that keeps the PD patient within the required protocols (see below). Assistance might also be provided by a motor on a solo stationary cycle.

Anecdotal information indicates that it is also likely that some PD patients will be capable of meeting these protocols on their own (i.e., without assistance from a captain or a motor), either initially, after some training or after completing a program of assisted exercise.

Standards

1. Prescreening Requirements

The sponsor of an exercise program must prescreen potential PD participants for the following questions. If any of the questions are answered “Yes”, the physician for the PD patient must address the identified concern(s) in their written clearance/permission for the patient’s participation in the program.

Pre-Screening Questions:	Yes:	No:
Have you taken any heart medications?		
Have you ever had a heart attack?		
Have you ever had heart surgery?		
Have you ever had heart failure?		
Have you ever had pacemaker/ implantable cardiac defibrillator/ rhythm disturbance?		
Have you ever had cardiac catheterization?		
Have you ever had coronary angioplasty?		
Have you ever had heart valve disease?		
Have you ever had congenital heart disease?		
Have you had a close blood relative who had a heart attack before age 55 (father or brother) or 65 (mother or sister)?		
Have you experienced unreasonable breathlessness?		
Do you take blood pressure medication?		
Are you a diabetic or take medicine to control blood sugar?		
Is your blood cholesterol >240 mg/dL?		
Females: Have you had a hysterectomy or are you postmenopausal?		
Have you experienced dizziness, fainting or blackouts?		
Do you smoke?		
Do you have musculoskeletal problems i.e. your doctor has recommended you not participate in exercise for muscular reasons?		
Do you have concerns about the safety of exercise?		
Are you physically inactive, exercising less than 30 minutes per day/ 3 days per week?		
Have you ever experienced chest discomfort with exertion?		

2. Participant Selection Requirements

Before selecting and accepting any PD patient for an exercise program, the sponsor must determine that the person satisfies all of the criteria for inclusion and does not have any of the criteria for exclusion:

Criteria for Inclusion:

1. The providing of consent after being given a copy of this Exhibit 2, Standards;
2. Clinical diagnosis of PD. (Idiopathic is the most common form of parkinsonism in which the cause for the condition is unknown);
3. Age between 30 and 75 years (older if approved by the participant's doctor); and
4. Written clearance/permission by the physician for the PD patient to participate in the exercise program after the physician has been given a copy this Exhibit 2, Standards, which clearance must address all concerns identified in the prescreening questions set forth above.

Criteria for Exclusion:

1. Clinically significant medical disease that would increase the risk of exercise-related complications (e.g. cardiac or pulmonary disease, uncontrolled diabetes mellitus, uncontrolled hypertension or stroke);
2. Dementia as evidenced by a score less than 116 on the Mattis Dementia Rating Scale; or
3. Other medical or musculoskeletal contraindications to exercise.

3. Exercise Program Requirements

Equipment and Fitting: Tandem Cycling

1. Tandem cycle
2. Stationary fluid or magnetic adjustable resistance trainer for the rear wheel (guideline: Cycleops brand is recommended)
3. Front wheel mount for the tandem (guideline: Cycleops or Krietler brand is recommended)
4. Pedals for both the captain/trainer and the patient should be either clipless pedals or pedals with cages (guideline: clipless style is recommended.) If the pedals are clipless, the patient should be familiar with or be taught about clipping in and out.
5. Step-stools for patients to get on and off the bike (guideline: preferable to have one on each side and stools with handles).
6. Bike computer for monitoring cadence, i.e., the pedaling rate during the cycling exercise.

7. Recommended Guideline: Heart rate monitor (HRM): the patient should be fitted with a heart rate monitor. (Guideline: HRMs with unique coding are recommended to prevent interference among multiple HRMs in a group setting). The chest strap of the HRM should be coated with a conducting gel or water to facilitate its operation. After each use, the HRM strap should be rinsed off with warm water and then dried with a towel. The heart rate readings should be available continuously to the captain so that the captain can adjust the cycling resistance to keep the patient's heart rate within the target zone. (Guideline: the cadence and heart rate monitor information should be provided to the PD patient during the exercise session so that the patient can monitor their performance and can learn in preparation for possible solo cycling exercise.)
8. Bike Fitting: all PD participants should be fitted to the cycle by an experienced bicycle fitter who should teach them the correct form and posture for cycling. Extra care and attention should be dedicated to the fitting process if the participant has any lower extremity contraindications to exercise.

Equipment and Fitting: Solo Cycling

1. Solo cycle, which can be either a stationary bike (including a motor assisted bike if available) or a road cycle on a trainer.
2. For the road cycle, stationary fluid or magnetic adjustable resistance trainer for the rear wheel (guideline: Cycleops brand is recommended)
3. Pedals should be either clipless pedals or pedals with cages (guideline: clipless style is recommended.) If the pedals are clipless, the patient should be familiar with or be taught about clipping in and out.
4. Step-stools for patients to get on and off the bike when the bike has a high crossbar (guideline: preferable to have one on each side and stools with handles). This may not be necessary for some stationary bikes, e.g., recumbent style cycles with step through frames.
5. Bike computer for monitoring cadence, i.e., the pedaling rate during the cycling exercise.
6. Recommended: Heart rate monitor (HRM): the patient should be fitted with a heart rate monitor. (Guideline: HRMs with unique coding are recommended to prevent interference among multiple HRMs in a group setting). The chest strap of the HRM should be coated with a conducting gel or water to facilitate its operation. After each use, the HRM strap should be rinsed off with warm water and then dried with a towel. The heart rate readings should be available continuously so that the patient can adjust the cycling resistance to keep his or her heart rate within the target zone. Note: HRM is recommended, not required.

7. Bike Fitting: all PD participants should be fitted to the cycle by an experienced bicycle fitter who should teach them the correct form and posture for cycling. Extra care and attention should be dedicated to the fitting process if the participant has any lower extremity contraindications to exercise.

Heart Rate Determination: Note: Recommended, not required.

1. For each PD participant, a maximum heart rate should be determined using the formula of 220 minus the age of participant. For example, the maximum heart rate for a 60 year old participant would be 160 beats per minute (220 minus 60).
2. The target heart rate zone for participants during exercise is 60-85% of their maximum heart rate.
3. Guideline: the target heart rate zone can alternatively be calculated using the Karvonen Formula, which incorporates a person's resting heart rate into the calculation and results in a slightly higher target zone.
4. Guideline: if a sponsor\participant wants a more individualized determination of maximum heart rate and target heart rate zone for a participant, they can have a cardiac stress test performed in a cardiologist's office, and use the results for the heart rate determinations.

Program Duration:

1. The cycling program should be considered an intervention that is suitable on a long-term basis for those individuals who are exhibiting improvements in functioning and do not develop any contraindications to exercise.

Parameters for Exercise Sessions:

1. Each exercise session should last at least one hour.
2. There should be 3 sessions per week.
3. Each one-hour exercise session consists of a 10 minute warm-up, a 40 minute main exercise set and a 10 minute cool-down. (Guideline: rest breaks may be necessary during the early weeks of a program especially for PD participants who have been sedentary or are unaccustomed to sitting in bike saddle for a period of time.)
4. During the warm-up, the patient's heart rate should gradually increase until the target heart rate is achieved after 10 minutes and the rate of pedaling should gradually increase to 80 RPMs.
5. During the main exercise set, the pedaling rate must be maintained between 80-90 RPMs and the patient's heart rate must be kept within the target heart rate zone (as determined

above, 60 to 85% of the patient's maximum heart rate). Based on heart rate monitor information, the captain on a tandem must adjust the biking resistance (gearing) to allow the patient to reach and maintain the desired heart rate range. On a solo cycle, the patient is responsible for selection of resistance; they should be instructed on proper use of the cycle prior to use. (Guideline: for patients who are relatively fit from an aerobic standpoint at the start of the session, a heart rate higher in their zone may be suitable and as patients become more fit over time, a gradual increase in their heart rate is recommended.)

6. During the cool-down, the patient's heart rate should gradually reduce to the level existing at the start of the warm-up while the cadence should gradually decrease to the preferred voluntary pedaling rate of the patient (typically 50-60 RPMS).
7. Patients should drink adequate amounts of water before, during and after each session. (Guideline: ACSM recommends that approximately 20 ozs. of water should be consumed during each hour of aerobic exercise.)
8. The cycling cadence and the patient's heart rate must be continuously monitored and adjustments made in resistance to keep the exercise within the specified parameters. The exercise is for the benefit of the PD patient, not for the fitness of the captain on a tandem or of a trainer in an exercise class for solo cyclists. (Guideline: while the captain/trainer should encourage the patient, learn about the patient and remain positive, they should also be monitoring the patient for any erratic or overly strenuous exertion and respond promptly, e.g., with a rest break, should such be encountered.)
9. Mounting and dismounting: tandems. Patient should get on the tandem first, with the captain assisting if necessary. The captain should not mount the bike until the patient has their feet in their pedals. At the end of the cool-down, the captain should dismount first and then assist the patient in dismounting.
10. Mounting and dismounting: solo cycles. Provide assistance as necessary for the patient to mount and dismount the cycle.