

Chapter 110. Clinical Center Cardiopulmonary Exercise Test (CPET) – Non-Invasive

This manual is intended to serve as a training and a reference document for persons who perform the CPET for the PVDOMICS Study using standardized procedures and techniques. This will aid in obtaining accurate test results and a safe testing environment.

110.1 Introduction to CPET

The cardiopulmonary exercise test (CPET) involves the assessment of cardio-pulmonary function during incremental exercise and combines the routine measurements of the electrocardiogram (ECG), blood pressure and power output with the analysis of exhaled gases.^{1,2} It is useful in a wide spectrum of clinical settings and helpful in clinical decision making. In clinical practice, CPET is considered when specific questions persist after consideration of basic clinical data (e.g., physical examination, chest radiograph, pulmonary function tests and ECG).

Cellular respiration involves the oxidation of carbohydrates, fats and glycogen stores using both aerobic and anaerobic metabolic pathways.^{3,4} The volume of oxygen (O_2) taken up each minute by the muscles for the oxidative process (VO_2), increases during exercise proportionate to the work rate that is being performed.⁵ In order to satisfy the increased metabolic needs of the exercising muscle, the lungs, heart, pulmonary circulation and peripheral circulation must respond in a coordinated fashion appropriate to the increase in metabolic demand.³ As exercise intensity increases, one or more of these essential systems may reach its maximal response, imposing a limitation to exercise. The assessment of maximum O_2 consumption ($VO_{2\text{ max}}$) and determining any limitations to further increases in VO_2 is an important diagnostic tool. The quantification and physiologic response of VO_2 , carbon dioxide (CO_2) production (VCO_2), and the minute ventilation (V_E) and other cardiopulmonary variables measured during a CPET allows the clinician to study the response of these systems under controlled metabolic stress.

Clinically, the most common indications for the CPET include:

1. Determination of the exercise capacity
2. Determination of the cause of a cardiopulmonary limitation to exercise
3. Identification of abnormal cardiopulmonary responses to exercise
4. Exercise prescription and monitoring response to exercise for training and rehabilitation
5. Evaluation of results of therapeutic intervention
6. Pre-operative evaluation
7. Impairment/disability evaluation
8. Selection of participants for cardiac transplantation
9. Evaluating unexplained dyspnea when initial cardiopulmonary testing is nondiagnostic

110.2 Quality Control

Quality Control (QC) is the periodic testing of a system to verify that it meets specifications. It is recommended that a mechanical calibration be performed following any movement or jarring of the equipment and a biologic calibration be performed every six months. Flow calibration and gas analyzer calibration should be performed prior to each test.

Ideally, each clinical center will have two biologic standards (lab personnel), so that if one of them is ill or leaves the area the center will still have a second person available to provide physiological calibration.

A biologic standard should be a healthy volunteer who does not smoke or have a respiratory disease (including asthma).

1. Biologic standards (two healthy laboratory personnel)

- 1.1 Obtain consent to repeated testing.
- 1.2 Test at least once every six months or as required by the manufacturer or your clinical center's protocol. Testing once every one to two months is encouraged, but not required.^{20,27,28}
- 1.3 The biologic standards should initially perform a maximal study, then use 40% to 50% of the maximum workload as their steady-state work rate.
- 1.4 For the steady-state tests, collect gas exchange and work intensity data on each biologic standard as 6 minutes of constant work rate is performed.
- 1.5 If the VO_2 or VCO_2 value obtained by averaging the last 2 minutes of the 6 minute test are outside the 95% confidence limits for a historical average for a particular biologic standard, repeat the test or use another biologic standard.
- 1.6 Take corrective action if the repeat values or other biologic standard's values are also outside the 95% confidence limits, and then repeat the test of the biologic standard to verify adequacy of the corrective procedure.
- 1.7 Add data to the quality control database only after the system is again performing properly. Recalculate averages and standard deviations to obtain updated values for the 95% confidence limits.
- 1.8 The time of day used to test the biologic standard should be consistent from session to session.

2. Collection of exhaled gases: utilizing appropriate valving, a 1 to 2 minute collection of exhaled gas can be obtained while a participant is in the steady state of exercise. Assessment of gas bag volume and fractional concentrations of O_2 and CO_2 can be used to calculate VO_2 , VCO_2 , and V_E . Though technically challenging, this method may be considered the gold standard validation method.²⁶

3. Establish mean and SD by repeated testing and apply rules for adequate quality assurance responses.

The QC technician should be familiar with all procedures to ensure that no technique errors are made. All QC testing data should be saved per the clinical center's normal protocol and should be readily available for review at all times.

110.3 Clinical Center Certification

Before CPET studies are performed on participants, each clinical center is required to complete the following list of requirements:

1. Review and become familiar with this MOP and study procedures
2. Establish a primary and a secondary contact person at each center who will be responsible for communication with and transmission of data to the Data Coordinating Center (DCC).
3. Submit one non-invasive CPET test on a "standard normal participant". The standard participant should be a healthy adult. You may use a laboratory employees for qualification testing if you like.
 - a. Prospective CPET laboratories will be evaluated based on their ability to: (1) follow a study qualification protocol, (2) generate good quality CPET data, and (3) transmit data to the core laboratory.
 - b. Test results will be compared to data available on normal individuals from the core laboratory and the published literature.
4. Await feedback from the core laboratory confirming that their center has qualified prior to scheduling study participants for testing.

110.4 Contraindications and Safety

Monitored exercise testing is considered relatively safe with a reported complication rate of 0.5 to 1.0 in 10,000 tests.^{20,23-25} Contraindications for performing cardiopulmonary exercising testing include those listed below. However, this list should not replace good clinical judgment. Any questions regarding exercise eligibility should be brought to the attention of the center's primary investigator.

110.4.1. Contraindications

1. Abnormal resting ECG
2. Current exercise-induced angina
3. Inability to cycle (e.g. arthritis)
4. Exertional syncope
5. Known potentially lethal exercise-induced arrhythmia (e.g., ventricular tachycardia)
6. Severe symptomatic aortic stenosis
7. Resting systolic blood pressure $\geq$ 200 mmHg

110.4.2 Criteria for immediately stopping the exercise test

In the vast majority of CPETs, participants should be verbally encouraged, both before and during the test, to give a maximal effort with the goal of achieving physiologic limitation. The most accepted criteria for exercise termination before symptom limitation are:

1. Chest pain suggestive of ischemia
2. Ischemic ECG changes
3. Complex ectopy or increasing ectopy with decreasing SpO₂
4. Second or third degree heart block
5. Fall in systolic blood pressure >20 mmHg from the highest value during exercise
6. Hypertension (>250 mmHg systolic; >120 mmHg diastolic)
7. Severe desaturation (SpO₂ ≤ 80% when accompanied by symptoms and signs of severe hypoxemia)
8. Sudden pallor
9. Loss of coordination
10. Mental confusion
11. Dizziness or faintness
12. Signs of respiratory failure

Note that exceeding a preset heart rate is not a useful criterion for stopping exercise. In situations in which the exercise is terminated because of the criteria listed above, the participant should be observed until they are stable and their physiologic variables have returned to baseline conditions.

110.4.3 Personnel Qualifications

The director of the laboratory performing the CPET should be a physician, preferably a pulmonologist or cardiologist certified in advanced cardiovascular life support, with knowledge of exercise physiology and with training in calibration, quality control, performance, and interpretation of CPET.

The director, based on the clinical situation and clinical judgment, should determine whether a physician needs to be present during the actual test or whether it is sufficient for the physician to be physically available in the proximity of the exercise laboratory, so as to be able to respond immediately in case of emergency.

The technicians should be trained in a field related to CPET such as exercise physiology, respiratory therapy, or pulmonary function testing. The technicians must have the basic knowledge of normal and abnormal exercise responses and be certified in basic cardiac life support. They should be able to recognize an abnormal rhythm and ST depression on an

ECG. The technician must have a minimum of 3 months of experience or internship in CPET before being given full responsibility for conduct of tests, and be competent in calibrating the equipment and performing quality control procedures.

110.5 Terms and Definitions

AT	Anaerobic Threshold
AT VO ₂	O ₂ Uptake at the Anaerobic Threshold
ATPS	Ambient Temperature and Pressure, Saturated
BP	Blood Pressure
BTPS	Body Temperature and (ambient barometric) Pressure, Saturated
HR	Heart Rate
HRR	Heart Rate Reserve
MVV	Maximum Voluntary Ventilation
OUES	Oxygen Uptake Efficiency Slope
RER	Respiratory Exchange Ratio (VCO ₂ /VO ₂)
VCO ₂	CO ₂ Output
V _D	Respiratory Dead Space
V _E	Minute Ventilation, Expired (L/min)
V _E / VCO ₂	Ventilatory Equivalent for Carbon Dioxide
V _E / VO ₂	Ventilatory Equivalent for Oxygen
V _I	Inspired Ventilation (L/min)
VO ₂	O ₂ Uptake
VO ₂ / HR	O ₂ Pulse
V _T	Tidal Volume

Continued on next page.

110.6 Equipment and Supplies

1. Cycle ergometer

- 1.1. Mechanical or electromagnetically braked (the electronically braked ergometer is strongly preferred because of its compatibility with incremental protocols)
 1. An upright cycle ergometer is preferred. A supine bicycle is an acceptable alternative in the case of invasive CPET.
- 1.2. Capable of calibration
- 1.3. Handlebars and seat that adjust to height

2. ECG system

- 2.1. Instrumentation should meet the specification set by the American Heart Association (AHA).^{11,12}
 1. Continuous display of a minimum of 3 leads
 2. Capacity to print copy of a 12-lead ECG

3. Blood pressure

- 3.1. Sphygmomanometer (cuff measurement method)
 1. Assorted cuff sizes
 2. Mercury column or calibrated Bourdon pressure gauge OR automatic blood pressure monitoring system
- 3.2. Direct method using in-dwelling arterial catheter
 1. Pressure transducer
 2. Recorder
 3. Intravenous (IV) administration set and associated pressure tubing
 4. 500 mL IV bag of heparinized saline solution with 1,000 units of heparin (2 units/mL) to be put under pressure for catheter flushing apparatus.

4. Pre-heparinized (dry heparin) syringes for arterial blood gas (ABG) harvesting are preferred

5. Appropriate standard precaution (SP) attire and gloves for technicians

6. Gas analyzers

- 6.1. O₂ and CO₂
- 6.2. Calibration tanks for 2 points within the physiologic range

7. Flow measurement device, typically including pneumotachograph or hot-wire anemometer, directional valves, and tubing (which may be provided as part of a commercial metabolic exercise system)

8. Data-acquisition computer, monitor and keyboard
9. Resuscitation cart
 - 9.1. Airway management equipment
 - 9.2. Defibrillator
 - 9.3. Airway suction apparatus, tubing and disposable ends
 - 9.4. Emergency medications (e.g., epinephrine, lidocaine, and nitroglycerine)
10. Supplemental O₂ equipment and delivery systems
11. Pulse oximeter
 - 11.1. Finger and ear probes
12. Chart displaying the Borg modified ratings of perceived exertion (RPE) scale¹⁴
13. Other optional tests require specific equipment
 - 13.1. Cardiac output determination using either CO₂ equilibration or foreign gas uptake techniques
 - 13.2. Spirometer for flow-volume curves before, during, and after exercise
14. Barometer (or other valid method to obtain barometric pressure) and accurate thermometer

110.7 Participant Preparation (Pre-Test Instructions)

110.7.1. Participant Instructions

1. The participant should be wearing loose-fitting and comfortable clothing and shoes suitable for exercise.
2. The participant should abstain from smoking and/or consuming alcohol at least 4 hours prior to test, and from eating a heavy meal 2 hours prior to test.
3. Typically, no medications are withheld prior to the CPET.

110.7.2. Procedure Explanation

1. Briefly explain the procedure, including the purpose of the procedure and the risks involved with CPET.
2. Answer the participant's questions before the test.
2. The explanation should be provided by personnel who are familiar with CPET and this PVDOMICS protocol and can accurately describe the test and all potential risks.

110.8 Participant Assessment and History

The participant's medical history, clinical diagnosis, and reason for the test should be reviewed by a physician or other trained professional prior to exercise testing. The review should include:

1. Current medications (especially bronchodilators, medications for control of blood pressure, and beta-blockers)
2. PF tests, blood gas data, chest radiograph, blood chemistry results, etc.
3. Current symptoms including chest pain, discomfort, or wheezing
4. The participant's exercise limitations and activities of daily living
5. If the participant needs to use supplemental oxygen during the procedure

The clinical center primary investigator or a designated certified professional should assess each participant to determine their ability to perform the CPET. Rescheduling may be necessary if the participant has not complied with the preparation criteria.

When speaking with the participant, utilize an interpreter if there is a language barrier. Ask the participant if they have complied with the preparation procedures and document the time of their last meal, all medications taken in the last 24 hours, and if they have exercised in the past 8 hours. Please note that recent exercise is participant reported and each participant may have a different definition of "exercise". This is okay, we are interested in ascertaining if they have recently tired themselves out.

110.9. ECG electrode placement

The modified 10-electrode (Mason-Likar) configuration is the preferred method of electrode placement for obtaining a 12-lead ECG.^{10,13,17}

The positions of the precordial leads are in the standard locations. The right arm (RA) and left arm (LA) limb electrodes are usually placed slightly below the right and left clavicle. The right leg (RL) and left leg (LL) limb electrodes are usually placed at the lower edge of the rib cage, or alternatively, at the level of the umbilicus at the mid-clavicular line.

Skin preparation is essential to reduce surface resistance and ensure a good ECG signal. To obtain the best ECG signal, the following steps may be used at the discretion of the personnel performing the ECG.

1. Shave hair (if applicable).
2. Use alcohol wipes to remove surface oils.
3. Abrade skin with fine emery cloth (240 grit sandpaper or mechanical skin preparation device). There are commercially available skin preps which include an abrasive and alcohol.

In addition, ensure that cables are adequately stabilized to reduce motion artifact.¹⁰

110.10. Arterial Line Placement (optional)

If arterial blood gases are indicated, arterial line placement to obtain multiple arterial blood samples may be required to fully assess gas exchange. This is especially true during the invasive CPET procedure (see MOP Chapter 111). In some situations, however, a single arterial blood sample may be taken during heavy exercise by radial artery puncture.

110.11. Pulmonary Function Tests (PFTs)

Pulmonary Function Tests will be obtained as per the PVDOMICS Pulmonary Function Testing MOP. Before proceeding with the CPET, ensure that the maximum voluntary ventilation (MVV) from the participant's most recent PFT is available.

110.12. Pulse oximetry

Pulse oximetry may be monitored during testing with either a finger probe or an ear probe. If an ear probe is used, rub the ear to improve perfusion prior to attachment of probe.

Ensure a good baseline reading for pulse oximetry probe by noting that the instrument indicates an adequate signal, pulsing with the heartbeat, and that heart rate measured by pulse oximeter agrees with ECG readings.

110.13 Pre-Test Procedures	
Confirm consent	Check to make sure that a current signed consent is on file for the participant.
Demographics	Identify the participant using two separate identifiers and record demographic information.
Participant instruction	Explain the purpose of the test. Explain that it is a maximum stress test and that the mouthpiece or mask must be in place for the duration of the test.
	Explain the end-points (attainment of maximal heart rate, development of limiting symptoms, or blood pressure, ECG or O ₂ saturation out of range) and reassure the participant about safety.
	Explain how to use of the Modified Borg Scale (Appendix 1). This scale will be used to assess both dyspnea (shortness of breath) and Rate of Perceived Exertion (RPE). The modified Borg scale will be used for all dyspnea and RPE assessments prior to, during, and immediately following exercise.
	Explain that they will need to point to a number on the scale because

	they will have a mouthpiece or mask in place.
Position participant on cycle ergometer	An upright bicycle will be used in order to ensure consistent measurements across clinical centers. However, a supine bicycle is an acceptable alternative in the case of invasive CPET (see MOP chapter 111). 1. Adjust handlebar and saddle height a. When the pedal is at bottom center, knee flexion should be about 20°. 2. Instruct the participant on pedal speed. 60 rpm is the target. a. Have the participant cycle briefly with no power to familiarize themselves with the equipment and to check the ECG signal for motion artifact.
Attach participant to mouthpiece/mask	Place mouthpiece in participant's mouth or attach mask and apply nose clip. Although sometimes uncomfortable, the mouthpiece is preferred to the mask since leaks can occur with a mask and cause erroneous results. Instruct the participant to maintain a tight seal around the mouthpiece to reduce the incidence of air leak. If the participant is using a mask, ensure that it fits tightly. Instruct the participant to breathe quietly for 2 to 3 minutes; feedback may be needed to avoid inappropriate breathing patterns (e.g., hyperventilation). Remind participant that they should not talk while the mouthpiece is in or during the test. Go through alternative communication signals with them (such as pointing at a number on the modified Borg scale rather than saying it, or nodding when you point to or say the correct number).
Pulse oximeter	Place pulse oximeter, if applicable. Finger or ear probe can be used. The ear probe is preferred because the contraction of the hand muscles while holding the handlebar of the cycle can alter blood flow to the finger. If the ear is used, prep the site by rubbing to ensure good blood flow. Pulse oximetry may or may not be accurate in exercise testing³⁶⁻³⁸ (Check pulse tracing to assess quality of signal if O₂ saturation reading seems inappropriate.)

Select Ramp Protocol	Participants will be assigned to one of three continuous ramp protocols depending on their current, self-reported physical abilities. The three ramps that will be used are a 10 watts per interval ramp, a 15 watts per interval ramp, and a 20 watts per interval ramp. An interval is defined as the time spent at a specific work rate. Follow the guidelines below to select the appropriate ramp for each patient based on their self-reported abilities. • If the participant becomes short of breath or fatigued moving between rooms in their house, use a 10 W ramp. • If the participant is able to walk around their house without difficulty but becomes short of breath or fatigued climbing one (1) flight of stairs, use a 15 W ramp. • If the participant is able to climb one (1) flight of stairs without difficulty (they do not become short of breath or fatigued in doing so) use a 20 W ramp. See Appendix 2 for further details.
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110.14 Resting Measurements	
ECG	Obtain resting ECG, which may differ morphologically (e.g., T-wave inversion) from standard ECG performed in the supine position with limb-lead configuration. Obtaining supine, upright, and hyperventilation ECGs has been recommended to document morphological changes.
Blood Pressure	Obtain resting blood pressure and assess for absolute or relative contraindication for testing. Cuff blood pressure measurement - The AHA recommends that the width of the bladder should be 40% of the circumference of the arm and the length of the bladder should be at least 80% of the arm circumference. - Measure blood pressure with the participant's arm relaxed and not on the cycle handlebar. - If using, mercury manometer or Bourdon gauge should be at eye level to avoid parallax - Note that if using an automated blood pressure unit, they are acceptable to use but may be unreliable at higher power outputs, likely because of motion artifact.

	Direct measurements of blood pressure are available with an arterial catheter.⁴⁰ - Pre-flush gauge and tubing with heparinized solution, clearing all bubbles. - View pulse wave-form to detect overdamping or underdamping of the signal. - Mount the pressure gauge at the left atrium level and set electrical output to read zero when gauge is opened to atmosphere.
Dyspnea	Assess and record resting dyspnea score using the modified Borg scale (Appendix 1) as feasible. Ask participant: “Using this scale from 0-10, where 0 is none at all and 10 is maximal, what number best describes your current shortness of breath?”
Rate of Perceived Exertion (RPE)	Assess and record resting RPE score using modified Borg scale (Appendix 1) as feasible. Ask participant: “Using this scale from 0-10, where 0 is none at all and 10 is maximal, what number best describes your current level of fatigue?”

110.15 Exercise Procedure	
Start exercise	Begin exercise following the appropriate ramp protocol (10 watts/interval, 15 watts/interval, or 20 watts/interval)
Monitor and record blood pressure, dyspnea, RPE, HR and ECG	Obtain blood pressure, dyspnea score, RPE score, heart rate, and work rate every 2 minutes, as feasible, during exercise as outlined in Appendix 3. Additionally, record VO₂ every 2 minutes as outlined in Appendix 4. 12-lead ECG should be continuously monitored during exercise. Obtain ECG, blood pressure, dyspnea score, RPE score, and VO₂ at the maximal work rate, as feasible. Maximal work rate (aka peak exercise) is defined as the point in time at which the participant is unable to maintain 60 revolutions per minute cycle rate.
Encourage participant	Encouragement may be needed with certain individuals to obtain a maximal effort. Encourage participant to reach an RER >1.10 and to maintain it for 30+ seconds.

Termination of test	At the termination of exercise ask the participant the reason for stopping the test (e.g., legs hurt, shortness of breath, or fatigue). Document the reason given. Obtain and record dyspnea and RPE scores immediately after the cessation of exercise.
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110.16 Post-Exercise Procedures	
Cool down	Recovery should include ECG and symptom monitoring during a cool-down phase of 2 minutes of unloaded pedaling (at 0 watts) followed by 3 minutes of rest.
ECG	12-lead ECG should be monitored continuously for 5 minutes post-exercise (cool down period).
Blood pressure, dyspnea, RPE, and HR	Blood pressure, dyspnea score, RPE score, and heart rate should be measured and recorded at each minute, as feasible, after cessation of exercise until the end of the cool down period.
Discontinue monitoring	Recovery values do not have to reach pretest levels but should be stable before monitoring is discontinued.

110.17 Reporting Results

Form 290 (Center Cycle Ergometer Non-Invasive Cardiopulmonary Exercise Test (CPET) Procedure Notes) or Form 291 (Center Cycle Ergometer Invasive Cardiopulmonary Exercise Test (iCPET) Procedure Notes) must be completed and entered into the study database. Note that only one of these forms will be filled out per participant. The paper copy of Form 290 or Form 291 should be maintained in the participant's study record at the clinical center.

At a minimum, the following results must be recorded either by the exercise system and software (data sent to the cardiovascular physiology core) or by the study coordinator on Form 290 or 291.

1. Maximum watts achieved during exercise
2. Duration of exercise in minutes
3. Reason for exercise termination
4. Whether or not the RER reached/exceeded 1.10
5. Resting RER (30 second average)
6. Peak RER (30 second average)
7. Resting HR (beats per minute)

8. Peak HR (beats per minute)
9. Resting oxygen saturation
10. Peak oxygen saturation
11. Resting respiratory rate (breaths per minute)
12. Peak respiratory rate (beats per minute)
13. Resting VO₂
14. Peak VO₂
15. VO₂ at AT (if identifiable)

110.18 Procedure notes

Record thorough notes on the procedure as several factors may influence test results. For example:

1.1. Participant effort

- 1.1.1. Participant should be encouraged to give a maximal performance, unless early termination is warranted.
- 1.1.2. Example variables to detect a maximal performance:
 1. HR must be close to the maximal predicted.
 - a. predicted HR = $210 - 0.65 \times \text{age}$
 2. V_{E,max}: between 60% - 80% of ventilatory capacity.
 - a. Ventilatory Capacity = MVV or FEV1 x 35 to 40
 3. SaO₂ <80% (In cases of severe hypoxemia a participant may terminate exercise.)
 4. Metabolic work: RER equal to or greater than 1.10 to 1.15
 5. Supervising clinician's observation of apparent effort.

1.2. Medications

- 1.2.1. Beta-blockers, calcium channel blockers, and similar medications may affect the heart rate response.
- 1.2.2. Bronchodilators may affect the ventilatory response

1.3. Exercise device selection and usage

- 1.3.1. Participant performance, coordination, and physical limitation with a particular exercise device can affect results:
 1. Weight support on handrails
 2. Inability to coordinate pedaling effort

3. Orthopedic constraints

1.3.2. Exercise device calibration

1. A poorly calibrated exercise device will affect reported work rate but not the overall VO_2max .

1.4. System leaks

1. Leaks associated with participant, connection interface, tubing, valves can affect results.

Cardiopulmonary exercise testing should be performed under the supervision of a physician appropriately trained to conduct clinical exercise tests and certified in advanced cardiac life support. The degree of supervision will be determined by the clinical condition of the participant being tested. It is recommended that the physician be present when participants are tested.

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Appendices appear on the following pages.

110.A.1 Appendix 1 – Modified Borg Scale

Modified Borg Scale

0	Nothing at all
0.5	Very, very slight
1	Very mild
2	Mild
3	Moderate
4	Somewhat severe
5	Strong
6	-
7	Severe
8	-
9	Extremely severe
10	So severe you need to stop

Use this scale to measure both perceived dyspnea and rate of perceived exertion (RPE) before, during, and after exercise.

110.A.2 Appendix 2 – Selecting the Appropriate Exercise Protocol

Follow the procedure below in order to select the appropriate exercise protocol for each participant in the PVDOMICS study.

Ask each participant:

1) *Do you become short of breath or fatigued when you walk around your house?*

If the answer to question 1 is “yes” → STOP, select a 10 watt/minute continuous ramp protocol

If the answer to question 1 is “no” → ask question 2

2) *Do you become short of breath or fatigued when you climb 1 flight of stairs?*

If the answer to question 2 is “yes” → select a 15 watt/minute continuous ramp protocol

If the answer to question 2 is “no” → select a 20 watt/minute continuous ramp protocol

110.A.3 Appendix 3 – PVDOMICS Non-Invasive Cycle Ergometer CPET Data Collection Schedule

Data should be captured as indicated below during the last 30 sec of each interval if possible.

Time Elapsed	Work Rate	Heart Rate	Pulse O ₂ sat	SBP	DBP	Dyspnea (Borg scale)	RPE (Borg scale)
(min)	(watts)	(bpm)	(%)	(mmHg)	(mmHg)	(0-10)	(0-10)
Pre-Exercise							
-1	Rest						
Exercise							
0	0						
Start ramp							
2							
4							
6							
8							
10							
12							
Recovery							
+1	0						
+2	0						
+3	Rest						
+4	Rest						
+5	Rest						
Peak							
____ : ____ minutes : seconds							

110.A.4 Appendix 4 – PVDOMICS Non-Invasive Cycle Ergometer CPET Additional Data Collection Schedule

All data should be captured during the last 30 sec of each interval

Time Elapsed (min)	VO ₂ (ml/kg/min)
Pre-Exercise	
-1	
Exercise	
0	

Time Elapsed (min)	VO ₂ (ml/kg/min)
Start ramp	
2	
4	
6	
8	
10	
12	

Time Elapsed (min)	VO ₂ (ml/kg/min)
Recovery	
+1	
+2	
+3	
+4	
+5	
Peak	
____ : ____ minutes : seconds	

110.A.5 Appendix 5 – Goldman Specific Activity Scale

This scale will be utilized by the study database to calculate the participant's NYHA functional class based on the maximum METS they achieve during the exercise testing.

METS Achieved	NYHA Functional Class	Summary of Criteria for Specific Activity Scale Classifications⁵³
≥ 7	Class I	Patient can perform to completion any activity requiring ≥ 7 metabolic equivalents
≥ 5	Class II	Patient can perform to completion any activity requiring ≥ 5 metabolic equivalents but cannot or does not perform to completion activities requiring ≥ 7 metabolic equivalents
≥ 2	Class III	Patient can perform to completion any activity requiring ≥ 2 metabolic equivalents but cannot or does not perform to completion any activities requiring ≥ 5 metabolic equivalents
< 2	Class IV	Patient cannot or does not perform to completion activities requiring ≥ 2 metabolic equivalents

110.A.6 Appendix 6 – CPET Calculations

In general, all calculations will be performed by a computerized data acquisition system or database software and will not need to be calculated by the technician. However, if the values below are not automatically calculated by either the system software or a database, manual calculations will be performed according to the equations below.

1. Expired volume (V_E) is calculated from the timed collection of expired gas, with gas volumes being corrected to BTPS conditions:

$$V_{E,BTPS} = \frac{V_{E,ATPS} \times (\text{ATPS to BTPS factor})}{t \text{ (min)}}$$

where:

$V_{E,BTPS}$ = expired minute ventilation (L/min) at BTPS

$V_{E,ATPS}$ = expired minute ventilation (L/min) at ATPS

$$\text{Conversion from ATPS to BTPS conditions} = \frac{(PB - PH_2O) \times (310)}{(PB - 47) \times (TA + 273)}$$

where:

PH_2O = water vapor pressure at the ambient temperature (AT). This MUST be obtained from tables of water vapor pressure versus temperature.

PB = barometric pressure

2. Inspired volume (V_I) is needed for other calculations and, if room air is inspired, can be obtained from:

$$V_I = V_E \times \frac{1 - FEO_2 - FECO_2}{0.7904}$$

where:

FEO_2 = mixed expired O_2 concentration

$FECO_2$ = mixed expired CO_2 concentration.

3. VCO_2 and VO_2 are calculated from timed gas collection and concentration of mixed expired gases (either direct measurement of a mixed expired gas sample, or calculated from

analysis of expired gas flow and concentration), corrected to mL/min at STPD conditions:²⁰

$$\text{VO}_2 = [(V_{I,\text{BTPS}} \times \text{FIO}_2) - (V_{E,\text{BTPS}} \times \text{FEO}_2)] \times \frac{\text{PB}-47}{0.863}$$

$$\text{VCO}_2 = [(V_{I,\text{BTPS}} \times \text{FICO}_2) - (V_{E,\text{BTPS}} \times \text{FECO}_2)] \times \frac{\text{PB}-47}{0.863}$$

where:

V_E and V_I are calculated as above

0.863 = conversion from L/min to mL/min and the ratio of (760 X 310/273) X 0.001 is the factor for the conversion from BTPS to STPD conditions

FIO_2 = fractional concentration of inspired O_2

FICO_2 = fractional concentration of inspired CO_2

FEO_2 = fractional concentration of mixed expired O_2

FECO_2 = fractional concentration of mixed expired CO_2

4. There are variables of interest that are derived from V_E , VCO_2 , VO_2 and heart rate (HR): the ventilatory equivalents (V_E/VO_2 , and V_E/VCO_2), the oxygen pulse (VO_2/HR), and the gas exchange ratio or respiratory exchange ratio ($\text{RER} = \text{VCO}_2/\text{VO}_2$)^{3,8,21}
5. Measures of pulmonary dead space to tidal volume ratio can be done by analysis of arterial blood gases using the classic Bohr equation (which gives the physiological dead space exactly):⁴¹

$$V_D/V_T\% = \{[(\text{PaCO}_2 - \text{PECO}_2)/\text{PaCO}_2] - (V_{D,\text{valve}}/V_T)\} \times 100$$

where:

$V_{D,\text{valve}}$ = respiratory valve and mouthpiece dead space

Utilization of the erroneously named “non-invasive V_D/V_T ” is inappropriate in CPET. It is usually misleading and can lead to radically wrong V_D/V_T values because PETCO_2 can be considerably different than PaCO_2 in the presence of significant gas exchange abnormalities which yield alveolar dead space.⁴²

6. Anaerobic threshold (AT), also known as ventilatory threshold (VT) or gas exchange threshold (GET), is determined from graphical analysis of data.⁴³ This study will use the term AT rather than VT or GET.
 - 6.1. The conventional method⁴¹ for determining AT uses ventilatory equivalents plotted against VO_2 . Usually, data are smoothed or averaged to reduce breath-by-breath variability, facilitating location of the AT. The AT coincides with the minimum of $\text{V}_\text{E}/\text{VO}_2$. The $\text{V}_\text{E}/\text{VCO}_2$ should either be constant or declining in the region around the AT. An increasing $\text{V}_\text{E}/\text{VCO}_2$ suggests the increase in both parameters is due simply to hyperventilation rather than to a change caused by lactic acidosis.
 - 6.2. AT can also be located using V-slope analysis,^{44,45} where the VCO_2 (vertical axis) is plotted versus the VO_2 (horizontal axis). The AT is the point where the slope of VCO_2 versus VO_2 increases; this can be located either manually or by using computerized analytic routines. If computerized analysis routines are used, the AT should always be verified by visual inspection of the data.
 - 6.3. Another approach is to plot the lactate concentration values in arterial blood against VO_2 (using either manual or computerized data analysis routines). The AT is the point where the rate of rise in lactate increases or the total lactate concentration exceeds a threshold value (usually about 2 mEq/L). Presenting the $\log(\text{lactate})$ versus $\log(\text{VO}_2)$ amplifies the change in slope, allowing easier identification of the threshold.⁴⁶
7. The normal alveolar-arterial O_2 gradient [$\text{P}(\text{A-a})\text{O}_2$] increases with age and during exercise. At 20 to 39 years of age, the mean $\text{P}(\text{A-a})\text{O}_2$ is 8 mmHg at rest, and 15 mmHg at maximal exercise. At 40 to 69 years of age, the mean $\text{P}(\text{A-a})\text{O}_2$ is 13 mmHg at rest, and 19 mmHg at maximal exercise. In this older group, at maximum exercise the upper limit of normal (i.e., 95% confidence interval) is 28 mmHg.³ A general guideline for the upper limit of adults is a $\text{P}(\text{A-a})\text{O}_2 < 35$ mmHg.⁸