A home-based intervention to promote mindful breathing awareness through pursed-lip breathing

training for COPD patients

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MAYO CLINIC

General Study Information

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Study Title: A home-based intervention to promote mindful breathing awareness through pursed-lip breathing training for COPD patients, IRB19-012772

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Research Question and Aims

Hypothesis:
We hypothesize that providing COPD patients with a mindful breathing module that is easy-to-use, prompts them to complete daily mindful breathing practice, and provides feedback will improve their breathing mechanics, emotional awareness, increase the time that they spend in heart rate coherence, and improve their quality of life.

Aims, purpose, or objectives:
The primary outcomes of the study are changes in breathlessness and emotions. Changes from baseline to three months on the two primary outcomes will be compared between the study arms using two-sample, two-sided t-tests with 5% type I error rates. Means, SDs, medians, ranges, and frequency distributions will be reported and plotted over time by study arm. Linear models will be used to assess the impact of treatment arm on three-month outcomes after adjusting for the corresponding baseline measure and other variables related to the outcome (age, degree of breathlessness at baseline using the mMRC dyspnea, and FEV1).

Background:
COPD:
COPD is a progressive lung disease that makes breathing difficult. Breathlessness usually worsens over time and eventually may make it difficult for people to carry out regular, simple daily activities, and cause anxiety and depressive symptoms. (8,35) In the United States COPD is the fourth leading cause of death and continues to increase.(2-6) It is also the third leading cause of hospital readmission in the US. There are currently an estimated 16 million Americans diagnosed with COPD(36) and many millions more who are believed to have the disease and not know it.37,38 It is estimated that the direct costs of COPD in the United States are $29.5 billion and the indirect costs $20.4 billion.(39)
COPD is demanding for the individual patient due to breathlessness (dyspnea) that increases during the more severe stages of the disease and impairs quality of life.(7,40) Breathlessness is the most common symptom and the use of pharmacological treatments alone is not effective; thus, additional non-pharmacological approaches such as breath retraining exercises are suggested.(7) Anxiety and emotional symptoms are frequently associated with symptoms of breathlessness/dyspnea and the cause of higher health care utilization.(40,41)

Pulmonary Rehabilitation (PR):
PR is an intervention that combines the promotion of physical activity and self-management. (42) It is regarded as an essential component of care for people with COPD and is supported by strong scientific evidence. (43-46)

PR reduces dyspnea, shortness of breath (13, 14), increases functional exercise capacity (13, 14), improves patients' health status and sense of control over their condition (13, 14), improves health-related quality of life (14), and reduces anxiety and depression associated with COPD (14). It also reduces acute exacerbations as well as decreases hospital bed days, the number of hospital admissions (47), and the overall burden on the health system. (14, 47-59)

Breathing Practice:
Breathing practice is an important component of PR. A commonly taught technique, pursed-lipped breathing (PLB) consists of instructions to breathe through the nose like smelling a flower without forcing and exhale slowly through the mouth while pursing the lips, as if they are blowing out a candle. Patients are taught to concentrate on the breath and nothing else, like meditation. PLB can ease dyspnea (20-23,51,60) which is the most disabling symptom of COPD(7), a common reason for seeking medical attention(7), and may cause people to limit their activity.(1) PLB can prevent the large airways from collapsing and can cause the release of more air from the lungs on exhale reducing dynamic hyperinflation. (24) Current guidelines for COPD suggest that using PLB also has positive effects in treating stress and anxiety related disorders(25) and it has an acute benefit to exercise capacity and parasympathetic outflow (stress).(26) Spontaneous pursed lips breathing can be a useful technique to increase walking endurance and reduce oxygen desaturation during walking in patients with moderate to severe COPD.(27) In a study of PLB with 16 COPD patients, researchers found that while practicing PLB patients had a significant decrease in respiratory rate and a significant increase in pulse oxygen saturation.(28) These effects have been demonstrated in previous studies.(29-32) However, there has been some variability found in the effects PLB, which may be due to difficulty in tracking compliance at home and the need for ongoing guidance by a respiratory health care professional. (22) Physicians and physical, occupational, and rehabilitation therapists teach PLB to their patients to ease shortness of breath; however, the benefits are short lived and up to 50% of patients lose them due to the lack of practice.61 Research suggests that regular practice of PLB may result in long-term benefit. Patients who participated in weekly PLB training (at a lab) demonstrate improvement after 12 weeks in exertional dyspnea and physical function.(62) Mindful PLB is a critical teaching ring PR as it's a practice that improves breathing mechanics, oxygenation and emotional buoyancy during breathlessness episodes. There is no remote system to foster the home practice of mindful PLB. (40)

Cardiovascular Benefits of mindful PLB:
A guided breathing practice can have significant benefit in the cardiovascular system, the source of the most prevalent comorbidities in COPD. Briefly, the heart has a natural variation, from minute to minute, beat to beat – even sitting at rest. This phenomenon, known as Heart Rate Variability (HRV) is a sign of health, the greater the variability, the better the health. Heart rate is intimately tied to the bodily expression of emotions: in states of anxiety, fear, and sadness, extremely prevalent in patients with COPD (33, 63-66), the variation tends to be disordered and chaotic. On the contrary in positive emotional states such as gratitude, the variation tends to be rhythmic. This state of rhythmic variation is known as Heart Coherence (HRC). (67)

When the heart is in a state of coherence, HRV synchronizes with the breath – a phenomenon known as Respiratory Sinus Arrhythmia. HRC is much more than a state of relaxation. It represents a dynamic balance within the Autonomic Nervous System and its two branches, the sympathetic and the parasympathetic, which work on the heart like an accelerator and brake respectively. On the in-breath, the sympathetic branch (accelerator) is active, and heart rate increases, while on the out-breath, the parasympathetic branch (brake) is

active, and the heart slows. Healthy heart rhythms have a beneficial effect on the emotional brain. Thus, HRC facilitates positive emotion and weakens negative emotion and improves thinking: cognitive performance can be faster and more accurate. HRC is not present all the time, but a few quiet periods of coherent heart breathing at various "breaks" in the day will be restorative and balancing.
Dysfunctional breathing patterns, such as in patients with COPD, are not only biomechanically inefficient but also reflect decreased physiological resilience. (68) Slow breathing with biofeedback assists patients in spending
more time in an optimal heart rate variability pattern for health.(68-70) HRV biofeedback has been used in the treatment of multiple chronic diseases, including COPD.(68,69,71,72) The use of biofeedback, to guide the user to breathe more deeply, has reported positive effects on dyspnea in patients with COPD,(22) as well as symptoms and quality of life in heart failure and hypertension.(73) The use of biofeedback assists patients in achieving a state of mindfulness as it helps them to stay focused on the present, provides a concrete goal and motivation.
The proposed HRV biofeedback training will provide patients with information on an on-going basis allowing the patient to see the effects of effort on HRC. Using HRV biofeedback training, most individuals with COPD may learn to engage in slow, effortless PLB (24) that will put them in a state of HRC and reduce dyspnea. The proposed system is critical to creating the "habit" of mindful breathing. Once the technique is learned, and the specific practice of breathing awareness is a habit, the individual no longer needs the support of biofeedback.

Health Coaching:
A key component of the researchers' PR program is health coaching. Health coaching has demonstrated effectiveness in facilitating patient improvement in various aspects of health (74-79) by affecting patients' knowledge, skill, self-efficacy, and behavior change (74). Health coaching utilizes motivational interviewing and goal-setting to facilitate behavior change. (80,81) Health coaching is a critical component of the current Chronic Care Model that involves patient-clinician collaboration and empowers patients to take on an active role in managing their health conditions and make important health behavior changes. The conceptual foundation of health coaching is Social Cognitive (Learning) Theory.(82) Health coaching has demonstrated effectiveness in improving patient health outcomes, including health behaviors.(83) In our previous awards we demonstrated the "boosting effect" of health coaching in PR and care of COPD.(84-87)
Regular feedback on a patient's health status and progress is central to the self-awareness that leads to behavior change and is also needed for proper coaching. (52) Since it is not practical or reliable (53) to collect this information daily from each patient, systems that transmit the necessary data to the health care professionals are needed. Multiple studies have found that providing regular feedback to the participant is effective in supporting behavior change. (54) Personalized feedback is more effective and preferred by patients.(54,55) In one study of COPD patients, there were clinically and statistically significant improvements in walking, QOL, self-efficacy, disability, dyspnea, and heart rate variability after using biofeedback on heart rate variability and feedback from pulse oximetry for 10 weeks.(56)

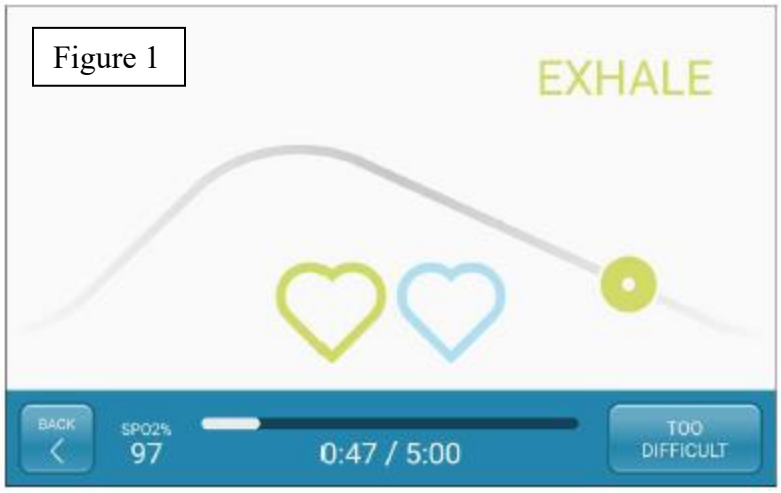
Existing PR system:
The existing PR system consists of an Android Computer tablet with Verizon service, a Nonin Pulse Oximeter and a Garmin Vivofit activity tracker. The home-based PR program is pinned on the Android tablet so that it is the home screen when the participant turns on the computer tablet and is the only accessible program on the computer tablet. The computer tablet is preloaded with a daily to-do list, daily exercises and daily questions.

The Nonin Pulse Oximeter and the Garmin Vivofit are connected to the Android tablet via blue tooth. A health coach at Mayo Clinic has access to the data through a health coach application.

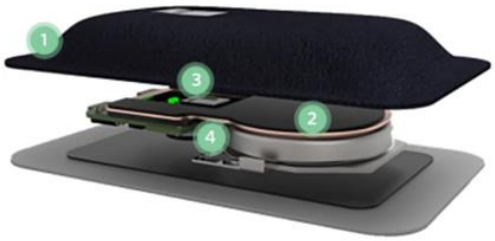
Pursed Lipped Breathing Module:
Minnesota Health Solutions and Spire Health will design and integrate a PLB module and integrate it with the existing home-base PR system (currently in use in 18-002453 and 17-009449, previously used in 14-00906). The Mindful Breathing Lab (Dr. Benzo) will complete a randomized control trial to evaluate the mindful breathing module. The study will evaluate the home-based PR system compared to the home-based PR system plus the mindful breathing module for its effects on breathlessness and emotions.

A mindful breathing module was created and tested for feasibility in IRB 17-004445. In this study, while wearing the Nonin Pulse Oximeter, participants inhale and exhale while following an animated ball. During an inhale, the ball climbs up a short hill, during the exhale the ball moves down a longer hill promoting pursed lipped breathing. The inhale duration is 2 seconds while the exhale duration increases from 2 to 8 seconds. The participant can tap the TOO DIFFICULT button the exhale duration will stop increasing. Please see figure 1 for an image of the mindful breathing module. In the new mindful breathing module, the breathing rate will be collected by the Spire Health Tag.

Figure 1



Spire Health Tags:
The Intervention system will incorporate the Spire Health Tag [redacted]. Each health tag contains a battery, tri-axis accelerometer, blue tooth radio, vibro-tactile feedback mechanism, photo plethysmography sensor, and force sensor to sense relative changes in abdominal and/or thoracic excursion. The health Tags can pick up respiration, pulse rate, activity and sleep duration and quality. The Health Tags adhere to existing clothing, can withstand the washer/dryer and last for about a year without charging. The tags are attached to clothes that are worn most like bras, underwear or athletic wear. The Health tags are attached with a fabric adhesive and can be removed by peeling the unit off. The Spire Health Tags will be integrated with the existing home-based PR system. Please see Figure 2 for images of the Health Tag.



1: Ultrasuede Fabric
Health Tags are placed against your skin so it is important that they be flexible, hypoallergenic, soft, and comfortable.

2: Respiration Sensor
As you breathe, our proprietary respiration sensor measures your thoracic excursion to assess respiratory patterns, events, and distress.

3: Pulse-Rate sensor (PPG)
Spire's Photoplethysmography (PPG) Pulse-Rate sensor measures your resting HR and also helps you determine how many calories you've burned.

4: 3-axis Accelerometer
Whether you're taking a walk or working out, Spire's 3-axis Accelerometer helps you log your steps and see how far you've gone.

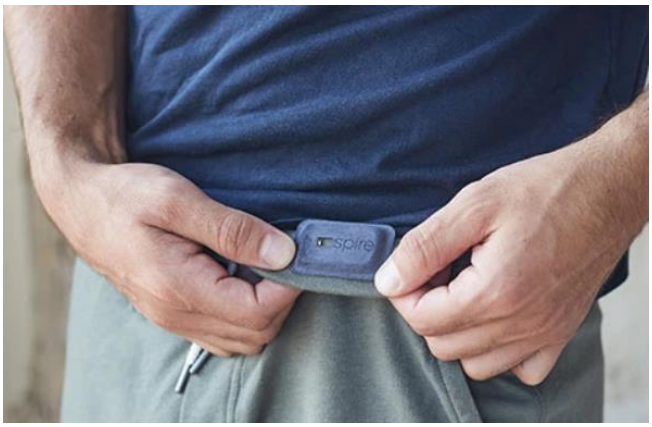


Figure 2

Study Design and Methods

Methods:

This project will involve two Phases: phase one in which mindful breathing by itself without any other device will be tested to make sure that is acceptable to patients and make a difference comparing to the usual protocol in use right now. Phase two will include a particular device that will guide the mindful breathing practice that we think will be more intuitive to practice and guide the mindful breathing and that device will be tested once we know that the acceptance to the mindful breathing practice, from phase one, is appropriate.

Phase 1: A total of 70 adults diagnosed with COPD will be enrolled in the study. Half of the participants will be randomized to receive the home-based PR with the Pursed Lipped Breathing Application (intervention) and half will receive the home-based PR (control). Randomization will take place in a REDCap database and will be in equal proportion.

Phase 2: A total of 70 adults diagnosed with COPD will be enrolled in the study. Half of the participants will be randomized to receive the home-based PR with the mindful breathing module which consists of the Pursed Lipped Breathing Application and the Spire Health Tags (intervention) and half will receive the home-based PR (control). Randomization will be take place in a REDCap database and will be in equal proportion.

Both groups entail one week of baseline where the participants wear an ActiGraph activity tracker and answer questionnaires. Baseline is followed by 12 weeks of home-based PR plus health coaching. The Intervention group also has the mindful breathing module loaded on the Android tablet. Both groups will also complete questionnaires and wear an ActiGraph activity monitor at 3 and 6 months.

Please see Figure 3 for a diagram of the intervention and Figure 4 for a diagram of the control scheme.

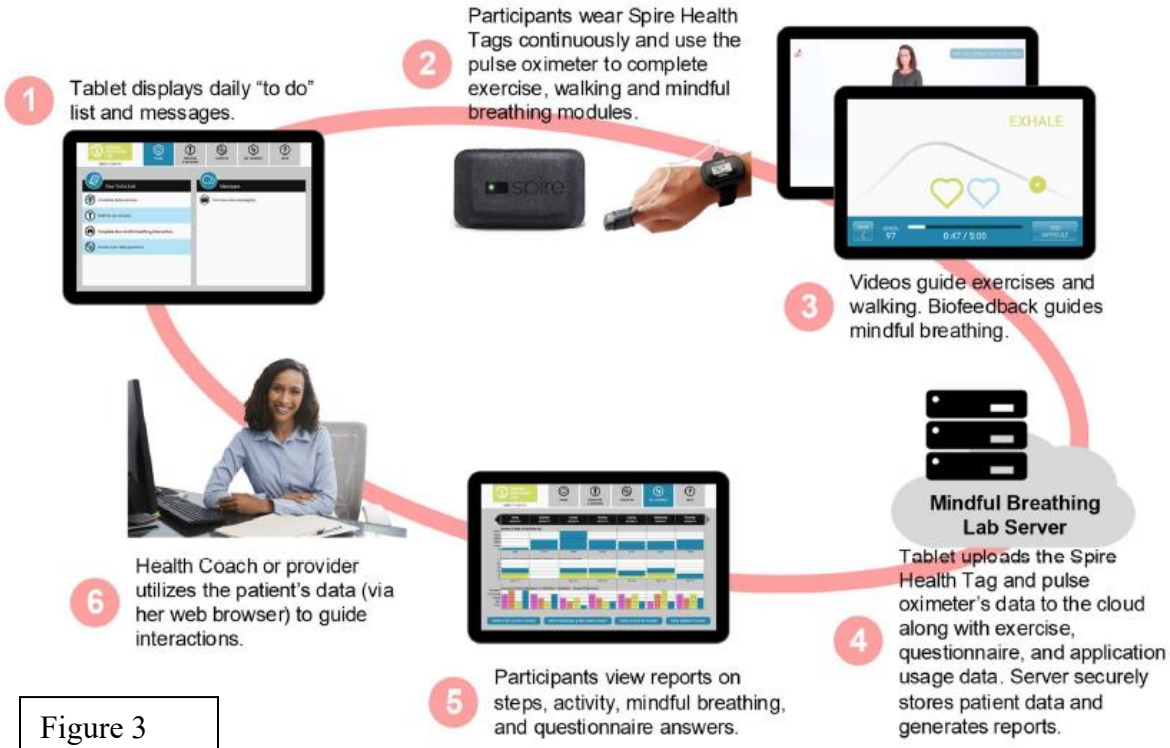


Figure 3
Intervention

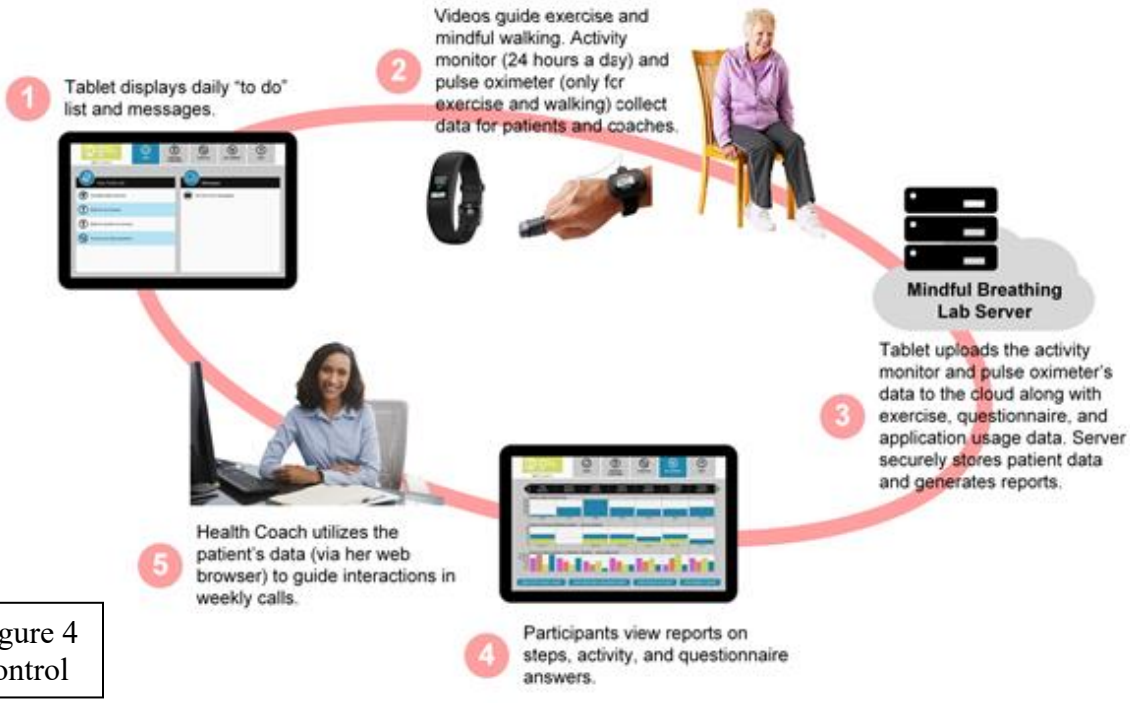


Figure 4
Control

Questionnaires:
Quality of Life will be assessed three times (baseline, 3 and 6 months) by the Medical Research Council (mMCR) questionnaire, the Chronic Respiratory Disease Questionnaire (CRQ), the Self-Management Ability Scale (SMAS30) and the Mindful Attention and Awareness Scale (MAAS). The questionnaires take about 20 minutes to complete.
At baseline additional health data will be collected from the medical record (chart review) to complete the Charlson comorbidity index, including lung function, demographics, living condition (living alone or not), GOLD stage, and comorbidities.

ActiGraph:
Physical activity will be measured three times (baseline, 3 and 6 months) by the ActiGraph activity monitor. The ActiGraph activity monitor has tri-axial accelerometers and will be wrist worn for seven days. See Figure 5. Important measures to be analyzed are daily number of steps, activity counts, minutes per day spent in daily physical activities of at least moderate intensity, and sedentary time (<2 metabolic equivalents).

Figure 5

The questionnaires and Act Graphs will be mailed to the participant with pre-paid shipping materials to send back.

Health Coaching:
All participants will receive a weekly coaching call to discuss their rehabilitation and health process. The calls are structured using motivational interviewing. The coach will review with the patient the data from the health coach system. Collaboratively, goals for rehabilitation for the following week will be set, based on information gathered and the patients' personal preferences. Each call lasts about 20 minutes. All calls will be taped to ensure compliance with the protocol.

Subject Information

Target accrual: 140

Subject population (children, adults, groups): Adults 40 years of age or older

Inclusion Criteria:

- Clinical diagnosis of COPD
- At least 10 pack years of smoking

Exclusion Criteria:

- Unable to do mild exercise (orthopedic-neurologic problems or confined to a bed)
- Unable to follow commands (cognitive impairment)
- Have a high likelihood of being lost to follow-up (active alcohol or drug abuse)
- Live in an area that does not have cellular service (Verizon)

Potential participants will have the option of meeting a study coordinator in person (if they are on campus for a clinical appointment), meeting via Video Anywhere through Epic, or meeting over the phone. If the patient desires, their consent can be digitally obtained and documented through PTRAX. The patient also has the option of receiving the consent via mail and mailing back the consent in a provided postage paid envelope.
Documentation of informed consent/HIPAA authorization will involve the use of the Research Participant Tracking (PTrax) Digital Signature Capture technology for research informed consent/HIPAA authorization forms. This is an institutionally approved process for documenting consent/HIPAA authorization only while the subject, and/or the subject's representative, is in the physical presence of the person authorized to obtain consent/HIPAA authorization. The study team may print a copy of the signed consent form/HIPAA authorization form for the subject or their representative. The consent form/HIPAA authorization form will also be available to the subject via the patient portal. Note: If the subject or their representative prefers not to use the Digital Signature Capture technology, the study team will provide a paper consent form/HIPAA authorization form for signature.

Review of medical records, images, specimens

☒ The study involves data that exist at the time of IRB submission **and** data that will be generated after IRB submission. Include this activity in the Methods section.
The study plans to conduct a retrospective chart review and ask subjects to complete a questionnaire.

Data Analysis

Sample Size

We calculated that sixty two participants will provide 80% power to detect 1 point of change in the two co primary outcomes (breathlessness and emotion as measured by the CRQ) with an alpha of 0.025. A 1 point change represents a clinically meaningful change.95 We expect about a 20 percent attrition rate (withdraw, not able to complete the 12 weeks of home-based rehab) and will therefore enroll 70 participants in each phase.

Analysis Plan
The primary outcomes of the study are changes in breathlessness and emotions. Changes from baseline to three months on the two primary outcomes will be compared between the study arms using two-sample, two-sided t-tests with 5% type I error rates. Means, SDs, medians, ranges, and frequency distributions will be reported and plotted over time by study arm. Linear models will be used to assess the impact of treatment arm on three-month outcomes after adjusting for the corresponding baseline measure and other variables related to the outcome (age, degree of breathlessness at baseline using the mMRC dyspnea, and FEV1).

The Chronic Respiratory Disease Questionnaire (CRQ) is a 20-question inventory assessing the areas of dyspnea, fatigue, emotion, and feelings of mastery. The fatigue, emotion, and mastery subscales ask patients to rate how often in the last two weeks they have been afflicted with a particular feeling or experience on a scale of 1 to 7, with higher ratings indicating less symptom impairment. The CRQ has shown to be valid and has high internal consistency reliability. Test-retest reliability is adequate in all subscales, but is particularly high in the subscales of fatigue (r=0.90), emotion (r=0.93), and mastery (r=0.91). The minimal clinically important difference for this instrument of 0.5 points is universally recognized. The Domains Dyspnea (breathlessness) and Emotions are the two co primary outcomes.
Physical activity will be measured at baseline, 3, and 6 months by the ActiGraph GX6 activity monitor, which has been used to assess physical activity in COPD populations. (92) The number of daily steps at baseline, 3,

and 6 months and across the two groups will be compared. Emotional Intelligence will be measured by the Trait Emotional Intelligence questionnaire at baseline, 3, and 6 months .(84) Mindfulness will be measured by the Mindful Attention and Awareness Scale at baseline, 3, and 6 months.(93) The participants HRC and respiratory rate will be tracked for the entire intervention period using the Spire Health Tags. At baseline additional health data will be collected from each participant's medical record to complete the Charlson comorbidity index, including lung function, demographics, living condition (living alone or not), GOLD stage, and comorbidities.

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