Home Pulmonary Rehabilitation for COPD

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General Study Information

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Study Title: Home Pulmonary Rehabilitation for COPD

Protocol version number and date: Protocol Version9, August 23, 2021

Research Question and Aims

Hypothesis:

Home-based pulmonary rehabilitation with proper self-management support through health coaching rooted in motivational intervention during pulmonary rehabilitation will improve physical wellbeing, quality of life, increase daily physical activity, and decrease health care utilization for patients with COPD.

Aims, purpose, or objectives:

The ideal system for a home PR program requires straightforward, accurate technology to monitor physiological parameters, patient engagement, and simple exercises to be performed at home, all ensuring participant safety. Feedback is critical: MI-based health coaching, proven effective in COPD,[6] can translate to higher self-efficacy, subsequently promoting better SM and improved QOL.[15, 16]

The **aims** of this project:

- Home-based PR will increase PR uptake and adherence, a significant existing gap in COPD care.
- The addition of formal SM support through health coaching during PR may promote behavioral change to prolong the effects of PR on critical COPD health outcomes.
- The home-based PR program may meaningfully engage participants in successful SM and translate into sustained improved physical wellbeing (QOL), increased daily PA, and decreased health care utilization for patients with COPD.
- The proposed home-based PR system using "off-the-shelf" hardware and a previously commercialized software (accomplished through our Small Business Innovation Research Grant, SBIR 5R44HL114162-03) will have a high likelihood of implementation and dissemination once proven effective.

Background:

Role of Pulmonary Rehabilitation in Chronic Obstructive Pulmonary Disease care

International guidelines for managing Chronic Obstructive Pulmonary Disease (COPD), one of the main causes of morbidity and mortality worldwide,[1] suggest that pulmonary rehabilitation (PR) programs and self-management support (SM) are a critical part of treatment. A compelling body of evidence confirms that PR programs deliver improved exercise capacity, reduced breathlessness, and improved health-related quality of life (QOL)[2] and are associated with fewer acute exacerbations and hospital admissions-the biggest costs burden in health care.[2, 7]

Adherence to PR is poor

Despite proven benefits, the proportion of people with COPD who receive PR is very small, with estimates from developed countries of <20%.[3] The current model of a center-based PR program fails to address the needs of many patients with COPD.[5] The most common patient barrier to attendance is travel to center-based programs, particularly for frail patients with more severe COPD who need transportation assistance.[3]

Home-based, unsupervised PR has been proposed as an alternative model[4] to hospital-based programs and has been found to be safe and effective compared with traditional programs in terms of improvement in exercise tolerance, disease-specific QOL, and degree of breathlessness and fatigue.[8] *However, despite initial results, the implementation and dissemination of home-based PR has been poor in the United States due to a lack of simple home-based PR systems that combine proper monitoring and meaningful feedback to the patient.*[8] There is a knowledge and practice gap regarding effective systems that can deliver home PR.[2, 5] Further research on feasible and effective home-based PR particularly oriented to a sustained behavior change is needed.

Aiming for home PR programs with lasting results

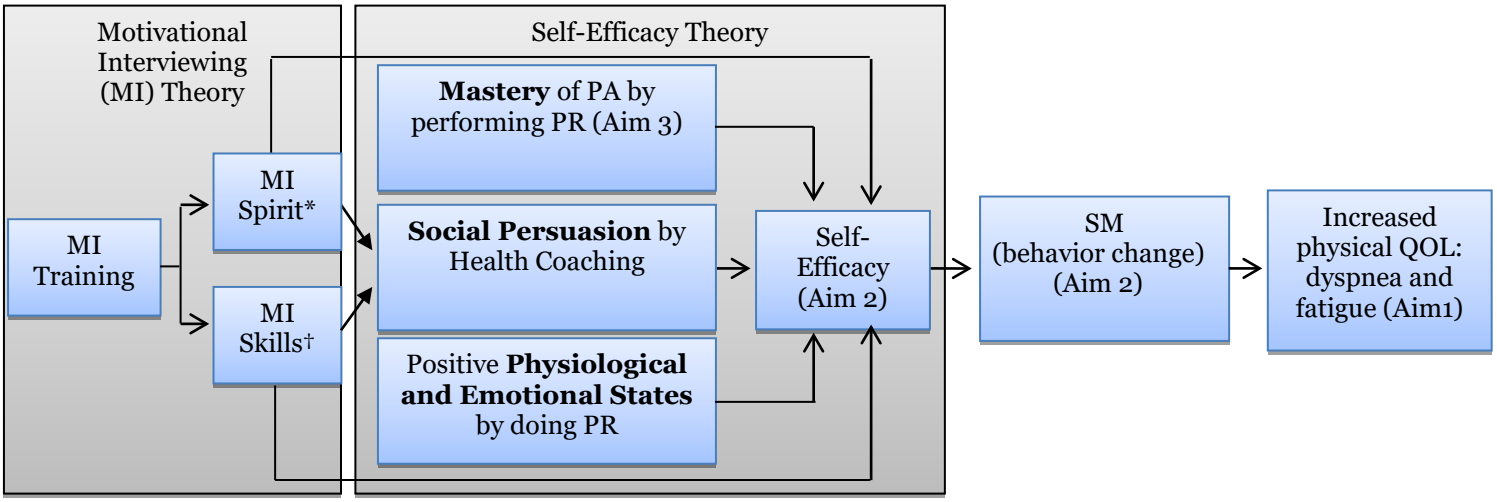
It is well documented that the effects of PR diminish over time, with deterioration in both exercise capacity and health-related QOL within six to 12 months of program completion.[9] One key reason for this decline is the lack of a behavioral change after completing PR (developing new habits). It is now postulated that undertaking PR in the home may promote effective behavior change through integration of physical activity (PA) routines into daily life.[5] Self-management support (SM), which creates ideal conditions for behavior change, is now recommended by guidelines as an essential part of chronic care, particularly in PR programs.[2, 10] A recent large randomized study of COPD SM[11] identified lack of patient engagement as the core problem in adopting new behaviors. In that study, significant effects on health-related QOL and health care utilization after the SM intervention occurred only in patients who were engaged in their care. Brief advice is not enough to promote behavior change; meaningful engagement is necessary.[12]

Health Coaching, promoting a behavior change

In our previous work, we developed and tested (R01 HL09468), an effective program for SM in COPD through health coaching[13] rooted in motivational interviewing (MI)[13, 14] that decreased COPD re-hospitalizations[6] and produced a sustained improved QOL at six and 12 months.

Theoretical Framework

The theoretical framework of the proposed intervention (Fig. 1) is based on two guiding theories: self-efficacy theory[15, 17] and MI theory.[16] In brief, training in MI prepares the health coach to initiate conversations in the spirit of MI (compassion, acceptance, evocation of the client's values, and collaboration) and skills (open questions, a non-coercive approach for change, and making the participant the expert and final decision-maker). The latter (spirit and skills) may not only impact social persuasion (part of self-efficacy theory) but also directly increase self-efficacy (confidence) that leads to higher SM abilities (behavior change). Pulmonary rehabilitation directly impacts the foundations of the self-efficacy theory: mastery in PA, by engaging in daily exercises (Aim 3, measured by activity monitor), social persuasion (weekly feedback from a trustworthy coach) and emotions and physiology (exercise is a known positive factor impacting emotions and COPD physiology). Self-efficacy (Sub aim 2 measured by CRQ Mastery) translates into SM or behavior change (Aim 2 measured by SMAS30) which in turn impacts physical QOL (Aim 1). We have recently confirmed and published the independent relationship between MI health coaching, SM and quality of life.[6, 18, 19] A proposed path analysis will confirm the proposed framework.



*Compassion, Acceptance, Evocation, Collaboration; †Open-ended questions, affirmations, reflective listening, and summaries

Fig. 1. Theoretical framework.

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Innovation

The project is truly innovative due to the purely home-based nature of the system, the simplicity and accuracy of data collection attained with using commercially available monitors, and the addition of health coaching to engage and provide weekly feedback to participants. Previous studies required participants in home-based training groups to attend SM education[4, 20] or weekly monitoring in the clinic or hospital.[21] These approaches fail to overcome the transportation and mobility-related barriers to attendance, perpetuating the present lack of adherence.

The proposed study will be the first of its kind combining monitored home-based PR with theory-driven health coaching to provide SM support, a novel addition to PR which may translate to greater participant engagement, better communication, and sustained behavior change.[13] **Currently, there is no research-proven, effective home-based PR system available.**

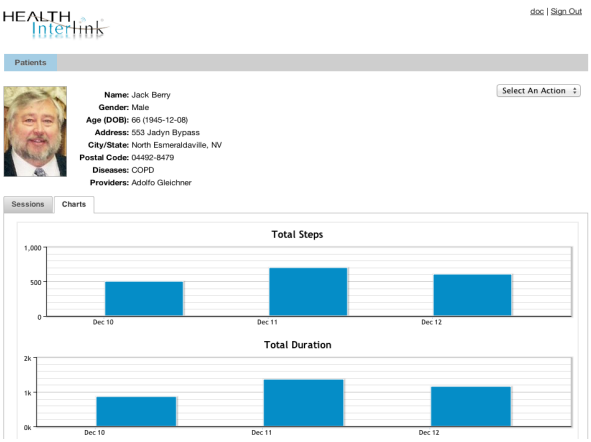


Fig. 2. Project 1 - coach application used.

Preliminary Data:
We present the preliminary data of four projects (tested in previous applications) representing critical components that support the proposed home-based PR system:

1. Creating the system using AMs and an Android™ receptor (R44 AG29087-02A1) and pilot of its effect on disease-specific QOL (Aim 1)
2. Effect of the proposed health coaching on sustainable improvement of QOL (Aim 1). (R01 HL09468)
3. Pilot testing the integrity of the transmission of physiologic data (R43 HL 114162-01)
4. Refinement of the system and Pilot testing of the whole proposed intervention (5R44HL114162-03)

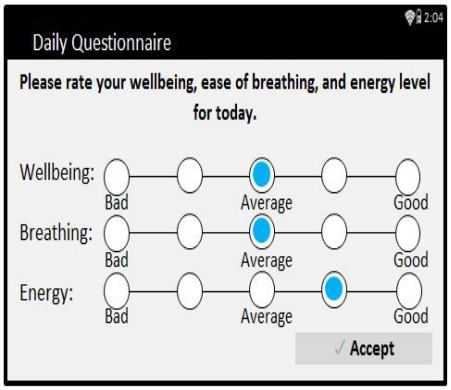


Fig. 3. Android™ screen of reported

Project 1 – Creating the System. SBIR project NIH (R44 AG29087-02A1 Kramer, PI; Benzo, Co I) provides the foundation for the proposed mobile system for home PR in this project. In this study, AMs with Bluetooth capabilities were fastened to the ankle and connected to an Android™ device (proposed in the present application). The device then transferred activity and patient-reported outcomes to a server, which generated a report (Fig. 2) for a coach who reviewed the data and provided support to participants. The system also included daily participant feedback about their symptoms (Fig. 3), which informed the coaching sessions. We tested 50 participants with severe COPD aiming to improve QOL as measured by the Chronic Respiratory Questionnaire (CRQ) (as in Aim 1). We found improved QOL at eight weeks, (Fig. 4) and this improvement was ***maintained at six months.***

Qualitative analysis reported the following participant themes: (1) the system was efficacious in motivating increased activity; (2) improved wellbeing; (3) appreciation of the coach interaction; and (4) interested in a wrist monitor that enabled them to view activity (Garmin monitor with display is proposed in this application; see Fig. 5). Coach interviews indicated that coaches found reports useful and actionable. The technology was friendly and did not interfere with participant- coach communication. All themes and requests of the previous study are now incorporated in this application.

	Baseline	8 Weeks	6 Months
CRQ Dyspnea	4.6 (1.3)	5.2 (1.1)*	5.6 (1.0)*
CRQ Fatigue	4.3 (1.2)	4.8 (1.4)*	5.1 (1.5)*
CRQ Emotion	5.3 (1.1)	5.6 (1.0)	6.0 (0.9)*
CRQ Mastery	5.3 (1.2)	5.7 (1.1)	6.0 (0.6)*

Fig. 4. Pilot 1. CRQ scale is 1-7, with higher scores indicating better health.*A clinically significant difference is ≥0.5 points. ($P<.05$)

Fig. 5. Garmin Vivofit™.

Project 2–Effect of the proposed health coaching on sustainable improvement of QOL (Aim 1). In a randomized study (N=215), [6] we tested the proposed MI-based health coaching telephone intervention (NHLBI R01 HL09468 Benzo, PI) to decrease COPD readmission and to improve QOL. We discovered significant improvements in Physical QOL (Aim 1) and Emotional QOL measured by the CRQ at six months post-intervention, and also observed that these benefits were maintained at 12 months (Fig. 6). Health coaching decreased ER visits and hospitalizations (see exploratory aim in this proposal).[6] The SM worksheet is shown in Appendix 1. Qualitative analysis also demonstrated that the SM support intervention was acceptable to patients and interventionists, increased self-efficacy for dealing with COPD, and promoted an effective working alliance with the coach (Fig. 7). Details of the intervention are published and publicly available.[13]

Characteristic	Control	Intervention	NNT	P Value
CRQ Emotional Function				
Δ6 Month – Baseline, mean (SD)	0.10 (1.0)	0.50 (1.0)		0.004
Δ12 Month – Baseline, mean (SD)	0.15 (0.9)	0.43 (1.0)		0.058
% improved >MCID at 6 months	14.1	29.9	6	0.018
% improved >MCID at 12 months	14.3	28.8	6	0.036
CRQ Physical Function				
Δ6 Month – Baseline, mean (SD)	-0.01 (1.0)	0.33 (0.9)		0.036
Δ12 Month – Baseline, mean (SD)	-0.04 (1.0)	0.27 (1.0)		0.016
% improved >MCID at 6 months	12.8	26.0	7	0.038
% improved >MCID at 12 months	11.4	19.2		0.199
ΔPhysical Activity Level at month 6	0.01	0.01		NS
ΔPhysical Activity Level at month 12	0.01	-0.10		NS
Died in First 12 Months, n (%)	12 (11.3%)	10 (9.3%)		0.620
Patient reported Prednisone/Antibiotic Use, n (%)				
Baseline to Month 3	40 (46.5%)	51 (56.7%)		0.178
Month 3 to Month 6	37 (44.0%)	46 (51.1%)		0.351
Month 6 to Month 9	35 (43.2%)	49 (57.6%)		0.063
Month 9 to Month12	34 (43.0%)	54 (65.9%)		0.004

NNT, Number Needed to Treat ; MCID, Minimal Clinically Important Difference

Fig. 6. Quality of life outcomes from health coaching

Project 3–Addition of physiologic monitoring to the system in Project 1: Feasibility and Signal Integrity. In R43 HL 114162-01 (Benzo, Kramer Co I) we tested participants with severe COPD, we confirmed the feasibility and integrity of heart rate and oxygen saturation transmission during the proposed PR exercise routine in a simulated patient's home, validating transmitted data from the monitor with in-site monitors (gold standard).

Project 4–Pilot Study Testing the Proposed System (home-PR plus coaching). The finalized proposed system, was finalized funded by NHLBI (5R44HL114162-03 Home-Based Management of COPD Patients), and was tested in a pilot study included health coaching. All participants were able to use the technology and were 100% compliant with daily activity measures. Participants highly rated the helpfulness of the study scale 0-10) and ease of technology navigation (9.67, scale 0-10). preliminary qualitative analysis is shown in Fig. 8.

Qualitative Interviews	N=24
Confidence in taking care of health (mean ± SD)	8.05 ± 1.99
Helpfulness of the intervention (mean ± SD)	9.60 ± 0.60
Frequency of calls (%)	
Too little	22%
About right	78%
Too much	0%
Frequency of calls at end of study (%)	
Too little	43%
About right	57%
Too much	0%
Recommend to others (%)	
Yes	96%

Fig. 7. Qualitative feedback of health coaching

What did you think about using the tablet?

"It helped to be able to follow along with someone, follow the pace"
"Very helpful. Very visual. Tablet was portable which allows people who need visual training to follow along."
"Wasn't that difficult, could see where if someone would stick with it they would benefit."

Were there things you didn't like?

"I mentioned to the day that you showed me this that the slow walking bothered to me, but then when you explained to me that the slow walking really helps me work on my balance, I really thought about it and plan to really work on it."

Is there anything we could do differently or that we need to change?

"I think the human component is very important, to feel that someone is checking up. It would be nice to have variation in the exercises. I don't think I could do the same exercises for 8 weeks. I really liked the pursed lipped breathing exercise."

Fig. 8. Qualitative pilot feedback of the home pulmonary rehabilitation program.

Study Design and Methods

Methods: *Describe, in detail, the research activities that will be conducted under this protocol*:

Pilot Study: When the technology is ready, we will conduct a pilot study enrolling fifteen or fewer participants. The participants in the pilot study will not be randomized and will receive the Intervention. The purpose of the pilot study is to observe how the technology works in real life and to refine the intervention if needed. The participants in the pilot study will complete all measures and activities of the randomized control trial, minus the randomization.

Randomized Study:
Participants will be randomly assigned in equal proportion to one of two treatments: home PR with health coaching or the attention waitlist control (Fig. 9). Participants randomly assigned to the intervention will receive three months of home PR followed by six months of usual care.

Participants randomly assigned to the active control group will receive three months of usual care plus educational materials and non-coaching calls (matching the number of contacts in the intervention group), followed by three months of home PR plus health coaching and three months of usual care.

Phase 2: Participants randomized to intervention will not change; three months of home PR followed by six months of usual care. Participants enrolled in the active control group will follow the scheme listed above; 3 months of usual care followed by three months of home PR and three months of usual care. During the control wait period they will receive a pamphlet of 12 Healthy Habits during the enrollment period as well as two letters during the control period. The letters will remind them to review the 12 Healthy Habits and will remind them that the exercise portion of the study will start soon.

Phase 3: Forty Mayo participants who have competed the intervention (the 12 weeks of home-based pulmonary rehab with health coaching) will be randomly selected to complete a qualitative interview to explore areas related to the intervention, quality of life and symptom severity. The purpose of the qualitative interview is to take an in-depth look at the appropriateness of the intervention as a potential method of treatment as well as examining the impact on the participant as a whole. Mayo Clinic participants who have completed the intervention portion of the study will be contacted via the telephone to inquire about their interest in participating in the interview. If interested, oral consent will be conducted. A mutually agreed upon time and date for the interview will be confirmed. (A phone script will be used.) The participants will receive $40 for consideration of their time.

The interviews will be recorded for subsequent transcription of the interactions. The transcribed interviews will be examined for common themes. Each interview will vary between 20 and 30 minutes and will be performed by a member of the Mindful Breathing Laboratory who is trained in Motivational Interviewing and Qualitative Interviewing. Additional members from the Lab will assist in the transcription of the interviews as well as theme identification. Data collection and analysis will be overseen by Dr. Benzo. (A guided interview script will be used.)

In addition, the five Mayo Clinic staff who served as health coaches on the study will also be offered the opportunity to be interviewed to learn their experiences in the program. The interviews will be conducted by Qualitative Expert, Dr. Jennifer Ridgeway, either in a private space or by phone call. The interview will be recorded so that it can later be transcribed and analyzed. An email inviting the health coach to participate will be sent to the health coach. The health coach will be orally consented and will have the option to opt out.

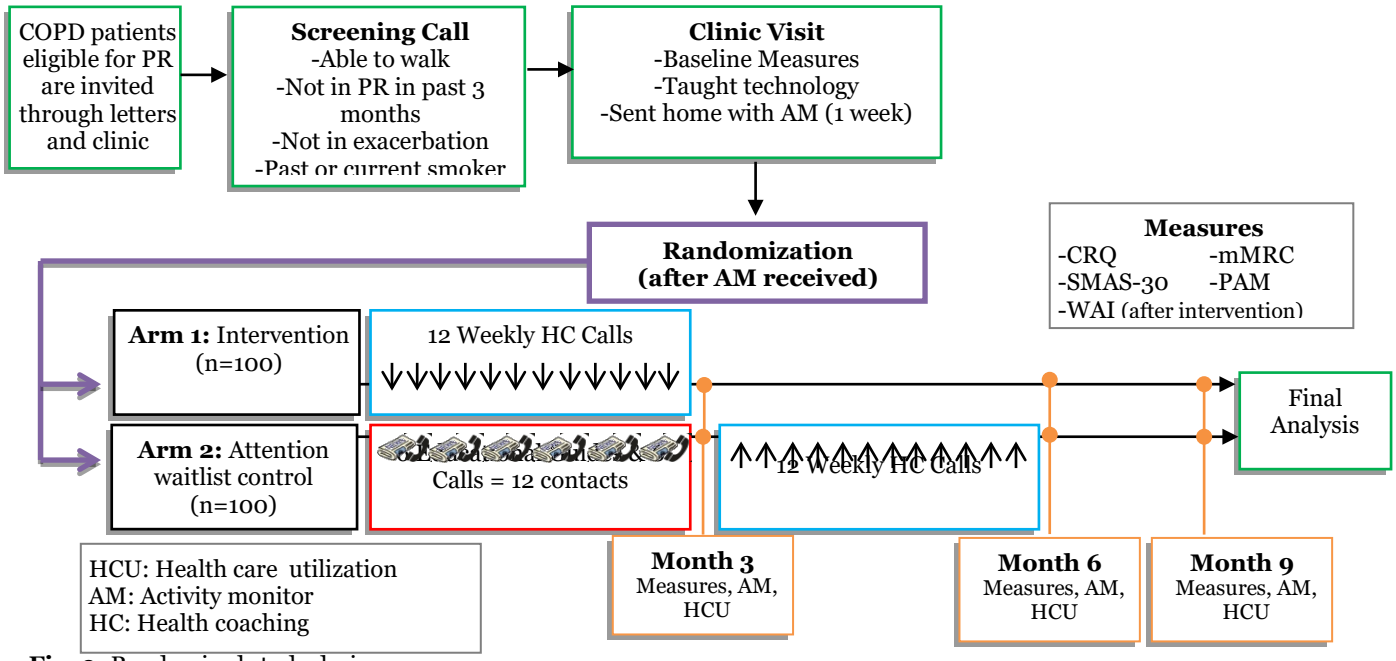


Fig. 9. Randomized study design.

Questionnaires:
Physical QOL will be assessed by the CRQ (Aim 1), SM abilities, self-efficacy (Aim 2), and daily PA and self-efficacy for exercise (Aim 3). These QOL components will be measured at baseline, three, six, and nine months after randomization in both groups. Qualitative analysis (Aim 4) will occur after the intervention in order to further understand the intervention's acceptability and to help interpret the comparative effectiveness findings from Aims 1-3.
Additional QOL questionnaires will include the Interpersonal Support Evaluation List (ISEL-12), the Meaning of Life Questionnaire (MLQ6), and the Longitudinal Analogue Self-Assessment (LASA6). Recent research has indicated that social support and sense of meaning of life are important indicators in the perception of quality of life. The added questionnaires will better measure these important factors.

Study Sites:
The clinical study sites include (1) Mayo Clinic—Rochester, Rochester, MN, (2) Mayo Clinic-Jacksonville, Jacksonville, FL, and (3) HealthPartners® Specialty Center-Regions Hospital, St. Paul, MN. The engineer site is Minnesota HealthSolutions, Maple Grove, MN. These study partners have collaborated for the past five years.

Recruitment
The study coordinator will utilize ACE to generate a list of eligible participants with research authorization (avoiding any HIPAA noncompliance) and send invitation letters. In addition, patients presenting to the clinic with COPD may be referred to the study by

their provider. The coordinator will approach potential participants through a screening call (review inclusion and exclusion criteria) and will schedule an enrollment visit and to demonstrate the Home Rehab and to obtain consent.

Subject Information

Target accrual:
400 total participants. Mayo Clinic Rochester has a target enrollment of 150 participants, Mayo Clinic Florida and Health Partners have a target enrollment of 70 participants each. Up to fifteen total participants will be enrolled in a Pilot Study.

Inclusion Criteria:

- Clinical diagnosis of COPD, confirmed by spirometry
- Age ≥40 years (to avoid recruiting participants with asthma rather than COPD)
- Current or previous smoker (≥10 packs per year)
- Confidence in using the proposed PR system
- English language fluency

Exclusion Criteria:

- Study candidate experiencing an acute COPD exacerbation (can be included after the acute event)
- Inability to walk (orthopedic-neurologic problems or confined to a bed)
- Currently in PR or finished PR in the last three months (unlikely to improve)
- Pregnant women
- Live in an area where cell phones do not work/

Research Activity

Randomization
Eligible participants (after the screening call) will visit the site for the consenting process. In the clinic visit, all consented participants will receive baseline questionnaires, and information about the system. They will complete the questionnaires during the visit, and take home the ActiGraph™ AM (Fig. 10), to wear for one week. On return of the AM, the study coordinator will randomly assign the participant to intervention or attention waitlist control through a centralized program, Research Electronic Data Capture (REDCap). Randomization will be stratified by whether the participant has poor lung function (forced expiratory volume [FEV1] <50% predicted) and whether the participant has severe dyspnea (recorded modified Medical Research Council Dyspnea Scale [mMRC] score, 3-4; scale, 0-4); critical factors that can make the study arms unbalanced regarding risk factors. The study coordinator will call the participant and inform him or her of the results of randomization. Intervention participants will be mailed the home-based PR system (pulse oximeter, tablet and Garmin Vivofit™). While blinding participants will not be possible, as most behavioral interventions, the arms will be blinded to the research team in charge of the data entry and statistical analysis and revealed only at study conclusion.

Clinic Visit: Face-to-Face Encounter
The participant will practice the use of the proposed system and the PR routine in the PR lab to ensure understanding and safety; therefore, no home visits are planned. The clinic visit is the best opportunity to evaluate the confidence of the individual in using the system. The study team will provide step-by-step instructions on how to perform the daily home-based PR routine (Fig. 11) and discuss the home environment where PR will take place to define the optimal conditions, particularly safety, for exercise. The participant will be asked to rate their confidence to use the technology presented and their confidence (self-efficacy) to perform the home rehabilitation routine on a scale from 0 (no confidence) to 10 (great confidence). A rating of six or greater will be deemed an acceptable confidence level to participate in the study.

Fig. 10.
ActiGraph™ wGT3X-BT.

Each participant will be asked to define a particular place and time they can perform the home-based PR. The physical and mental environment is critical for the successful adoption of new behavior (PR). Each participant will learn about the weekly calls with the coach to discuss their rehabilitation and monitored measures (steps, level of shortness of breath, wellbeing and fatigue). They will then go over the daily answers to wellbeing questions (mood, energy, and breathlessness as tested in the pilot study) (Fig. 3). After performing the PR routine (to ensure safety and understanding) and reviewing use of the monitors, a plan for the following week will be discussed. The coach will also confer with the participant and caregiver to identify possible exercise-related fall hazards in the home environment (see Human Protections section).

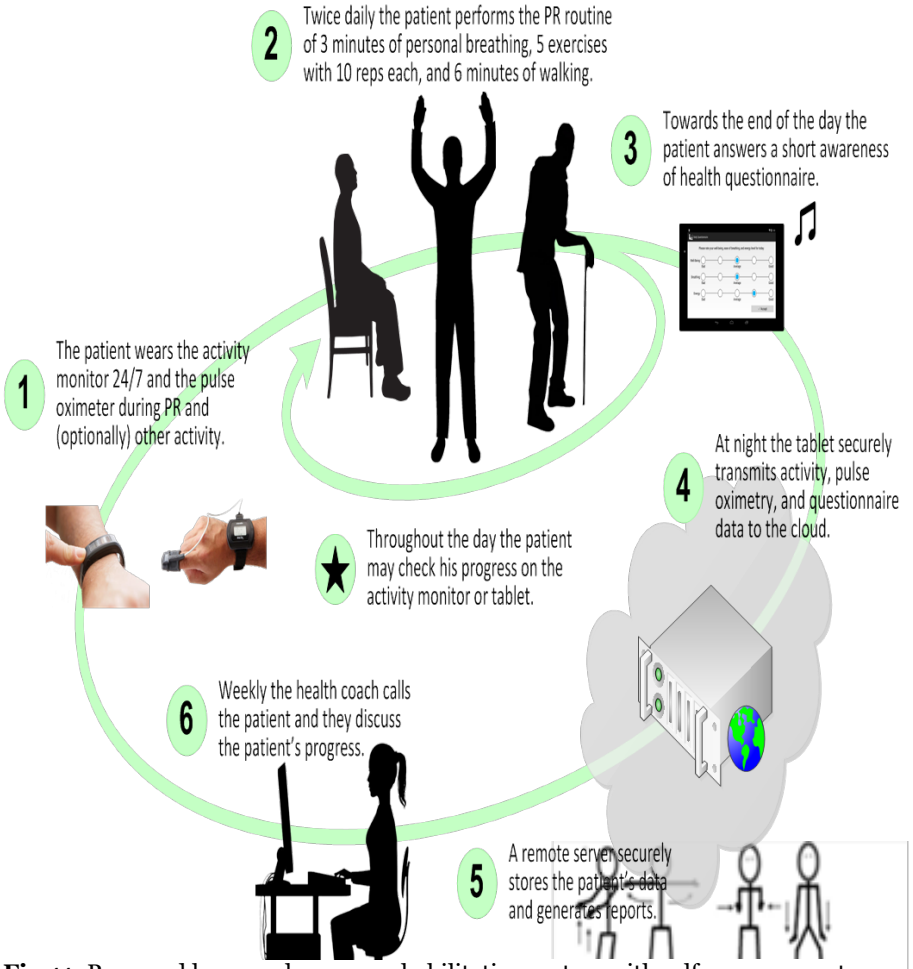
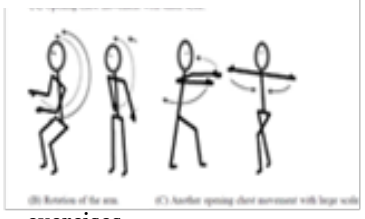


Fig.11. Proposed home pulmonary rehabilitation system with self-management support.

Strategies for promoting recruitment and retention

A thorough explanation of the technology and measures required will contribute to a better understanding of the study and decrease the risk of dropout. In the screening visit, the study coordinator will clearly and carefully explain the benefits of enrolling and the duties in this study from the perspective of potential participants. These benefits include access to home-based PR and a coach, who is describe safety and benefits of the proposed exercise in the home, the weekly call with a coach, the steps, oxygen and heart rate monitoring, and SM support. All tasks related to study participation (e.g., questionnaires and utilization of AMs) will be carefully explained. We believe that the proposed study design will be attractive to both intervention and control participants.



exercises.

Intervention Group

Participants are to engage in the home PR at least six days a week. The Garmin Vívofit™ AM (Fig. 5) is to be worn at all times (battery lasts one year) to capture daily steps and metabolic equivalent of task (METs) per day. The PR routine begins with a slow breathing awareness exercise, "pursed lips breathing," followed by upper-extremity exercises (Fig. 12) and a 6-minute walk (in the home or outside) finishing with another slow breathing-awareness exercise.

Participants will complete two 6-minute walks, either right after or at another time of day. The exercise protocol lasts about 24 minutes, which is the amount of dedicated exercise time associated with a risk reduction in hospitalization and improved QOL[23, 24] and is recommended by current PR guidelines.[2] The proposed protocol is currently being used by the PI of this proposal in a prospective COPD trial (NIH NCI R01CA163293-03). The PR coach will contact the primary care or referring provider before PR to introduce the provider to the study as well as coordinate and develop a strategy in case of a COPD exacerbation (a common cause of PR abandonment).

The proposed home-based PR system (Fig. 11) consists of three commercial devices and two software application. The devices are a Garmin Vívofit™ AM, a Nonin 3150 WristOx$_2$® Pulse Oximeter (PO), and a 7" Android™ tablet with 3G/4G cellular service. The AM and PO wirelessly communicate with the tablet via Bluetooth. During the upper extremity exercise routine (Fig. 12) and 6-minute walks, the PO measures the participants' heart rate (HR) and oxygen saturation (SpO_2). Near the end of the day, the tablets

periodically sound a musical alarm and display a short health status questionnaire (as demonstrated in the pilot study, Fig. 3)[25] asking participants to rate their wellbeing,[25] ease of breathing, and energy level. At night, the tablets securely transmit the device data and wellbeing questionnaire answers to a remote Web server, which securely stores the data and generates reports. Health coaches call the participants weekly to discuss their progress in PR and SM (see below).

Participant software application: When the participant turns on the Android™ tablet, the application logs in, and the participant accesses two main screens (see appendix for all graphics). First Screen:

1) The top left corner of the screen displays the participant's step count, step goal, and remaining number of steps. The top center of the screen shows a motivational message (based on the participant's progress). The top right corner displays the weather, an important factor for the PR coach to consider when interpreting a participant's PA. The remainder of the screen displays the daily PR activities.

2) To initiate one of these activities, the user selects the corresponding activity from the "To-Do" column. Selecting "Exercise" from the "To-Do" column initiates a video guiding the user through the PR exercises. Similarly, selecting "Walk" from the "To-Do" column starts a 6-minute countdown once the application detects that the participant has initiated walking. Before displaying the exercise and walking videos (asked to be followed), the application verifies that the participant is wearing the AM and PO to assure measure and compliance (during exercise an increase in heart rate is expected). When the participant finishes the selected activity, it appears in the "Done" column. The application provides instructions before and between each activity.

The second screen plots historical data, allowing the participant to see trends as in the pilot study. From this screen, the user is able to view daily steps, average heart rate, SpO_2, and questionnaire answers. The user also is able to select the historical window (e.g., last week, last month, last quarter).

Coaching Calls (weeks 1-12) content for PR feedback plus SM: *After the in-person visit, coaching calls will occur weekly for 12 weeks following the published protocol*:[13]

1) Set the call agenda. Listen for the participant's exercise description, ask which exercises were successful, and affirm. 2) Provide feedback of monitored sessions and generate dialog by listening for "change talk" (participant's comments on anticipated activities he or she wants to do). 3) If problems arise, resist the urge to attempt to solve the participant's problems and barriers. 4) Listen carefully and kindly (ambivalence from the participant in changing their behavior). 5) Discuss how behaviors connect to the participant's values and strengths. 6) Collaborate in setting goal(s) for the following week. 7) Discuss the process of action planning: elicit the participant's preferences/desires for behavior change. 8) Elicit the participant's choice; do not assign goals, and use the participant's language to describe the goal. 9) Assess confidence for goal completion, reaffirm commitment to the action plan, and express optimism. 10) Thank the participant and plan the next call.
   All calls will be recorded to ensure compliance with the protocol and MI principles (10% of all calls will be reviewed). Recorded files are saved on the restricted research drive, accessible only to study staff. The recorded files are to be deleted off the drive after analysis of the intervention is completed and study is finished. Only ten percent of the calls are reviewed, and that is to feedback and training to the health coach.

Coach Training

Details of the health coach training have been published and publicly available.[13] In brief, the health coach intervention is purposefully designed to be delivered by PR professionals, respiratory therapists, or nurses, the most common providers of care in PR, as opposed to psychologists. Training includes: 1) face-to-face education on theory and strategies associated with SM education and MI in general (six hours); 2) reading materials detailing skills and strategies associated with SM education and MI; 3) role play-based experiential learning of intervention strategies with participant vignettes (five hours); and 4) recorded and reviewed intervention sessions in which interventionists provide tailored training to discuss strengths, missed opportunities for use of intervention strategies, and any deviations from the intervention protocol (10 hours over six months). The rationale for the latter is that training sessions that incorporate feedback from coded sessions increase skill retention. All training sessions will be audio or video recorded for future review to minimize drift from intervention protocol.

Health Coach Software Application: (see Appendix 1 for full size graphics and reports).

The health coach software application provides three types of reports. The overview report (Fig. 13) allows health coaches to succinctly ascertain the status of their participants and flag anyone who may be experiencing problems. The health coach may select a

participant from the overview to display the trend report (Fig. 14). The trend report allows the health coach to review the participant's progress between weekly health coaching sessions. Finally, the health coach may select a day from the trend report to display a detailed report (Fig. 15). These three reports are updated after the results of the pilot studies (preliminary data projects 1 and 3) are generated.

While participant monitoring does not occur in real time, any significant physiologic abnormality measured during rehabilitation and transmitted to the server (O_2 saturation less than 80% or heart rate >140 or <40 beats per minute) prompts a message to the coach to call the participant to investigate the event. The PI also is alerted within 24 hours by text message if a physiologic abnormality is measured to ensure the appropriate response. In 5R44HL114162-03 Home-Based Health Management of COPD Patients, the remote rehabilitation and health coaching systems have been pilot tested together and found feasible, accurate, and acceptable to participants.

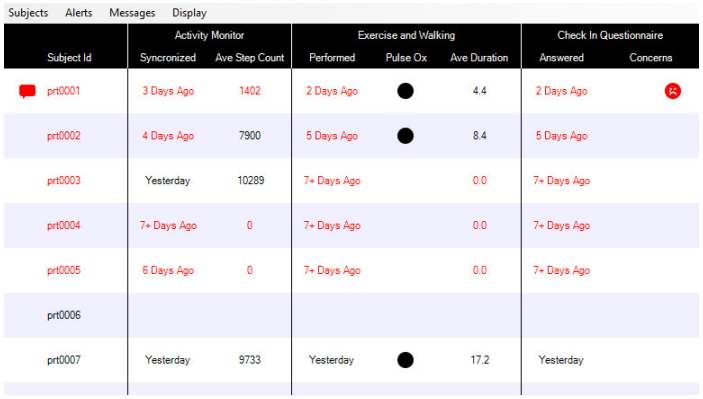


Fig. 13. Overview report.

Attention Waitlist Control Group Procedure

Our experience with behavioral studies has shown that retention in a pure control arm is very poor when the active intervention seems intuitively very useful to participants. A waitlist randomized attention control design not only permits each participant to receive an active intervention if assigned to control initially but also maximizes retention and helps fulfill immediate expectations.

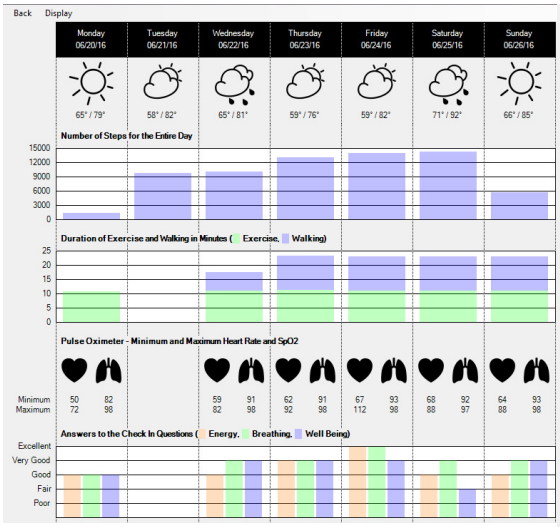


Fig. 14. Weekly individual report.

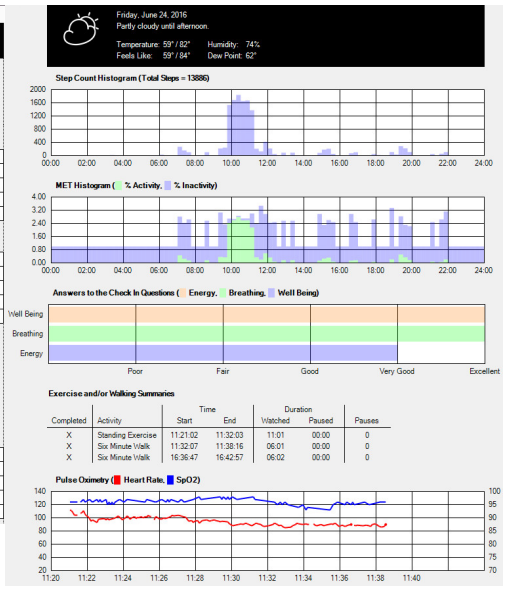


Fig. 15. Detailed report.

During the control group period, participants receive a educational materials on healthy habits for physical activity based on the 12 Habits of Highly Healthy People featured by Mayo Clinic. The control group will also receive two letters aimed at acknowledging the materials. National Institute of We plan to control for a likely Hawthorne effect that can be observed in the control group as participants may receive more attention than normal. Hence, the difference observed in the control group over time will be deducted from the effects observed in the intervention group when interpreting the results of the study as part of our analysis. The control group then receives the active intervention at month four after being randomized and upon completion of the active control period and the three month measures.

Questionnaires

Questionnaires pertaining to quality of life are administered in the project. The questionnaires are reviewed and entered into REDCap in a timely basis. If a participant indicates a score of 3 or higher on the PHQ 9, the PI will be notified.

Review of medical records, images, specimens – Category 5

The target population consists of patients who have COPD receiving outpatient care at Mayo Clinic (Rochester). We plan to enroll 200 patients in the study through referral from the Mayo Clinic Pulmonary Division ACE Database. Once enrolled, study staff will review the medical records and will document the most recent Pulmonary Function Test data and demographics.

HIPAA Identifiers and Protected Health Information (PHI)

Check all that apply:	INTERNAL	EXTERNAL
Name	X	
Mayo Clinic medical record or patient registration number, lab accession, specimen or radiologic image number	X	
Subject ID, subject code or any other person-specific unique identifying number, characteristic or code that can link the subject to their medical data	X	
Dates: All elements of dates [month, day, and year] directly related to an individual, their birth date, date of death, date of diagnosis, etc. **Note:** Recording a year only is not a unique identifier.	X	
Social Security number		
Medical device identifiers and serial numbers		
Biometric identifiers, including finger and voice prints, full face photographic images and any comparable images	X	
Web Universal Resource Locators (URLs), Internet Protocol (IP) address numbers, email address		
Street address, city, county, precinct, zip code, and their equivalent geocodes	X	
Phone or fax numbers	X	
Account, member, certificate or professional license numbers, health beneficiary numbers		
Vehicle identifiers and serial numbers, including license plate numbers		
Check 'None' when none of the identifiers listed above will be recorded, maintained, or shared during the conduct of this study. (exempt category 4)	☐ None	☒ None

Data will be stored in Mayo Clinic's REDCap database. Mayo Clinic Florida and Health Partners will only be able to see data from their site. Mayo Clinic Rochester will have access to data entered into REDCap as they are the coordinating site for this trial. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing:1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Health Coaches located at Mayo Clinic Rochester may fill in as Health Coaches at other sites to cover vacations, absences and employment gaps in health coaches. Mayo Clinic Rochester Health Coaches only have access to data in REDCap (demographics and health coach notes) and not the medical record.

Data Analysis and Data Safety Monitoring

DSMB
See Data Safety Monitoring Charter.

Analysis Plan

There are three *distinct* quantitative study hypotheses (inform different aspects of the process). Hypothesis 1 (Aim 1) states that participants on home-based PR will have higher physical (dyspnea fatigue) QOL at month three than participants in the waitlist control group as measured by the CRQ physical summary score. Hypothesis 2 (Aim 2) is that participants on home-based PR will have better SM abilities at month three than participants in the waitlist control group. The SMAS-30 will be used to test this hypothesis. Hypothesis 3 (Aim 3) is that participants on home-based PR will have more daily PA than participants in the control group at month three. This will be measured by steps and minutes spent in sedentary, light, and moderate activity measured by the ActiGraph[34, 35] and greater self-efficacy for exercise. This study has two activity monitors, the ActiGraph, a gold standard activity monitor used for outcome measures (7-day wearing) at baseline, 3, 6 and 9 months. The Garmin Vivofit PR activity monitor used daily during PR period will NOT be used as an outcome measure, just for health coaching and participant awareness of physical activity (participant will keep this activity monitor after PR).

For the continuous study outcomes, changes from baseline to three months will be compared between the study arms using two-sample, two-sided t-tests with 5% type I error rates. Changes in QOL and number of steps will be compared between the two treatment sequences using two-sample two-sided t-tests. No adjustments will be made for multiple testing. Means, SDs, medians, ranges, and frequency distributions will be reported and plotted over time by study arm. Additional analyses will compare changes from baseline to three months. 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, and FEV1. Repeated measures mixed models will be used to estimate the intervention effect over the three months of the comparison study. Although there is a crossover element to the study design, crossover analyses will not be used due to the anticipated carryover effect in the intervention arm. Intent-to-treat analyses will also be performed to determine the sensitivity of the results to dropouts and missing values. In the intent-to-treat analyses, if a month three measure is missing for any reason, it will be described as not changing from baseline. Health care utilization (number of ED visits, hospitalizations, and length of stay) between baseline and three months will be treated (analyzed) as both binary (for incidence rates) and continuous (for the number of events). The binary endpoints will all be compared between groups using Fisher's exact test. Logistic regression models will also be fit to look for differences in these outcomes by arm after adjusting for age, mMRC, FEV1, baseline levels of anxiety, depression, and fear, and baseline health care utilization (before starting the study). While significant missing-ness (>5%) in the Aim 1 outcome is not expected, imputation is planned in case it is.

Descriptive summaries of the changes between baseline, three, six, and nine months will be used to assess the effect of the delayed intervention on the control arm and the residual beneficial effect on the intervention arm. These results will be only descriptive and exploratory. No formal hypothesis testing will be done. All data will be stored in REDCap and analyzed using SAS (Cary, NC).

Missing Values treatment: Initially, Little's test for missing completely at random (MCAR)[36] will be used along with Potthoff and colleagues assessment of missing at random (MAR+).[37] Contingent on either MCAR or MAR data, imputation will be considered in order to respond to the level of missing-ness and to be able to use the optimal amount of information in our model. In case of participant withdrawal, all available data will be used.

Path analysis: The hypothesized framework will be tested using structural equation modeling (SEM), which allows us to examine multiple dependent variables in one model and concurrently describe multiple paths of direct and indirect effects among the theoretical constructs. We will use two steps in SEM analyses. First, the validity of the measures will be assessed by fitting a measurement model and investigating whether the items are strong indicators of the latent constructs (e.g., self-efficacy and quality of life). The second step involves testing the effect of the predictor variables (e.g., MI training, mastery in PA, social persuasion, physiological and emotional states) on the outcome variables (e.g., self-efficacy, self-management, and physical QOL) with a particular interest in the role self-efficacy has in increasing self-management and physical QOL. In addition to the direct effects of MI training on self-efficacy, self-efficacy on self-management, self-management on physical QOL, mediating effects can be tested, such as the effects of MI training on self-management and physical QOL, or effects of self-efficacy on physical QOL by estimating their indirect effects. The model will be tested using lavaan, the R software package for SEM.[38] The model fit will be examined by its model $\chi 2$, goodness-of-fit index (GFI), and root mean square error of approximation (RMSEA).

Qualitative Analysis (Aim 4): Perceptions of the participants and the interventionist will be captured using qualitative methods. Qualitative inquiry in randomized controlled trials help interpret results and variation in results.[39] It can also help ensure that interventions meet stakeholder needs and therefore aid in future transferability of interventions like the proposed system. This is increasingly important as trials move out of controlled settings and into the social context of natural settings,[40] including participant homes.

This qualitative approach is part of an embedded mixed-methods design, a design commonly used when individuals' perspectives inform experimental results.(33) This aim also helps us better understand the contextual factors related to implementation. As such, it

reflects the principles of a type 1 hybrid effectiveness-implementation design, the rationale for which is to study barriers and facilitators to widespread implementation alongside the intervention's effectiveness, speeding future translation into practice.[41]

The interview instruments will be informed by the quantitative study aims, and quantitative results will guide the qualitative sampling plan. Specifically, the purposive sampling for interviews and in order to increase the breath of representativeness of the interviewees , we will use baseline scores on the Patient Activation Measure to stratify the population available for interview recruitment, and we will aim to interview 10 patients with lower levels of activation at baseline (Stages 1 and 2 indicating lower participant engagement) and 10 patients with higher levels (stages 3 and 4 indicating higher engagement) AND patients with high severity defined by a MRC dyspnea score 3-4 (10 participants) vs. low severity -score 0-2-(10 participants). This variation in the sample will better ensure a range of experiences in the data and allow understanding of different opinions and outcomes. Patient activation in particular has been shown to impact adherence to self-care regimens, including home monitoring.

Data Collection

The primary method of qualitative data collection will be individual semi-structured interviews with a sample of participants in the intervention arm (n=40) and study interventionists (n=4). Interviews will be conducted at approximately week 12 (around the time of the last interventionist call). We will use an interview guide—reviewed by experts (patients and clinicians)—to ask a combination of broad, open-ended questions and focused questions eliciting information about: 1) the participant's impressions of the program; 2) impressions of program effectiveness or perceived benefits; and 3) participant's prior experience with coaching. The interview guide will be informed by program theory, (i.e., self-efficacy theory and MI)[15, 16] and the underlying constructs of measures from Aims 1-3.

To understand the feasibility and acceptability of the program, participants will be asked if they would recommend the program to another patient with COPD and what, if anything, they would change. Questions will also elicit feedback on the use of technology and barriers and facilitators to long-term adoption. We will ask interventionists to assess perceptions of how well the program fits within the current clinical services delivery system and which methods should be modified to enhance feasibility, acceptability, and durability of the intervention. Interventionists will be interviewed twice during the study in order to assess program delivery, including whether the intervention is being delivered as expected, at different points in the study implementation. Interviews will be conducted by a qualitative research analyst not involved in the intervention. They will take place *by phone and be audio recorded* and transcribed verbatim. After each interview, the interviewer will take detailed notes that describe the context of the interview, emerging themes or issues that arose in the interview, areas for clarification, and other comments. These notes and transcripts will be used in analysis. Per the reviewers' suggestions, we purposefully included a qualitative expert, Jennifer Ridgeway, to conduct this analysis and work collaboratively with Dr. Matthew Clark, as they have previously reported qualitative analysis together.[42]

Qualitative Analysis Plan

Qualitative methods will use directed content analysis. This approach is useful when existing theory informs research questions, and researchers are interested in extending the theory or using it to make predictions or look for relationships among variables.[43] At least two investigators will review the data and use an iterative process to develop labels or codes and then higher-order categories that represent key themes related to the study aims. These will be informed by the theoretical assumptions in Aims 1-3. A coding framework will be independently applied to transcripts before the investigators discuss and agree on coding. Data will be entered into NVivo software (NVivo 10.1, QSR International Pty. Ltd.) or another system for text data management to facilitate queries.

Integration with Aims 1-3: The function of the mixed-methods design is elaboration of the quantitative data on effectiveness with the qualitative findings. After initial quantitative and qualitative analyses are complete, the investigators will place findings side-by-side to explore connections as well as divergent findings that need further exploration. This includes within- and between-case analysis to understand the perspectives of participants who differed on comparative effectiveness outcomes (Aim 1-3) as well as those who differed in important baseline characteristics such as participant activation.

Sample Size: We will enroll at total of 200 participants, with 100 in each arm. Sample size calculations are based on two-sample, two-sized t-tests comparing the two groups at 3 months. **Aim 1**: We calculated the sample size based on estimates from our previously published data[6]. From this research, the CRQ has a SD of about 1.13. A total sample of 189 participants (94 or 95 per group) is needed to detect a difference of 0.5 (the minimal clinically important difference) in the CRQ with 80% power. Based on our previous health coaching application (R01HL09468 Benzo, PI),[6] we expect 5% attrition**.** We will therefore enroll 200 participants, 100 in each arm. **Aim 2**: A sample size of 128 is needed to detect a half SD change in SMAS-30 based on COPD studies using this measure. **Aim 3**: The number of steps recorded by the AM is considered a valid measure of PA in patients with COPD and the elderly. The clinically meaningful difference in steps is estimated at 1100. Therefore, a sample size of 170 participants (85 per group) is needed considering a SD of 2500 steps from our previous study.[6] Aim 4: The sample size of 40 completed participant interviews is within standards for qualitative research, but interviewing and analysis will take place concurrently and iteratively to inform the sampling plan. We will continue interviewing until saturation (the point at which interviews are not yielding much new information) is reached; the sample

will be increased as needed to more fully understand variation in the data,[44] especially between those who have low (versus high) levels of initial participant activation or those who differ in comparative-effectiveness outcomes. We will ensure ample participants to represent a range of opinions and investigate variation, rather than statistical testing. In regard to interventionist data collection, we will invite all interventionists (n=4) in the study to complete an interview; based on our pilot data, we expect high participation.

Limitations: While comparing the proposed intervention to center-based PR would be the ideal study , it would not be feasible because most participants cannot attend PR weekly (about 70%)[3] and the study would be unlikely to accrue sufficiently. This study is geared to capture the population willing to do home PR, and individuals who are confident using technology: results may not be generalizable to all individuals with COPD. We realize that some participants randomly assigned to the control group will receive center-based PR, and we plan to document and adjust our model analyses accordingly (intention-to-treat analysis) despite this limitations, the study will address a critical need in COPD care: bringing PR to all individuals with COPD.

Conclusions

The proposed study will be the first of its kind combining monitored home-based PM with theory-driven SM support through health coaching. *Since there is no system available for home-based PR delivery the results of this application are critically needed in the field of COPD. We envision that the proposed intervention is feasible (already tested) and using commercially available software and hardware will be ready to be disseminated if effective. Health Coaching will bring higher participant engagement, better participant provider communication, and possibly improved outcomes. Inclusion of qualitative inquiry will strengthen our understanding of our results and provide further information for implementation/ dissemination*

Timeline: This project will take five years to complete. The first year will be spent on institutional approvals (two months); development of materials (four months); training of health coaches on site; database creation; and the start of the clinical trial. Years 2-4 will involve the accrual of all subjects and the completion of the clinical trial. A Method Paper will be produced and published in Year 2. The final year will involve the end of the clinical trial (first quarter) data analysis, triangulation of the quantitative with the qualitative analysis manuscript publication, and preparations for grant renewal.

	YEAR 1				YEAR 2				YEAR 3				YEAR 4				YEAR 5			
Task	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Database Development																				
HC Training																				
Recruitment																				
Clinical Trial																				
Monthly Team Meetings																				
Qualitative Interviews																				
Data Analysis																				
Publication																				
Renewal																				

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