Comparing Effectiveness of Self-Management and Peer Support Communication Programs amongst Chronic Obstructive Pulmonary Disease Patients and Family Caregivers

Study Protocol

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JHM IRB - eForm A – Protocol

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1. Abstract

a. Provide no more than a one-page research abstract briefly stating the problem, the research hypothesis, and the importance of the research.

Chronic Obstructive Pulmonary Disease (COPD) is a prevalent global condition that results in high mortality, morbidity, symptom burden, and functional limitations that impact the quality of life. COPD is the third leading cause of death in the US and a leading cause of hospitalizations. COPD patients report unmet needs in regards to information about their disease and how to manage and cope with it at an intellectual, emotional, and social level. Many COPD patients lack the information and skills that they need to correctly use their inhaled medications, manage 'breathlessness episodes', and detect early signs of a COPD exacerbation. Pulmonary rehabilitation programs are established to help COPD patients increase their exercise capacity and reduce fatigue and dyspnea with daily activity. While clinical trials testing these programs have demonstrated significant improvements in health-related quality of life, and reduced dyspnea and fatigue amongst participants, it remains unclear how best to engage and motivate patients to participate in them.

Self-management support interventions which involve "collaboratively helping patients acquire and practice the skills needed to carry out disease-specific medical regimens, change their health behavior to adjust their roles for optimal function, improve day-to-day control of their disease, and improve their well-being", have been demonstrated in several trials to improve health-related quality of life, and reduce symptom burden, hospitalizations, and ED visits amongst COPD patients. However, it is still unclear which self–management support strategies employed in 'real world' settings are most effective in engaging, motivating, and enabling patients to successfully follow recommended treatments, adopt desired health behaviors, and thus achieve the desired improvements in their health outcomes.

Studies that involve 'expert patients' or 'peer mentors' in delivering self- management support to other patients who have a similar health condition have shown significant benefit to participants including: increased motivation; enhanced self-efficacy; and improvements in self-care behavior, disease control, clinical outcomes, and quality of life. Using peer-to-peer communications to help advance self-management amongst patients is particularly promising as peer mentors possess 'credibility' and can serve as 'role models', as people 'who understand, have been there, and done that'. These elements are key to achieving behavior change, according to Social Learning Theory.

The overall goal of this proposal is to compare the effectiveness of two health communication and dissemination strategies that are designed to engage patients and family caregivers in successfully managing COPD in 'real-world' settings. Both strategies aim to; advance patient understanding of COPD, its treatment options, and self-care tasks; support them in coping with the disease; and enable them to adopt a variety of positive behaviors, including adherence to treatment plans, smoking cessation, joining pulmonary rehabilitation programs, and assuming an active, healthy lifestyle. One strategy relies on the

healthcare professional (HCP) as the primary communicator about COPD self-management (Health Care Professional Arm), whereas the other uses a dual approach that involves both healthcare professionals and peer mentors delivering such communication (Health Care Professional PLUS Peer support Arm). Peer mentors are COPD patients and caregivers who have successfully managed COPD and have received foundational training on peer mentoring. Specifically we aim to: 1) Conduct a randomized controlled trial in which the 'HCP' and 'HCP PLUS Peer Support' strategies are tested in 'real-world' healthcare settings; 2) compare the impact of these strategies on patient satisfaction, experience, activation, self- efficacy, self-care behavior, health status, quality of life, use of Emergency Department (ED) and hospital services, and survival; and, 3) compare the impact of these strategies on caregiver satisfaction, experience, self-efficacy, stress, and coping skills. Study participants will be adult patients with moderate to severe COPD and their caregivers. Three hundred and twenty five patient participants will be recruited in 'real world' clinical settings from one urban and one suburban hospital and their specialty and primary care practices. Each patient will have the opportunity to include one family-caregiver with them in this study. The primary study outcome is the change in health-related quality of life at 6 months post-intervention compared to baseline. Secondary outcomes include: Combined number of COPD-related hospitalizations and ED visits, patient experience and satisfaction, patient–reported health status for physical, mental, and social well–being; symptom burden; patient activation and self- efficacy; medication adherence; smoking cessation rates; participation in pulmonary rehabilitation; physical activity levels; caregiver stress, coping skills, and self-efficacy. We hypothesize that the 'HCP PLUS Peer Support' strategy will achieve superior results compared to the HCP strategy.

2. **Objectives** (include all primary and secondary objectives)

The overall goal of this proposal is to compare the effectiveness of two health communication and dissemination strategies that are designed to engage patients and family caregivers in successfully managing COPD in 'real-world' settings. Both strategies aim to advance patient understanding of COPD, its treatment options, and self-care tasks; support them in coping with the disease; and enable them to adopt a variety of positive behaviors, including adherence to treatment plans, smoking cessation, joining pulmonary rehabilitation programs, and assuming an active, healthy lifestyle. One strategy relies on the healthcare professional (HCP) as the primary communicator about COPD self-management (HCP Arm), whereas the other uses a dual approach that involves both healthcare professionals and peer mentors delivering such communication (HCP PLUS Peer Support Arm). Peer mentors are COPD patients and caregivers who have successfully managed COPD and have received foundational training on peer mentoring. Specifically we aim to: 1) Conduct a randomized controlled trial in which the 'HCP' and 'HCP PLUS Peer Support' strategies are tested in 'real-world' healthcare settings; 2) compare the impact of these strategies on patient satisfaction, experience, activation, self- efficacy, self-care behavior, health status, quality of life, use of Emergency Department (ED) and hospital services, and survival; and, 3) compare the impact of these strategies on caregiver satisfaction, experience, self-efficacy, stress, and coping skills.

The proposed study will answer the research question: Amongst COPD patients and their caregivers, would a dual strategy that combines healthcare professional and peer mentor delivery of COPD self-management education and support result in greater improvements in health status and quality of life, and reductions in acute healthcare services' utilization, compared to relying on healthcare professionals alone in these communications? Would such dual strategy result in reduced caregiver stress and improved coping and satisfaction?

3. **Background** (briefly describe pre-clinical and clinical data, current experience with procedures, drug or device, and any other relevant information to justify the research)

Chronic Obstructive Pulmonary Disease (COPD) is a prevalent global condition that results in high mortality, morbidity, symptom burden, and functional limitations that impact the quality of life. In year 2000, around 2.75 million people died from COPD worldwide[1] with 119,000 of those deaths occurring in the U.S. In that year in the US , COPD resulted in 1.5 million ED visits and 726,000 hospitalizations.[2] In year 2010, COPD continued to be amongst the top 10 causes of hospitalizations in the United States accounting for 703,000 hospitalizations that year.[3] According to the 2011 Behavioral Risk Factor Surveillance System (BRFSS), 6.3% of U.S. adults (about 15 million individuals) reported being told that they have COPD by their health-care provider[4] and about 12% of the U.S. population ≥65 years have COPD.[4] COPD is the third leading cause of death in the US and a leading cause of hospitalizations.[3] A recent analysis of age standardized death rates in the US between 1969-2013, showed that whereas death rates from most common killers such as cardiovascular disease and cancer have decreased, the death rates from COPD have doubled.[5] About 75% of total costs for treating COPD are spent treating acute exacerbations mostly in the hospital setting, [3] and about 20 % of hospitalized patients get re-hospitalized within 30 days of their discharge.[6] Significant disparities in hospitalization rates exist among COPD patients, with patients residing in low income areas and blacks experiencing higher number of re-hospitalizations than patients residing in high income areas and white patients, respectively.[3] Psychosocial distress, single marital status, and the need for social services intervention are all associated with higher re-hospitalization rates among COPD patients.[7]

COPD results in significant functional limitations and reductions in the quality of life, with 64.2% of COPD patients reporting shortness of breath that impaired their quality of life.[4] Depressive symptoms among COPD patients are associated with higher mortality and symptom burden and poorer physical and social functioning.[8] COPD results in increased burden, stress, and affects the health and professional life for family-caregivers of COPD patients.[9]

Patients with COPD report unmet needs in regards to information about their disease and how to manage and cope with it at an intellectual, emotional, and social level. [10-13] More than half of COPD patients lack the skills required for proper inhaler use.[14, 15] This has been associated with increased symptoms and functional limitation; treatment with steroids and antibiotics; and, emergency room and hospital visits.[16] COPD patients lack the necessary information and skills for how to manage 'breathlessness episodes' and how to detect early signs of an acute COPD exacerbation.[17, 18] Pulmonary rehabilitation programs have been established to help COPD patients increase their exercise capacity and experience less fatigue and dyspnea with daily activities. While clinical trials testing pulmonary rehabilitation programs have demonstrated significant improvements in health-related quality of life, and reduced dyspnea and fatigue, amongst participants, [19] it remains unclear how to engage and motivate patients to participate in pulmonary rehabilitation.[20, 21] Pulmonary rehabilitation remain largely underused as treatment option , despite medical guidelines recommendations and healthcare insurance plans coverage, with as little as 1-14% of COPD patients being referred to these programs.[22] Self- management support interventions which involve "collaboratively helping patients acquire and practice the skills needed to carry out disease-specific medical regimens, change their health behavior to adjust their roles for optimal function, improve day-to-day control of their disease, and improve their well-being",[23] have been demonstrated in multiple clinical trials to result in significant improvements in health related quality of life , reduced symptom burden, and reduced hospitalizations and ED visits amongst COPD patients.[24] However, it is still unclear how to provide self –management support in real world settings so that patients are engaged, motivated, and enabled to successfully follow recommended treatments, adopt desired health behaviors, and thus achieve the desired improvements in their health outcomes. [23, 25] Studies that involve 'expert patients' or 'peer mentors' in delivering self- management education and support to other patients who have a similar health condition have shown significant benefits to participants including increased motivation, self-efficacy, and self-care behaviors; as well as, improved disease control, clinical outcomes, and quality of life.[26-40] Such 'peer to peer' programs have been successfully implemented and sustained in real world settings to help patients suffering from many different conditions including weight problems/obesity, mental health and addiction problems, chronic disease, pulmonary disease, and cancer. Examples of these programs include peer-led support groups, dyadic peer-to-peer mentorship or 'buddy' programs, and online peer support groups. Peer support benefits are attributed to the provision of emotional, informational, and appraisal support (peer affirmation of the "appropriateness of one's emotions, cognitions, and behaviors").[41] Benefits have been demonstrated for both people providing and receiving peer support. Using peer to peer communications to help advance self-management amongst patients is particularly promising as peer mentors bring in the 'credibility' and 'role modelling' as people 'who understand, been there, and done that'. These elements are key to achieving behavior change, according to the Social Learning Theory. [42, 43] Peer support also strengthens the social support structure that patients have and reduces their isolation. The latter is particularly relevant to patients with COPD whose medical illness often makes them reluctant to 'go out' with family and friends given their functional limitations and need for portable oxygen. In persons with COPD, receiving positive social support is associated with reduced hospitalizations, fewer exacerbations and better health status.[44, 45] There is evidence that the number of interpersonal relationships in the COPD patient's social network has important implications for their health outcomes.[46]

Studies show a significant role that family caregivers play in caring for COPD patients especially when they become more dependent,[47,48] and that this role can positively impact patients' healthcare behaviors (e.g. improved adherence),[49] or negatively influence it (for example, when a caregiver is overprotective which leads to patient becoming more dependent and less active).[50] Studies also show that caregivers experience distress and increased burden when caring for COPD patients and that can negatively influence their emotional wellbeing, professional life, and quality of life overall . [48, 50- 51] Findings from a survey administered to participants in support groups for COPD revealed positive impacts with 90% of participants reporting that they have a better understanding of COPD, 72% feeling less lonely, and 61% feeing less anxious. Survey patient respondents (N=347) reported that the group definitely help them with health decision making (76% of participants); communication with doctors (61% of participants); communication with family, friends, peers, and neighbors (41%); and adjusting their activities so they can do more at home (50%) and outside it (44%). Participants reported making positive changes in behaviors with 50% becoming more active, 31% taking medicines more regularly, 23% joining pulmonary rehabilitation, and 9% stopping smoking. Seventy one percent of respondents reported that they have taken steps that have resulted in keeping them out of the hospital. Ninety percent of participants encouraged other COPD patients to join a COPD peer support group.[52] Caregivers participating in COPD peer support groups also reported similar benefits, with 100% having better understanding of COPD, 78% gaining confidence in managing COPD, 71% feeling less lonely as a COPD caregiver; 64% feeling more supported in their caregiving responsibilities activities; and, 78% reporting that participation in the peer group helped them keep their loved one out of the hospital.[52]

4. Study Procedures

a. Study design, including the sequence and timing of study procedures (distinguish research procedures from those that are part of routine care).

Study Phases

The study will be conducted in two phases: Phase 1 starts with intervention development (phase 1a), followed by peer mentor recruitment and training (phase 1b). Phase 2, randomized controlled trial and assessment of experience with study intervention, implementation barriers, and lessons learned. **Phases 1a and 1b are already underway (IRB application is # IRB00103197). The current application is for Phase 2 of this study.**

Summary of Phases 1a and b: Phase 1a involves development of study intervention, materials, and protocol with a joint study team that includes patients, caregivers, interdivisional/multidisciplinary professional team (physicians, nurses, respiratory therapists, case managers, social workers), and healthcare leaders.

Phase 1b involves partnering with COPD patients and caregivers who are 'candidates' for peer mentor role to co-develop the peer support intervention materials and pilot test the peer mentor training. In this phase, the peer mentors will receive foundational training on peer mentoring and provide feedback on it. Candidate peer mentors are COPD patients and family- caregivers who have successfully managed COPD and who will be nominated by their healthcare team as successful COPD self-managers. All patient peer mentors will be graduates of pulmonary rehab and current non-smokers thus serving as positive role models. Specifically, the peer mentors will be 1) moderate-severe COPD patients who have successfully stopped smoking, participated in a pulmonary rehabilitation program, and have been nominated by pulmonary rehabilitation center staff or their pulmonologist for this role; or 2) a family- caregiver of a COPD patient who meets above criteria, is not a current smoker, and is nominated by the pulmonary rehabilitation program staff or pulmonologist for this role.

To recruit the peer mentors we are collaborating with the pulmonary staff program teams at the Johns Hopkins Bayview Medical Center and the Howard County General Hospital, and the pulmonologists at both study sites (JHBMC and HCGH). The peer mentors will receive training on how to mentor other people who have COPD. This training includes both general peer mentoring skills, as well as discussion about COPD –specific topics. Training topics include listening, empathy, motivational interviewing, telling own story, as well as discussion of common questions and challenges with COPD. The training will take about 10 hours, and its format, number of sessions etc. will be determined based on feedback from the participants.

Participants in phase 1b who successfully complete all training activities and the requirements for serving as a volunteer at Johns Hopkins will be offered the opportunity to participate as peer mentor (also called BREATHE Pal) in phase 2 of this study. In their role as BREATHE Pals, the peer mentors would help provide peer support to other patient and caregiver study participants.

Phase 2 involves conducting a randomized controlled trial to compare the effectiveness of two strategies to support COPD patients and improve their quality of life. Both strategies aim to advance patient understanding of COPD, its treatment options, and self-care tasks; support them in coping with the disease; and enable them to adopt a variety of positive behaviors, including adherence to treatment plans, smoking cessation, joining pulmonary rehabilitation programs, and assuming an active, healthy lifestyle. One strategy relies on the healthcare professional (HCP) as the primary communicator about COPD self-management (HCP Arm), whereas the other uses a dual approach that involves both healthcare professionals and peer mentors in delivering such communication (HCP PLUS Peer Support Arm). Phase 2 specific aims are : 1) Conduct a randomized controlled trial in which the ‘HCP’ and ‘HCP PLUS Peer Support’ strategies are tested in ‘real-world’ healthcare settings; 2) compare the impact of these strategies on patient satisfaction, experience, activation, self- efficacy, self-care behavior, health status, quality of life, use of Emergency Department (ED) and hospital services, and survival; and, 3) compare the impact of these strategies on caregiver satisfaction, experience, self-efficacy, stress, and coping skills.

Study Population and Setting

The study participants are adults receiving treatment for COPD and their family caregivers. The patient participants must be older than 40 years, with no significant cognitive dysfunction, severe mental illness, or active substance abuse. Family caregivers must be 18 years or older and chosen by the patient participant to get enrolled with them into the study. The reason for these requirements is the nature of the proposed intervention (group-based with active engagement and participation).

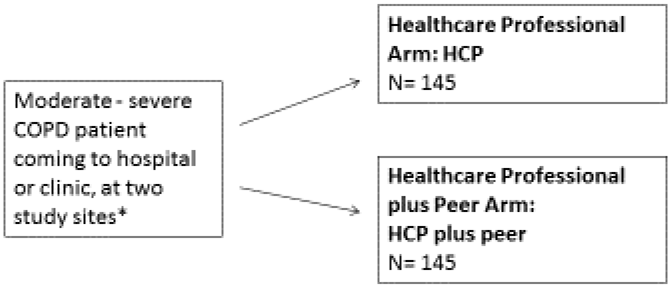
We will conduct this study at Johns Hopkins Bayview Medical Center (JHBMC) and Howard County General Hospital (HCGH), and their affiliated pulmonary and primary care clinics (some of these clinics are part of Johns Hopkins Community Physicians). JHBMC is an academic center in Baltimore, Maryland that serves an urban, inner-city population with a large percentage of low-income and ethnic minority patients, as well as patients from the Baltimore-

Washington DC region. JHBMC has a 550-bed hospital, a nationally recognized pulmonary center, pulmonary specialty clinics, a pulmonary rehabilitation center, and multiple primary care clinics. HCGH is a community hospital in Columbia, Maryland that serves a suburban population with a large percentage of middle class patients, as well as patients from the Baltimore-Washington DC region. HCGH is a 300 bed community hospital, and includes pulmonary specialty clinics, a large pulmonary rehabilitation center (about 2000 people complete the acute rehabilitation program), and multiple primary care clinics. Both hospitals and their affiliated clinics are part of the Johns Hopkins Health System.

Study structure

We will conduct a randomized controlled trial (RCT) to implement and test study interventions at two study sites, recruiting COPD patient participants from an urban academic hospital (Johns Hopkins Bayview Medical Center) and its affiliated hospital based clinics and a suburban hospital (Howard County General Hospital) and its affiliated clinics. Participants will be recruited from both hospital and ambulatory service settings.

Below is a schematic depicting Phase 2 trial design:



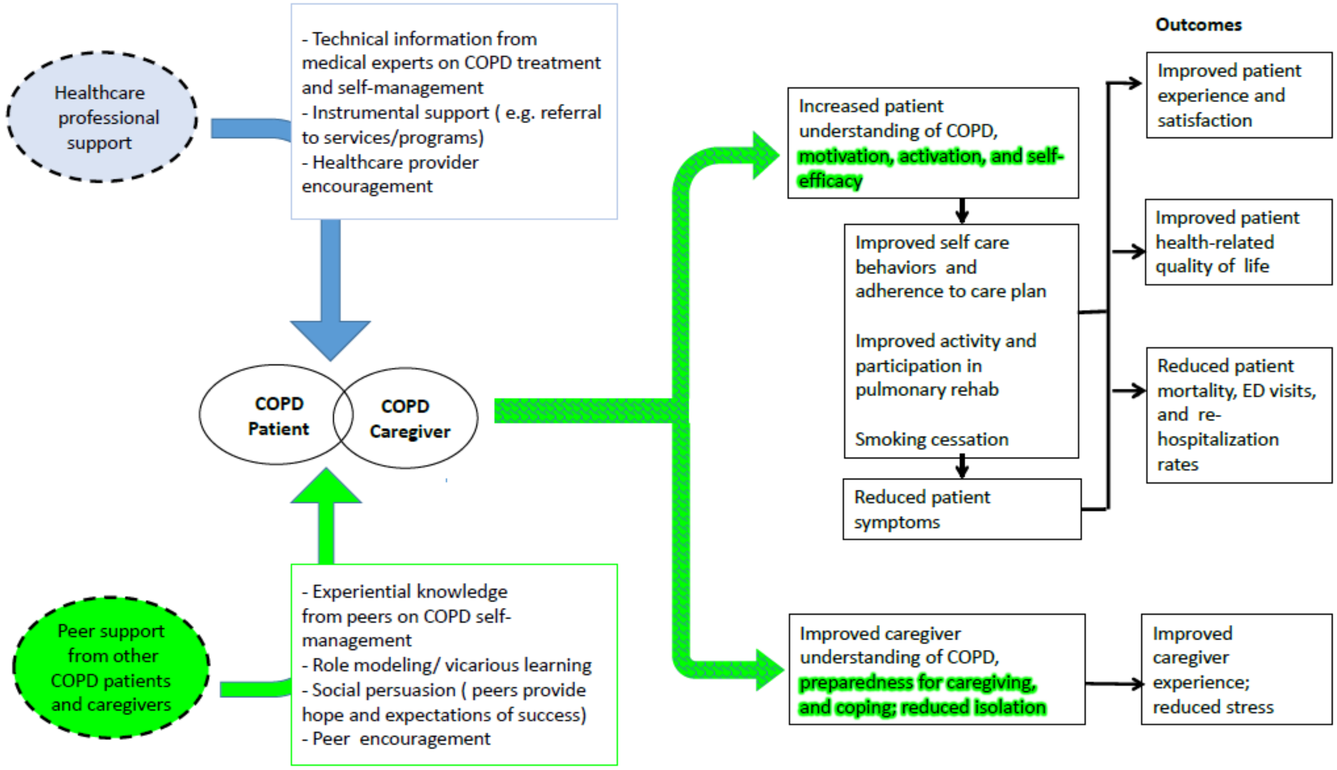
* Randomize within site and service setting

In the HCP Arm, we will employ a healthcare professional delivered, clinic-based approach for engaging patients and families. It involves delivery of self-management education and support on an individual basis to individual patients (and their family caregivers, if applicable).
In the HCP PLUS Peer Support Arm, a dual strategy will be followed where HCP support is provided as in the first arm, and a peer support program is added.

This strategy employs a partnership model, is co-led by peer mentors and healthcare professionals, and brings together groups of patients and family caregivers to discuss COPD and chronic disease management topics, and share tips on how to cope with COPD and manage it. The peer mentors (called ‘BREATHE pals’ in this study) are COPD patients and caregivers who have successfully managed COPD, and have received foundational training on peer mentoring and facilitation of peer conversations. Peer mentors will be nominated by their medical providers as successful COPD self-managers and all patient peer mentors will be graduates of pulmonary rehab and current non-smokers thus serving as positive role models. The peer mentors are also formal ‘volunteers’ within Johns Hopkins Bayview and HCGH and have thus met the requirements for interacting with patients within these healthcare facilities.

Study conceptual model

The conceptual model (see below) clarifies the different mechanisms by which healthcare professionals and peers can help enable and support COPD patients and caregivers in adopting the recommended self- management strategies that will lead to improvements in patient outcomes and caregiver experiences.



The traditional medical expert model involves healthcare professionals (HCPs) from various disciplines (doctors, nurse educators, respiratory therapists, etc..) providing the necessary medical/ technical information about COPD; the instrumental help in regards to referring patients to the necessary treatment services and recommended programs (e.g. pulmonary rehabilitation, smoking cessation programs etc..) ; and, the encouragement and support that would help enable them to gain confidence in their ability to implement recommended self-care practices and desired behaviors. Though all of the above healthcare professional contributions are essential to caring for COPD patients, they may not be sufficient to induce and maintain positive behavior changes particularly amongst patients who are less engaged and motivated and who have low self-efficacy. These patients often fail to adopt the desired evidence-based behaviors that would lead to achieving improvements in patient-centered outcomes such as improved health related quality of life and reduced need for frequent use of emergency room and hospital services.

According to the Social Cognitive Theory, self- efficacy mediates behavior change and achieving the former requires practice and mastery of the necessary skills, modeling of desired behaviors (also referred to as vicarious or observational learning), and social persuasion. (Bandura, 1986) Patients who are successfully managing COPD (for example, those who have stopped smoking, participated in pulmonary rehabilitation, maintain activity, and use available COPD treatment options effectively) are very well positioned to help other COPD patients and their caregivers learn from their practical knowledge on managing COPD in their daily living. More importantly those ‘successful COPD self-managers’ are capable of offering COPD patients what no other healthcare professional can offer, mainly the role modeling of desired behaviors and the persuasive message that these behaviors are indeed achievable by other people with a similar health condition. In addition to helping provide experiential knowledge, role modeling, and social persuasion, peers can help provide emotional and appraisal support and therefore facilitate success in adopting recommended behaviors and reducing feelings of isolation.[41] Caregivers who have successfully supported family members with COPD can similarly provide informational, social, emotional, and appraisal support for other caregivers and help them in learning about how they can support someone with COPD and cope with the burdens of caregiving for someone with this health condition. The attached conceptual model depicts key contributions that healthcare professional support provides to COPD patients and their caregivers (blue arrow), and the additive contributions that peer support would introduce (the green arrow). A dual approach which involves pairing expert healthcare professional services with peer support, allows patients to receive (1) the technical information that they need, and the referrals to services that will enable them to adopt recommended behaviors; and (2) the peer support that increase the likelihood that they will become more motivated, activated, and achieve the self- efficacy needed to successfully manage COPD. Those areas that peer support is most likely to positively impact amongst both COPD patients and caregivers are highlighted in green in the model.

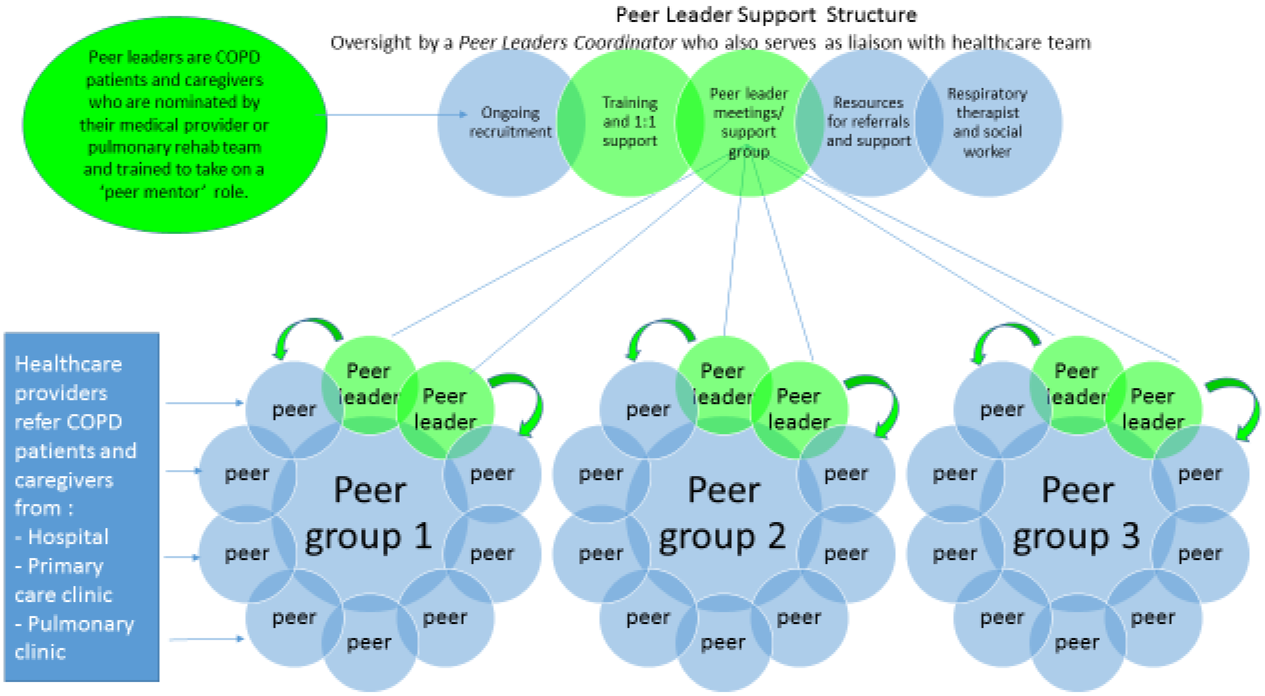
Description of Study Arms

HCP Arm- employs a healthcare professional delivered approach for engaging patients and families. It involves delivery of self-management education and support on an individual basis to individual patients and their family caregivers if applicable. The program will aim to deliver COPD education and support services per ATS/ ERS guidelines for treatment of COPD. The program will include provision of patient-centered self-management education materials, a community resources guide, and follow-up phone support by a respiratory care practitioner (RCP). The RCP will explain the provided materials, answer any questions that the patients/caregivers may have, and discuss any challenges that they are having in managing their health.

HCP PLUS Peer Support Arm –employs a dual strategy where HCP support is provided as in the HCP Arm and a peer support component is added. The peer support is provided via participating in a peer support program that uses groups and 1:1 conversations to provide peer support. In this program COPD patients and family caregivers will be connected with 'expert' patients and caregivers also referred to as 'peer mentors'/'BREATHE Pals'. These mentors are COPD patients and caregivers who have successfully managed COPD and have received foundational training on peer mentoring. Peer mentors are nominated by their medical providers as successful COPD self-managers and all patient peer mentors have completed an acute pulmonary rehabilitation program and are current non-smokers thus serving as positive role models. Peer mentors are trained to listen and share their experiences with having COPD and overcoming its challenges, without provision of any medical advice. They are also trained about HIPPA and keeping all their conversations with program participants confidential. The peer support is provided using multiple channels including group and 1:1 conversations. All program participants will be invited to 8 group sessions over 6 months period. The sessions will be led by 1-2 peer mentors and discuss COPD self-management topics. At each of these sessions, a social worker would be present to support the peer mentors and facilitate any 'difficult conversations' that may arise. The group leaders will be trained to promote a friendly and non-hierarchal group environment. The program will encourage all participants to use group formats as often as possible to maximize benefits of peer and social support. Participants in the peer support program will also receive 1:1 peer support via having phone conversations with the peer mentors.

The peer mentors/Breathe Pals will have their own support structure to ensure continued participation, interest, and reciprocal benefits. Based on earlier studies we anticipate that the

BREATHE Pals will also benefit from participating in the peer support program via connecting with others peers in general and peer mentors in particular. The figure below depicts the BREATHE Pals (referred to in the visual as peer leaders) support structure. A Peer Support Program Coordinator will provide support and guidance for the BREATHE Pals. The coordinator is a licensed clinical social worker who will help train the BREATHE Pals and hold regular peer leader meetings in which they get to discuss their current efforts and any challenges that they may be facing. The social worker will be available to also provide support for BREATHE Pals on individual basis as needed.



Study procedures

i. Recruitment and Consent Procedures

There are four types of participants in this study: 1) Patient participants (patients receiving treatment for COPD at the hospital or clinic setting); 2) Caregiver participants (family members or friends helping the patient participant with their healthcare); 3) Patient peer mentors (COPD patients who have completed phase 1 of this study and indicated interest in participating in this trial as a peer mentor/BREATHE Pal in the Peer Support Program); 4) Caregiver peer mentors (COPD family caregivers who have completed phase 1 of this study and indicated interest in participating in this trial as a peer mentor/BREATHE Pal in the Peer Support Program).
The Patient Participants will be asked if they are interested in inviting a family caregiver to join in them in this study; however, they can enroll without a family-caregiver. The patient participants will be randomized to one of the two study arms in this trial (HCP or HCP PLUS Peer Support) and their respective Caregiver Participant, if they have one enrolled, would participate with them in that study arm. The Patient and Caregiver Peer mentors will only participate in the HCP PLUS Peers study arm serving as 'BREATHE Pals' in the Peer Support Program.

Below we detail the recruitment and consent approaches for each of these types of participants.

Patient and Caregiver Participants

Step 1- Patient identification and discussion about the study

Multiple approaches will be used to recruit patient participants from the hospital and clinic settings. We will start with recruitment from JHBMC and HCGH hospital medical units, as well as the pulmonary clinics at both hospitals, and the JHCP primary care clinics. For the latter, we will start with clinics that are on either of the hospital sites or the closest to these hospitals and additional clinics may be added as need be. We will collaborate with the healthcare providers to identify patients who are receiving care at the hospital or clinic, who have been diagnosed with COPD by a physician, are receiving treatment for it, and are at least 40 yrs old. The recruitment process will likely vary by setting and site, depending on logistical considerations (i.e. setting, space, staff) and healthcare team preferences.

At the hospitals, we will use patient census and diagnosis lists that are maintained by the hospital nursing and case management teams to identify in a timely manner admitted patients at the two study sites who have COPD early during their hospital stay. We have utilized this recruitment approach successfully in an earlier study to help streamline the process of hospital based recruitment and reduce recruitment time demands on clinical staff (IRB00054456). For patients who have COPD and are receiving treatment for it at one of 4 Bayview medical units (MedA, MedB, PCU, Bridgeview) or at one of the HCGH med-surg units, a study team member will contact the patient's provider to determine whether the patient's clinical status allows them to talk about the study. Patients who are clinically stable will then be approached by a study team member who will share materials about the study (Brief study video; Patient Hospital Flyer; Caregiver Hospital Flyer), and inquire about their interest in participating in the privacy of their own room.

At the outpatient clinics, we will use multiple approaches to ensure successful recruitment based on the clinic set up and patient flow:

(1) Recruitment materials will be available in clinic waiting areas, and for healthcare team members to provide to their patients (Brief study video; Patient Brochure; Caregiver Brochure). Contact information for the research study team will be provided on the recruitment materials. Interested patients have the option to fill in a contact information card (tear out part of the Patient Brochure) with times that they would like to be contacted and leave it in a sealed envelope with their healthcare provider at the clinic site. A study team member will then pick up their card and contact them via phone. This approach will be particularly helpful at clinic sites where the clinic lacks a private space for the study team member to discuss the study with interested patients.

(2) A study team member will be available at select sites to approach any patients who are referred by their healthcare provider to the study. To reduce burden on providers and streamline the recruitment process, we will collaborate with the healthcare providers to identify COPD patients who are coming for a clinic visit on that day and a study team member will then provide these patients with study recruitment materials and check on their interest to learn more about the study.

(3) Furthermore, at select clinic sites, we will collaborate with experienced data analysts at ICTR's Center for Clinical Data Analysis (CCDA) following applicable data trust privacy and security regulations, to identify patients with diagnosis of COPD in EPIC who have visited these clinics in the past 6 months, and contact these patients via mailed letter (See Study Notification Letter; this approach will be used at sites where medical director is a study team member) .

Step 2- Screening for Eligibility

Once the study team member talks with the interested patients about the study, s/he will check whether they meet basic eligibility criteria and if so s/he would describe the study in detail, and if the patient is interested to join the study, they will proceed to step 3 if in the hospital and not being discharged soon. Otherwise, the patient will be scheduled for a study enrollment visit. (Initial Contact Eligibility - In Person Script; Initial Contact Eligibility - Telephone Script). The patient will be asked if they have a family caregiver who is 18 years or older whom they would like to include with them in the study. and if so they are invited to ask that caregiver to come with them to the study enrollment visit or enroll with them while at the hospital. The patient will be informed that they can still participate in the study even if they don't have or don't want to include a family caregiver with them in the study. The study team member will also provide the patient, as needed, with a caregiver brochure or flyer to share with their caregiver (Caregiver Hospital Flyer; Caregiver Brochure). These materials will be provided in person or via mail. If the patient is enrolled in the hospital but family-caregiver is unavailable, a separate enrollment visit will be scheduled for the family- caregiver.

Step 3: Patient and Caregiver Study Visit, Written Consent, and Randomization
At the study Enrollment Visit (or during enrollment in the hospital) , additional eligibility data will be collected and if patient meets those, written consent, baseline assessment, and randomization will occur. A trained study team member will:
1) Conduct a spirometry test and confirm that results meet criteria for enrollment into the study
2) Obtain written consent and conduct the baseline interview
3) Tell the participant their randomization results
4) Refer the participant to the healthcare professional for their in- person education session
To start with the study team member will describe the study in more detail to the patient and caregiver (if applicable), the two study arms will be described, and the patient and caregiver will be told what will happen in either arm of the study. After written informed consent is obtained, (Patient Consent Form) all patients will complete the baseline assessment (REDCap Survey- Patient section). The caregiver, if applicable, will also provide written consent (Caregiver Consent Form) and complete a baseline assessment (REDCap Survey – Caregiver section).   All assessments will be obtained using structured interview format and participant responses will be directly entered by the study team member using an electronic device into a redcap database. After assessment is completed, a study team member will open a sealed envelope that would have the patient's randomization assignment. They will inform the patient of their random assignment and inform the family caregiver (if applicable) that they are assigned to that same study arm with their loved one. Both patient and caregiver, if applicable, will then be invited to their in- person session with the Respiratory Care Practitioner therapist (RCP) which will take place right after their Enrollment Visit for participant convenience, unless the participant had expressed their interest in alternative date and time. (If patient is enrolled at the hospital, the RCP session will be scheduled to take place while at the hospital or soon after their discharge.)

Patient and Caregiver Peer Mentors

Few COPD patients and caregivers will be recruited to perform peer mentor roles as BREATHE Pals in this study (N= 12- 36). To be eligible for this role, these participants must have:

(1) Successfully completed Phase 1 of this study in which they receive special training for this role (Peer Mentor Training Outline)
(2) Have applied for and met the requirements for becoming a Johns Hopkins volunteer at the respective study site (Johns Hopkins Volunteer Requirements). As part of these requirements, the peer mentors are asked to sign a confidentiality agreement (Confidentiality Agreement).

(3) Be willing to participate in phase 2 of this study as BREATHE Pals for at least 6 months

Eligible candidates will participate in a group meeting in which the BREATHE Pal role will be described in detail, and if still interested will have an individual follow up conversation (in person or via phone depending on candidate preference) to go over the written consent for Peer mentor participants in this study. (Peer Mentor Consent Form)

ii. Intervention procedures

All study participants will receive a HCP support intervention in this study. Those randomized to the “HCP PLUS Peer support” Arm will also have the opportunity to participate in a Peer Support Program. Below we describe the procedures for both study interventions.

HCP support intervention
In this intervention a HCP (trained respiratory care practitioner) would hold a 1 hour individual session with each study participant and their caregiver (if applicable). The session will be held at the site where the participant usually receives their care. The respiratory care practitioner will discuss with the participants COPD self-management, review medication use, and provide them with informational materials and resources. The RCP will ensure that the patient participant is demonstrating proper inhaler use technique. The RCP will go over COPD self-management following a written guide that will be provided to each participant (COPD Patient Education Guide). This guide has been developed by the study co-investigators in an earlier study and covers areas recommended by the American Thoracic Society and European Respiratory society (ATS/ERS) for COPD patient education. The RCP and the participant will decide together on the areas of the guide that they would like to spend more time on during this session. In addition, the participant will be provided with a resource guide for various local services and programs that COPD patients may find helpful (BREATHE Resource Guide). Caregivers will also be provided with Tips on Being a Caregiver (Caregiver Tips) and a caregiver frequently asked questions resource document that has been developed by the COPD foundation (FAQ for caregivers). The RCP will provide her contact information to the patient and their caregiver, if applicable, in case they wanted to meet and discuss the provided materials further. In this intervention, the RCP will not provide any medical advice or treatment services. Instead they will refer the participant to their medical provider for any specific questions on changes in their treatment plan. The RCP session will take place in person within 2 months of participant enrollment into the study. If the patient missed one appointment for RCP visit, they will be scheduled for another. If they missed the second appointment the RCP will reach out to them and offer to hold that session via phone.

Peer support program intervention
The Peer support program will offer patient and caregiver participants who are randomized to the “HCP PLUS Peer support” Arm, peer support services that will be delivered via multiple channels including 1:1 and group conversations. In this program, the patient and caregiver participants will have the option to connect with other peers. Each patient and caregiver participant in this study arm will be ‘matched’ with a peer mentor (referred to as BREATHE Pal). The Breathe pal will talk with the participant at regular intervals at peer group ‘Get together’ events and/ or via phone (based on participant preference and their attendance of group events). The group events will take place at the study sites and will be co-led by 2 BREATHE Pals in presence of a social worker. At these events, select topics about COPD self-management will be discussed, and the messages delivered by the RCP will be reinforced.

The BREATHE Pals are people who have COPD, who have successfully stopped smoking and completed acute pulmonary rehabilitation program, and/or their family-caregivers. They are identified via nomination from a pulmonologist or a pulmonary rehab team member for this role, have successfully completed phase 1 of this study that includes receiving training on becoming a COPD peer mentor, and have applied to and met the requirements for becoming a volunteer at JHBMC or HCGH. The BREATHE Pals will receive ongoing support from a Johns Hopkins licensed clinical social worker who will provide guidance and support to the peer mentors and coordinate peer support program services. The social worker will attend the 'Get together 'events, to provide support for the BREATHE Pals without taking over the leadership of these events. The social worker will ensure that the BREATHE Pals are following study protocol and not engaging in provision of medical advice. They would also help facilitate any difficult conversations that the group may have. The social worker will help match the BREATHE pals with patient and family- caregiver participants who are in the HCP PLUS Peer Support Arm. The matching will occur based on preset criteria, aiming to match participants with BREATHE Pals based on gender, patient or caregiver status, and oxygen therapy use to the extent that may be possible. Matching will also occur within study sites to the extent possible.

Peer support group conversations will be orchestrated at 8 'Get Together' events spanning a 6 months period. All participants who miss an event or were not interested/able to attend an event (based on preference, life circumstances, or health status), will be offered the option of attending a similarly themed 'BREATHE group call' to catch up on missed event conversations and their 'matched' BREATHE Pal will also contact him/her via phone to check in on them, answer any questions they have, and encourage them to attend the next Get together event. At end of these phone calls, the peer mentor has the option of talking about their call with the social worker. If a patient or a family caregiver expressed the need for additional healthcare or social support services, or if the peer mentor felt that they need it, they would inform the social worker who will facilitate the patient or family-caregiver access to these services.

At the group events (in person or group call), the group participants led by the BREATHE Pals will discuss COPD and its challenges, and share their experiences in coping with and managing it. See summary table below on general topics for discussion. The topics pertain to advancing patient understanding of COPD and its treatment options, introducing effective coping skills, and reinforcing a variety of positive behaviors including adherence to treatment plans, smoking cessation, joining pulmonary rehabilitation programs, and assuming an active, healthy lifestyle. The Breathe pals will use the COPD Patient Education guide and a set of commonly asked questions and answers (Commonly Asked Questions and Answers) as their content guide/reference for the group conversations and follow up phone conversations. Each meeting will include: 1) Education about COPD management strategies based on the themes in table below; 2) discussion of patient experiences and challenges related to using these strategies; and, 3) encouragement to set goals and problem solve challenges. The sessions will follow a sequence of themes from 1-8 and then repeat. A study participant may thus join the sessions sequence at any time point and continue for 8 sessions thus getting to participate in all 8 themes. If at any point the number of participants attending the sessions exceeded 20 people, the group will be split into two and new participants may join either group according to their preferred group meeting time.

The table below depicts the session themes and sample opening questions for group discussion:

Theme	Session Topic	Topics to be Discussed	Corresponding pages in the COPD Patient Education Guide
Theme#1	Ways to Breathe Easier Family-caregivers I	Ways to perform daily activities with less shortness of breath Pursed-lip breathing Small group activity (in separate patient and caregiver groups) –discussion of general experiences with COPD and providing/ receiving help and support	p. 21-26, 47-50 Addendum-Tips and resources for caregivers
Theme #2	Recognizing Signs of a Flare-Up	COPD exacerbations or flare-up and how to manage those "Action plans" and how to use	p. 31-34 Review Action Plan
Theme #3	Coping with COPD Family Caregivers II	COPD impact on life Managing feeling out of breath Managing feelings of anxiety and depression **Small group activity** (in separate patient and caregiver groups)	p. 23-26, 39, 47-50 Breathless-ness cycle
Theme #4	Getting the Most of your COPD Medications	COPD treatments Inhaler use Rescue vs. Maintenance Inhalers vs. Nebulizers Managing medication costs	p. 7-12
Theme #5	Getting Acquainted with Oxygen Usage	Oxygen therapy- when is it needed and how to use safely Traveling with oxygen Getting comfortable using oxygen in public	p. 13-20, 53-55
Theme#6	Becoming More Active	Importance of staying active Becoming more active Pulmonary rehabilitation and its benefits	p. 39-46
Theme#7	Lifestyle Modifications with COPD	Diet Changes Planning a Daily Routine/Pacing Yourself Support for Smoking Cessation Prevention/Being Proactive about COPD	p. 47-52

Theme #8	Preventing Breathlessness	Irritants you should avoid Protecting yourself from infections	p. 27-30

The BREATHE Pals will use the COPD education guide as a ‘content reference’ and review its contents as applicable in the group meetings.

The BREATHE Pals will have a set of suggested ice breaker activities to choose from for use at the various in-person sessions. Examples of those include sharing a personal story related to the topic of the meeting or sharing coping strategies such as pursed lip breathing or mindfulness to start the discussion. Additionally, time will be reserved that allows for socializing among group participants at the end of each meeting (approximately 30 mins). Any individual participant concerns can be discussed at that time between the participant and their BREATHE Pal and/or the social worker.

The Get together events will provide an open forum for COPD patients and their caregivers to share their experiences with COPD, and how they have managed its various impacts on their lives. These events will have a set of engagement rules for the participants (referred to as ‘group agreement’) that will be revisited periodically and posted in the room. Those include: “What is said in the group stays in the group; we listen to, support, and learn from each other; everybody’s opinion is important; when someone is talking, we allow the person to complete what they are saying before we speak; there are no right or wrong questions; we will reduce distractions (cell phones, computers, IPads, notebooks are not permitted- necessary calls may be made outside the room); we will start and end on time” . The social worker, who will also be attending the Get-togethers, will help support the BREATHE Pals in making sure that these rules are observed.

The Breathe pals will use ice breaker activities such as sharing a personal story related to the topic of the meeting or sharing coping strategies such as pursed lip breathing or mindfulness to start the discussion at each of the Get togethers. Additionally, time for socializing among group meeting participants will be allotted for people to talk with other participants at the end (approximately 30 mins).

Given that the patient and caregiver participants may wish to discuss some topics pertaining to how they relate to and support each other without the presence of their loved one, at least two opportunities will be provided where the group will be divided into a patient and a caregiver subgroup for part of the Get Together and time will be taken to discuss patient-caregiver matters separately.
As a quality control measure, we will audio-record a sample of the peer group conversations and those audio-recordings will be reviewed for adherence to guidelines protocol. The patients and family-caregivers will be reminded at the start of each conversation/session that it will be audio-recorded and will be informed that they may choose not to have the audio-recorder on or ask that it be stopped anytime during the session. The audio files will be saved on a secure password protected Hopkins drive directly after session conclusion. The drive will only be accessible to the PI and designated team members and stored files will be kept for 7 years in accordance with the DHHS regulations and would then be destroyed.

iii. Safety Management

The interventions employed in this study are minimal risk interventions where no medical treatments or advice will be provided. All treatment services will remain under the control of the study participants and their healthcare providers. The RCP who will be delivering the HCP intervention, and the social worker who will facilitate the Peer Get-togethers and provide oversight and support for the BREATHE Pals, are both licensed Healthcare professionals who are employed within Johns Hopkins. The roles they will perform in delivering the study interventions are well within their professional scope of practice. These professionals will be trained on intervention procedures and if a study participant requires additional medical treatment or social support services, they will not provide treatment services themselves but rather facilitate the study participant's access to these services at the respective sites where the participants receive their care.

The peer mentors will be specifically trained not to provide any medical advice and to refer study participants who request such advice or report on specific healthcare or social needs to the social worker. The peer mentors, in addition, will be instructed to turn to the social worker with any concerns that they may personally have about any participants, or if they feel distressed or burdened by their BREATHE Pal role. All peer mentors will have the opportunity to regularly meet with the social worker to discuss their volunteer efforts and any needs or concerns that they may have.

Given that many of our study participants will have severe COPD and other co-morbidities, and that frequent hospitalizations and occasional deaths are anticipated in this patient population, we will establish a Data Safety and Monitoring Board (DSMB). The primary responsibilities of the DSMB will include monitoring of participant safety, data quality, and adverse events tracking. The DSMB will meet regularly, either in person, or via conference call. They will receive data reports prior to the meeting that contain information about participant recruitment, retention, participant characteristics and adverse events. In addition to the DSMB members, meeting attendees will also include the study Principal Investigator and the study Biostatistician.

We will follow the following procedures to ensure safety and track adverse events in this study: Adverse Events in this study will be identified and assessed for severity and tracked whether or not they are related to the study treatments. For the purposes of this study, serious adverse events include: death, hospitalization, or fall due to intervention related activities. These events will be assessed during routine data collection calls at 3, 6 and 9 months post enrollment. A log will be kept for unanticipated problems. Any participant deaths that occur within 30 days of receiving a study intervention, whether expected or unexpected, will be promptly reported in accordance with JHM policies. All pertinent adverse events will be included in the data reports to DSMB and to the IRB at continuing review time.

Study Measures and Outcomes

The primary outcome measure is change in health-related quality of life as measured by the Saint George's Respiratory Questionnaire (SGRQ) total score at 6 months post-intervention compared to baseline. Additional secondary patient outcomes that we will measure in this study include overall patient experience and satisfaction; patient activation; patient–reported health status; PROMIS informational support, emotional support, and social isolation domain measures; loneliness; anxiety and depression; and symptom burden. We will also measure the combined number of COPD-related and all cause hospitalizations and ED visits per patient at 6 months post-intervention start. Other process/impact measures will include patient self- efficacy, and medication adherence; joining pulmonary rehabilitation; smoking cessation; caregiver stress, coping skills, and self-efficacy.

We will collect data on patient demographic characteristics, disease severity, co-morbidities, health literacy, history of healthcare utilization, anxiety and depression, mental health. Similarly, we will collect caregiver participants' age, gender, employment, relationship to patient, caregiving responsibilities, health status, and distance from patient home, and transportation means.

Below is a description of main patient study measures with comments on validity.
1. Disease-specific health-related quality of life will be measured with the St. George's Respiratory Questionnaire; 76 items, 3 subscales (symptoms, activity, and impacts), each with score 0-100. The minimum clinically important difference is 4; 8 units reflect moderate change; and 12 units very efficacious treatment.
2. Combined # of COPD- related ED and hospital visits per patient from enrollment to 3, 6, and 9 months (also calculated separately for hospital and for ED visits).
3. Patient activation measure Pam -13 item. This instrument has been widely tested with patients with various medical conditions. It has been psychometrically tested and used in multiple research studies. The 13-item measure has similar psychometric properties to the original 22-item version which shows good precision and validity.
4. Understanding COPD questionnaire: Will use the sections on 'understanding of COPD' and 'self-efficacy and use of key self-management skills". Good test-retest reliability (ICC range: 0.87 to 0.96) and internal consistency (Cronbach's Alpha range: 0.78 to 0.95). The instrument has been shown to be responsive to in studies of pulmonary rehabilitation. We will also use an adapted version of this questionnaire to measure self-efficacy among caregivers.
5. Medication adherence – Morisky scale. This is an 8-item scale that has been validated and used in multiple studies. The instrument was initially tested with hypertension patients but has since been used with different patient populations.
6. Social and other support- The Patient-Reported Outcomes Measurement Information System (PROMIS) item bank - four validated domains will be used: Social isolation; Informational support; Emotional support. .
7. Ways of Coping Questionnaire. Validated questionnaire with reliability of .76 - .88 and established construct validity.

Caregiver outcomes include self-efficacy, stress and coping, informational and emotional support, and experience with the intervention.

Please refer to 'Study Outcomes Table' attachment for full list of Patient and Caregiver outcomes and time points of data collection.

Data collection and outcomes assessment

It is not possible to 'blind' the patients, their families, or the healthcare professionals to the study assignment in this type of intervention. However, we will have the study research coordinators and any other personnel who are involved in outcome assessment blinded to the study participants' arm assignment.

All participants will be interviewed in person, upon enrollment , prior to randomization, by a trained study team member. They will then be interviewed via phone by a research team member, who is blinded to their study arm assignment at 3, 6, and 9 months post enrollment. Six attempts will be made to reach patient/caregiver at each data collection period. At the enrollment visit, baseline data will be collected on demographics, bio-psychosocial status, as well as COPD knowledge, self-management skills, patient activation, and health literacy levels (BREATHE2 REDCap survey; BREATHE2 Outcomes Table). At their last follow up call, patient and caregiver participants will be asked if willing to share their perspective about study interventions, their experience with those, and suggestions for improvement. If interested, a future 30-60 min interview will be scheduled to take place via phone or at the healthcare facility per participant preference. (See 'Exit Interview Questions' attachment)

Information will be collected post enrollment on whether the patient has visited the ED or been re-hospitalized. If so, the name of ED or hospital will be collected and patient's permission to check the medical records from that hospital /ED will be obtained. The medical record will then be reviewed to determine whether the visit was COPD-related. This determination will be carried out by two physician reviewers. A third physician will adjudicate any unresolved conflicts.

Patients will receive a small monetary incentive for participation in the study at each data collection time point. Data will be directly entered using a tablet device into a secured research database (Research Electronic Data Capture- REDCap)

We will similarly collect data from caregiver participants who will be surveyed upon enrollment, and at 3,6, and 9 months follow up post enrollment.

Peer mentor patient and caregiver participants will complete mentor specific assessment pertaining to their experiences as a peer mentor at the end of study. We will also conduct interviews with patient and caregiver peer mentor participants to better understand their experiences in this study and recommendations for improvement and future dissemination.

b. Study duration and number of study visits required of research participants.

Study duration for all participants is 9 months. Peer mentor participants will be invited to extend their participation in this study beyond 9 months, if interested and approved by study social worker to do so.

One visit will be required from patient and caregiver participants at the enrollment time to obtain baseline assessment and meet the respiratory care practitioner, except for hospitalized patients whose hospital length of stay allows for those to be conducted prior to their discharge. This visit will occur at the study site where the participants receive their medical care.

Patient and caregiver participants randomized to the HCP PLUS Peer Support Arm will be invited to also attend 8 Get together events at the study site where they receive their healthcare.

Peer mentors will be asked to also attend the 8 Get together events as well as monthly peer mentor meetings or conference calls with the Peer support program coordinator (clinical social worker.

c. Blinding, including justification for blinding or not blinding the trial, if applicable.

Blinding for intervention arm assignment is not possible for this study's interventions. Outcomes assessors, however, will be blinded to the participants' arm assignment.

d. Justification of why participants will not receive routine care or will have current therapy stopped. **N/A**

e. Justification for inclusion of a placebo or non-treatment group. **N/A**
f. Definition of treatment failure or participant removal criteria. **N/A**
g. Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely. **N/A**

5. Inclusion/Exclusion Criteria

Peer Mentor (PM) Participants

Inclusion criteria:

1) Having moderate- severe COPD or being a family-caregiver for one
2) AGE >/= 40 YEARS if patient PM and >/= 18 YEARS if family-caregiver.
3) Never smoked or have successfully stopped smoking for at least 3 months
4) If patient PM, completed an acute pulmonary rehabilitation program
5) Nominated by pulmonary rehab staff member or pulmonologist
6) Successfully completed Phase 1 of the BREATHE2 study (**IRB application is # IRB00103197)**
7) Consented to participate as peer mentor in Phase 2 of BREATHE2 study (RCT phase)

Exclusion criteria for peer mentors are: Non- English speaking; planning to move from area, unable to attend group meetings at study site.

Patient Participants

Inclusion Criteria:

1) Receiving a physician diagnosis of COPD AND treatment for it (defined as receiving treatment at hospital or clinic for COPD)
2) Age > or = to 40 years

Exclusion criteria for patient participants are: Non- English speaking; cognitive dysfunction impairing ability to provide informed consent and follow instructions; active substance abuse or unstable psychiatric condition; terminal illness (i.e. less than 6 months life expectancy) that is non-COPD related; planning to move from area; living at a facility, such as Hospice or nursing home; unable to provide contact information.

Caregiver participant:

Inclusion Criteria: Invited by an enrolled patient participant to join them as caregiver (person involved in their healthcare); 18 yrs or older
Exclusion Criteria: Non-English speaking; Unable to provide contact information

6. Drugs/ Substances/ Devices

a. The rationale for choosing the drug and dose or for choosing the device to be used. **N/A**
b. Justification and safety information if FDA approved drugs will be administered for non-FDA approved indications or if doses or routes of administration or participant populations are changed. **N/A**
c. Justification and safety information if non-FDA approved drugs without an IND will be administered. **N/A**

7. Study Statistics

a. Primary outcome variable.

Change in Health-related Quality of Life at 6-month follow up compared to baseline, as measured by Total score on the St. George Respiratory Questionnaire.

b. Secondary outcome variables
Please see table below

Outcome	Baseline	3 months post	6 months post	9 months post	**Measure/Instrument description**
Patient Outcomes					
Age, Gender, Marital Status, Race/Ethnicity, Living alone Y/N	✓				
Spirometry : FEV1 % predicted and FEV1/FVC	✓				
Addiction to drugs or alcohol, mental health dx.	✓				CAGE questionnaire; Drug use coded diagnosis at the time of baseline assessment
Education, Income, Occupation	✓				
Health Literacy	✓				One item question on ease of filling of medical forms
mMRC Dyspnea Scale	✓	✓	✓	✓	One item
Medical hx. (Ht, Wt, previous PFTs, oral steroid use, class of inhaler treatments)	✓				Medical record
Number of hospitalizations in prior 1 year to enrollment	✓				Patient/Caregiver self-report
Time since last hospitalization (in mons)	✓				Patient/Caregiver self-report
No. of years since receiving COPD diagnosis	✓				Patient/Caregiver self-report
Smoking Status	✓	✓	✓	✓	Yes/No, pack-years Readiness to quit using 4 stages
Home oxygen use	✓		✓	✓	No oxygen/oxygen continuously/oxygen with activity and/or sleep
Depression treatment	✓				One item on receiving treatment for depression: currently/during past 2 years/never
Health status	✓	✓	✓	✓	Patient self-report
Functional status	✓		✓	✓	Katz Index of Independence in Daily Living
Patient anxiety and depression	✓		✓		PROMIS anxiety (8 questions) and depression (4 questions) measures Response options: Never/rarely/sometimes/often/always
Cognitive status	✓				Minicog

Patient participation in study interventions				✓	HCP and Peer support program participation Participation in other programs
Co-morbidities	✓		✓		Charleson co-morbidity index based on coded diagnosis from medical record at baseline Patient self-report at 6 months on new heart conditions or cancer
Major life events			✓		Loss of caregiver, change in living status, new health conditions or terminal diagnosis, other
Patient Activation	✓	✓	✓	✓	Patient Activation Measure (PAM 13)
Self-efficacy	✓	✓	✓	✓	Understanding COPD Questionnaire- Select questions)
Self- care behaviors: Physical activity, smoking status, etc.	✓	✓	✓	✓	Select questions from Understanding COPD questionnaire, change in smoking status, physical activity
Medication Adherence	✓		✓		Morisky Medication Adherence Scale (4 items)
Patient perceptions of caregiving	✓		✓	✓	Perceptions of caregivers' support and their preparedness to assist with COPD management; caregiving activities received
PROMIS support measures	✓	✓	✓	✓	PROMIS item bank- 4 domains will be used (each domain has 4 items): 1) Social isolation; 2) Informational support; 3) Emotional support; 4) Instrumental support. There are 5 response options: Never/rarely/sometimes/usually/always
Hope	✓	✓	✓	✓	Herth Hope index (12 item instrument) with 3 subscales
Participation in pulmonary rehabilitation	✓	✓	✓	✓	Percentage of patients enrolled in pulmonary rehabilitation; Mean number of sessions attended per week
Post hospitalization ED visits and readmissions (COPD - related and all cause)	✓	✓	✓	✓	Measure: Average number of visits per patient in the 6 months post enrollment (calculated as Combined ED and hospitalizations; ED only; Hosp. only). Based on patient self-report (Y/N ; circumstances/reasons for seeking these services) followed by medical records confirmation
COPD - specific quality of life : Total score; domain scores	✓		✓	✓	St. George's Respiratory Questionnaire (SGRQ)
Mortality		✓	✓	✓	Mortality data collected from caregivers, hospital and ED records, and vital Statistics records
Caregiver Outcomes					
Family – caregiver preparedness for caregiving	✓	✓	✓	✓	Preparedness for Caregiving Scale adapted from Understanding COPD questionnaire
Caregiver stress	✓	✓	✓	✓	Zarit stress index, Ways of Coping Questionnaire
PROMIS measures	✓	✓	✓	✓	PROMIS item bank- 2 domains will be used (each domain has 4 items): 1) Informational support; 2) Emotional support. There are 5 response options: Never, rarely, sometimes, usually, or always.
Patient and Caregiver Satisfaction and Experience			✓		Adapted from CAHPS plus additional intervention specific items

c. Statistical plan including sample size justification and interim data analysis.

We hypothesize that the dual strategy of using ‘HCP PLUS Peer Support’ to engage and support COPD patients and caregivers will have superior outcomes to the ‘HCP only’ strategy in the following areas: a) Improved health- related quality of life and survival, and reduced numbers of COPD-related hospital and ED visits; b) improved patient activation, self-efficacy, and self-care behaviors; c) improved self- efficacy and coping skills. These improvements will be noted at 3, 6, and 9 months compared to baseline.

The main analysis approach for assessing the change in the primary outcome measure from baseline, as well as changes in secondary outcome measures from baseline, will consist of performing analyses of the treatment effect between the two study groups under intention to treat, adjusted for baseline measure, site, and recruitment setting. The health- related quality of life in hypothesis (a) will be measured using the SGRQ. For Hypothesis (b) patient activation will be measured using PAM, self- efficacy and self- care behaviors will be measured using the ‘Understanding COPD questionnaire’, Morisky scale, and additional items on physical activity, smoking cessation, and participation in pulmonary rehabilitation. For hypothesis (c), caregiver self- efficacy will be measured using ‘Preparedness for caregiving’ scale and an adapted ‘Understanding COPD questionnaire’ items for caregivers; and, coping skills will be measured using the ‘Ways of Coping Questionnaire’.

The primary outcome of this study (hypothesis a) will be evaluated with a linear mixed random-effects (RE) model. The primary hypothesis about change in HRQOL from baseline to 6 months, will be evaluated by a hypothesis test of the interaction term between study group and the 6-month time variable. The mixed RE model reflects the study’s interest in comparisons of change at the individual level, where the changes may be subject-specific and reflective of potentially unmeasured variables.

For secondary outcomes, we will fit appropriate generalized mixed RE models based on the type of outcome variable. Differences in change in outcome from baseline between study groups will be assessed by including interaction terms between the time variables and study group. Initially, models will be adjusted only for baseline measure, site, and recruitment setting. We will also consider adjusting for patient characteristics such as age, gender, presence of caregiver, home oxygen use, and prior hospitalization. For a more detailed description of the statistical analysis please refer to the statistical analysis plan in the supplemental study documents section (SAP_BREATHE2_2019Jun26).

Given the nature of the HCP PLUS Peer Support intervention, it is not possible to guarantee full adherence from all of the patients. As a result, traditional ITT statistical methods might be bias due to the effects from non-adherent participants. To correct for this bias, we would implement an instrumental variable approach to estimate the effect of the intervention on the change in the HRQOL. For this analysis we will divide the group of patients assigned to the HCP PLUS Peer Support group into adherent and non-adherent participants.

We will define as adherent participants all those patients who experienced at least 4 or more encounters with their peer mentor either by attending to a get-together, participated in a BREATHE call, or by having a phone conversation with their BREATHEpal. For this analysis, we will instrument patient adherence with the patient’s randomized assignment to either the control or the treatment group. Additional sensitivity analysis will be performed using different definitions of intervention adherence: (1) those participants with at least 2 encounters with their peers (get—togethers, BREATHE calls, or phone conversations) and (2) those participants who experienced at least 4 or more encounters with their peers either by attending to a get-together, participated in a BREATHE call, or by having a phone conversation with their BREATHE pal containing discussion of COPD-related issues (determination based on BREATHE pal notes.) For a more detailed description of our complier-average causal effect analysis and IV approach, please refer to the statistical analysis plan in the supplemental study documents section (SAP_BREATHE2_2019Jun26).

The sample size calculation will be based on an overall comparison of the change between the baseline and 6-month measurements of the patients on the St. George scale (primary outcome) in the two arms (interaction term). The unadjusted per-arm sample size is based on a power of 0.80, alpha of 0.05, a minimally clinical significant difference in change scores of 4 points and a meta-analysis estimate of variability. The estimated sample size is 145 patients per arm, after accounting for a 15% attrition rate, assuming a within-patient correlation between measurements of 0.8.

Heterogeneity of Treatment Effects (HTE) HT-1

The goal of the HTE analyses in this study is to consider the difference in treatment effect between the two arms, taking into consideration differences in the arms that are not obviously accounted for in the balance created by the randomization scheme. Patient characteristics such as disease severity or caregivers' presence may show differences in the intervention's effect and thus are important avenues to explore for hypothesis generation. In this hypothesis generating HTE analysis, we will consider the following subgrouping variables: age (4 categories), gender, disease severity, baseline PAM score, and caregiver presence. Within the HCP PLUS Peer Support group, we will also consider subgrouping by the propensity for adherence to treatment.

HT-2, HT-3

Subgroup treatment effects will be estimated by including a three-way interaction between the subgroup variable, the study assignment variable, and the 6-month time variable in a generalized linear mixed RE model. We will test for a difference in treatment effect between subgroups by a hypothesis test of the overall three-way interaction in this model. We will report estimates of subgroup treatment effects with corresponding 95% confidence intervals (CIs). For a more detailed description of the heterogeneity of treatment effect, please refer to the statistical analysis plan in the supplemental study documents section (SAP_BREATHE2_2019Jun26).

d. Early stopping rules.
   No early stopping rules.

8. Data Management Plan

Blinded team members will perform follow-up data collection by telephone 3, 6, and 9 months after a participant enrollment in the program. Authorized team members will collect the necessary study instruments using the secure web-based application, REDCap. This application is equipped to satisfy HIPAA requirements, and allows mechanisms to maintain the blinding requirements of the study. In addition, REDCap has the ability to export all data in different formats to be analyzed by different statistical software such as Stata, R, and Excel, while also providing with an updated data dictionary and other metadata from all the collected instruments. The team will also rely on internal Access databases for event tracking and logistics.

Once the data is collected, the research team member in charge of data management will monitor the quality and consistency of the data collected. All study data, raw data and analytic files, will be kept for

seven years in a Secure Analytic Framework Environment (SAFE) desktop. SAFE is a virtual desktop that provides JHM investigators with a secure environment to analyze and share sensitive data such as PHI and PII. This virtual environment complies with federal and institutional requirement to protect patient data. With respect to data recovery and preservation, the SAFE environment takes a snapshot of all data stored 3 times a day. Two of these are kept for 2 days, while one is retained for 6 weeks.
Study findings will be reported at trials.gov along with the study protocol and SAP. Study results we would also be shared with the scientific community in presentations and peer-reviewed publications. Results will also be shared with the study partners and recruitment site leaders.

9. Risks

This is a minimal risk study. Patients who participate in either study arm will not have any change made to the medical treatments that they receive. Patients will not have any procedures or receive any medications.
As part of their training the peer mentors in this study will learn the difference between sharing their experiences as peers and providing medical advice. We will also record a select set of meetings and those will be reviewed to ensure that conversations do not constitute medical advice but rather good exchange of information and practical advice from peers about how to address day to day challenges of living with COPD.

a. Medical risks, listing all procedures, their major and minor risks and expected frequency. Medical risks are minimal as the study participants will be in control of the treatment plan. No procedures or medical treatments will be provided to the study participants.

The risks associated with the intervention are negligible and mainly pertain to patient confidentiality. It is possible that the intervention may lead to few patients/ family members demanding more 'face time' from their clinicians to answer questions/address concerns about COPD, and that this demand while an encouraging sign of patient engagement and activation may on few occasions not be welcomed by some clinicians.

It is also possible that a patient may not feel comfortable with the peer mentor leading their group and in that event, we'll make accommodations so that they can get connected with another peer mentor. The peer mentors may get attached to a particular participant who is very sick or dies. In that case the peer mentors are instructed to turn to the clinical social worker leading the program who will provide grief counseling and be there for ongoing support. The monthly meetings that the peer mentors will have will also provide another ongoing source of support.

A Data Safety and Monitoring Board has been established for the study. The Board has 3 researchers and a patient advocate. The researchers have many years of experience in clinical management of COPD, research methodology, and community based research. The patient advocate has COPD and has participated in advocacy efforts led by the COPD Foundation. The board will meet twice a year during the study period. The Board has the responsibility for monitoring study data for evidence of adverse effects attributable to study interventions.

b. Steps taken to minimize the risks.
None of the patient information will be released to their physician, health care organization, or any other party without the patient's permission. Phone contacts to locate the study subject will not suggest the content of the study. All study data will be stored in locked file cabinets at Johns

Hopkins Armstrong Institute for Safety and Quality (not the clinical sites) . Personal identifiers will be removed as soon as possible.

c. Plan for reporting unanticipated problems or study deviations.
Unanticipated problems will be reported to the IRB per IRB specified guidelines and a log will be kept for unanticipated problems and study deviations. Any participant deaths, whether expected or unexpected, will be promptly reported in accordance with JHM policies, except when the death meets one of the exceptions to prompt reporting criterion.

d. Legal risks such as the risks that would be associated with breach of confidentiality.
There are minimal risks for breach of confidentiality that we would address by taking all possible measures to secure study participants personal health information and restrict access to it. All collected data will be kept in a secure database and secured shared drive. No PHI will be saved on personal devices.

e. Financial risks to the participants.

No financial risks.

10. Benefits

a. Description of the probable benefits for the participant and for society.

All patients in this study may experience benefits from having an in person meeting with a healthcare professional to learn about COPD and evidence based recommendations for their condition, double check their inhaler use technique, and receive educational materials and a community resource guide. They may also benefit from having the opportunity during their 9 month study period to call the RCP and ask questions about COPD and discuss any difficulties in managing it.
Study participants randomized to the HCP PLUS Peer Support arm may benefit from meeting other peers and gaining new knowledge about management of COPD.
This study may bring societal benefits if the developed study intervention was demonstrated later to result in improved outcomes for COPD patients and their caregivers.

11. Payment and Remuneration

a. Detail compensation for participants including possible total compensation, proposed bonus, and any proposed reductions or penalties for not completing the protocol.

1) PATIENT PARTICIPANTS: Participants will receive a total of $80 over the 9 months study period for his/her time and participation. The compensation will be given as follows: $20 for the Enrollment visit. The participant will receive $15 each for completing a phone interview at 3 months, and then at 6-month follow-up. S/he will also receive $30 for completing the 9-month final follow-up interview.

2) PEER MENTOR PARTICIPANTS: Peer mentor participants (both patient and caregiver peer mentors) will receive a total of $500 over the 9 months study period in appreciation of his/her service as a BREATHE Pal in this study. The peer mentors will receive $ 50 after each Get-together

and then $100 at the end of study period. Parking will be covered and meals will be provided at the group meetings.

3) CAREGIVER PARTICIPANTS: Caregiver participants will receive a total of $60 over the 9 months study period for his/her time and participation. S/he will receive $15 for the first scheduled study visit during which researchers will go over the study consent form and ask him/her questions about his/her health. S/he will receive $15 each for completing a phone interview at 3 months, and then at 6-month follow-up. S/he will also receive $15 for completing the 9-month final follow-up phone call.

12. Costs

a. Detail costs of study procedure(s) or drug (s) or substance(s) to participants and identify who will pay for them.

There will be no costs associated with study participation.

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Supplemental Document

Statistical Analysis Plan

NCT#02891200

Version Date: June 26, 2019

IRB Approval Date: 7/24/2019

Statistical Analysis Plan (SAP) for BREATHE2 Study

Study Description

The overall goal of this study is to compare the effectiveness of two health communication and dissemination strategies that are designed to engage patients and family caregivers in successfully managing COPD in *real-world* settings. Both strategies aim to (1) advance patient understanding of COPD, its treatment options, and self-care tasks and (2) support them in coping with the disease; and enable them to adopt a variety of positive behaviors, including adherence to treatment plans, smoking cessation, joining pulmonary rehabilitation programs, and assuming an active, healthy lifestyle. One strategy relies on the healthcare professional (HCP) as the primary communicator about COPD self-management (HCP Group), whereas the other uses a dual approach that involves both healthcare professionals and peer mentors delivering such communication (HCP PLUS Peer Support Group).

The study will compare the impact of these strategies on the outcomes of health-related quality of life, mortality, and use of Emergency Department (ED) and other hospital services, as well as intermediate measures such as patient activation, self- efficacy, and self-care behavior, as described in the BREATHE2 Study Conceptual Model shown in Figure 1 below. At the same time, the study will compare the impact of these strategies on caregiver self-efficacy, stress, and coping skills. We will also assess both patient and caregiver experience and satisfaction within the HCP PLUS Peer Support Group.

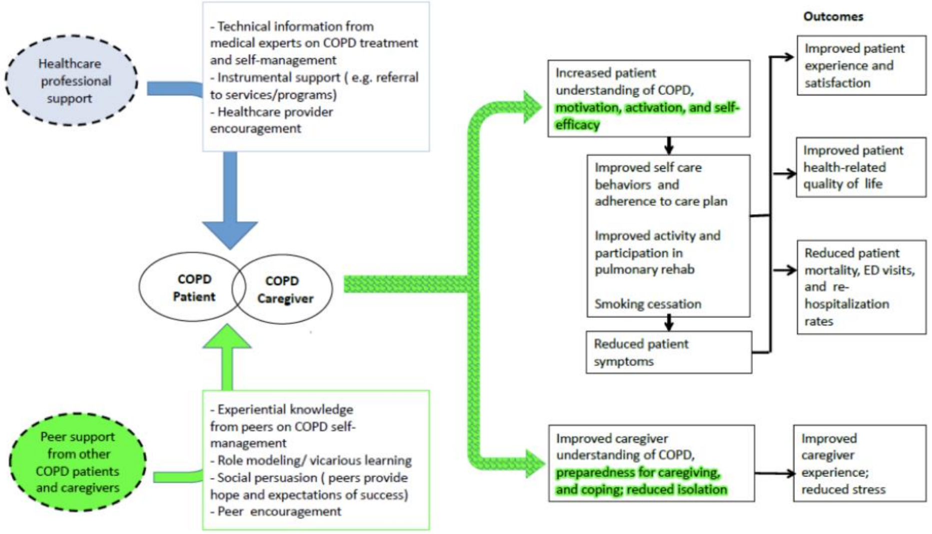

Figure 1. BREATHE2 Study Conceptual Model

Study Design (PCORI Standard IR-1)

Phase 1 of this study involved intervention development followed by peer mentor recruitment and training. Phase 2 of this study, which is addressed by this SAP, involves rigorous testing of the study intervention in a randomized controlled trial (RCT) at two study sites: (1) Johns Hopkins Bayview Medical Center (JHBMC) and affiliated pulmonary and primary care clinics and (2) Howard County General Hospital (HCGH) and affiliated pulmonary and primary care clinics. (some of these clinics are part of Johns Hopkins Community Physicians). Thus within each study site, patients were recruited from two clinical settings: (1) inpatient recruitment within the hospital and (2) outpatient recruitment from the affiliated clinics.

We consented and enrolled 290 persons who met the initial eligibility criteria of receiving a physician diagnosis of COPD and treatment for it. Patient participants were randomized to one of the two study groups in this trial (HCP or HCP PLUS Peer Support) and their respective Caregiver Participant, if they have one enrolled, participated with them in that study group. Then patients were randomized 1:1 to the HCP or the HCP PLUS Peer Support.

Our primary study outcome is the change in quality of life (QOL) over the 6 months post discharge. Other patient measures include patient activation self-efficacy, self-care behavior, health status, used of Emergency Department (ED) and other hospital services, and survival. Caregiver measures include caregiver self-efficacy, stress, and coping skills.

Intervention Description

All study participants will receive a Health Care Professional (HCP) support intervention in this study, which involves a 1 hour session with the respiratory care practitioner (RCP), and the ability to follow up with them with any questions. They would also receive the BREATHE binder with educational materials on COPD self-management and a resource guide.

Those randomized to the HCP PLUS Peer Support group of the study will also have the opportunity to participate in a Peer Support Program. This program will offer patients and their caregiver support services to be delivered via multiple channels including one-on-one and group conversations. In this program, the patient and caregiver participants will have the option to connect with other peers. Each patient and caregiver participant in this study group will be *matched* with a peer mentor (referred to as BREATHE Pal). The BREATHE pal will talk with the participant at regular intervals at peer group *Get together* events and/ or via phone. The group events will take place at the study sites, and will be co-led by two BREATHE Pals in the presence of a social worker. At these events, select topics about COPD self-management will be discussed, and the messages delivered by the respiratory care practitioner will be reinforced. Participants who are unable to attend these in-person events have the option to participate in BREATHE calls, where the same topics are discussed via a conference call.

Study Objectives

We hypothesize that the dual strategy of using *HCP PLUS Peer Support* to engage and support COPD patients and caregivers will have superior outcomes to the *HCP only* strategy at 3-, 6-, and 9-months post enrollment compared to baseline in the following areas:

a) Improved health- related quality of life measured with the St. George's Respiratory Questionnaire.
b) Improved survival and reduced numbers of COPD-related hospital and ED visits.

c) Improved patient activation, self-efficacy, and self-care behaviors

Data Collection for Phase 2

All participants will be interviewed in person, upon enrollment, prior to randomization, by a trained study team member. At the enrollment visit, baseline data will be collected on demographics, bio-psychosocial status, as well as COPD knowledge, self-management skills, patient activation, and health literacy levels. Participants will then be interviewed via phone by a research team member, who is blinded to their study group assignment at 3-, 6-, and 9-months post enrollment. Similarly, we will collect data from caregiver participants who will be surveyed upon enrollment, and at 3-, 6-, and 9-months follow up post enrollment. Due to the study end date, it will not be possible to collect 9-month follow-up data for participants who enrolled later in the study.

Additionally, information will be collected post enrollment on whether the patient has visited the ED or been re-hospitalized via Chesapeake Regional Information System for our Patients (CRISP). CRISP will be used determine whether the visit was COPD-related using a set of pre-determined discharge diagnoses.

Study Outcomes and Hypotheses

The study groups will be compared for the following outcomes:

Primary Outcome for Patient Participants:

1. Change in health-related quality of life (HRQOL) as measured by the St. George Respiratory Questionnaire (SGRQ) total score, from baseline to 6 months post-enrollment.

   Hypothesis: Patients in the HCP PLUS Peer Support group will have a larger improvement in HRQOL (larger negative change in SGRQ score) at 6 months post discharge compared to baseline, than patients in the *HCP only* group.

Secondary Outcomes and Intermediate Measures for Patient Participants:

Secondary Outcomes:

1. Change in HRQOL based on SGRQ total score at 9 months post enrollment.

   Hypothesis: Patients in the HCP PLUS Peer Support group will have larger improvement in HRQOL (larger negative change in SGRQ score) compared to baseline, than patients in the *HCP only* group.

2. Total number of COPD-related hospitalizations and ED visits at 3, 6, and 9 months post-enrollment.

   Hypothesis: Patients receiving the HCP PLUS Peer Support will have a lower rate of COPD-related hospitalizations and ED visits than patients in the *HCP only* group.

3. Total combined number of *all cause* hospitalizations and ED visits at 3, 6, and 9 months post-enrollment.

   Hypothesis: Patients receiving the HCP PLUS Peer Support will have a lower rate of hospitalizations and ED visits than patients in the *HCP only* group.

4. Total combined number of *all cause* hospitalizations and ED visits at 3, 6, and 9 months post-enrollment.

   Hypothesis: Patients receiving the HCP PLUS Peer Support will have a lower total number of *all cause* hospitalizations and ED visits than patients in the *HCP only* group.

5. Change in HRQOL based on SGRQ domain scores at 3, 6, and 9 months post-enrollment.

   Hypothesis: Patients receiving the HCP PLUS Peer Support will have larger improvement in HRQOL (larger negative change in SGRQ score) compared to baseline, than patients in the *HCP only* group.

6. Mortality rate at 3, 6, and 9 months post-enrollment.

   Hypothesis: Patients receiving the HCP PLUS Peer Support will have a lower mortality rate compared to patients in the *HCP only* group.

Intermediate Measures:

7. Change in PROMIS support domain scores (Instrumental, Informational, Depression, Anxiety, Social Isolation, and Emotional Support) at 3, 6, and 9 months post-enrollment.
   Hypothesis: Patients receiving the HCP PLUS Peer Support will have larger positive change in PROMIS scores compared to baseline, than patients in the *HCP only* group.

8. Change in Herth Hope Index total score at 3, 6, and 9 months post-enrollment.
   Hypothesis: Patients receiving the HCP PLUS Peer Support will have larger positive change in Hearth Hope Index scores compared to baseline, than patients in the *HCP only* group.

9. Change in Patient Activation Measure (PAM) scores at 3, 6, and 9 months post-enrollment.
   Hypothesis: Patients receiving the HCP PLUS Peer Support will have larger positive change in PAM scores compared to baseline, than patients in the *HCP only* group.

10. Change in patient's understanding and self-efficacy, as measured by the *Understanding COPD questionnaire's* three components (About COPD, Symptom Management, and Accessing Help and Support) at 3, 6, and 9 months post-enrollment.
    Hypothesis: Patients receiving the HCP PLUS Peer Support will have larger positive change in understanding and self-efficacy levels compared to baseline, than patients in the *HCP only* group.

11. Morisky adherence levels at 6 months post-enrollment.
    Hypothesis: Patients receiving the HCP PLUS Peer Support will have a higher level of adherence compared to patients in the *HCP only* group.

12. Participation in pulmonary rehabilitation at 3, 6, and 9 months post-enrollment. **Hypothesis**: Patients receiving the HCP PLUS Peer Support will have greater level of participation in pulmonary rehabilitation than patients in the *HCP only* group.

13. Change in smoking status at 3, 6, and 9 months post-enrollment.
    Hypothesis: Patients receiving the HCP PLUS Peer Support will have a higher smoking cessation rate than patients in the *HCP only* group.

Handling of Missing Data (PCORI Standards MD-2, MD-4)

There are two types of missing data, at the respondent level (unit non-response) and at the specific question level (item non-response). At the respondent level, missing data occurred because of patient death, withdrawal from study, or inability to be reached via phone for an interview. Comparisons of missingness by several patient characteristics at baseline will be performed with Fisher's exact or Chi-Square tests to examine any potential systematic pattern to the missing data. For the specific case of the SGRQ instrument, values of 100 (the worst possible QoL score) will be imputed for any assessment in which a patient was not available because of death.

With respect to data at the specific question level, missing data will be handled according to each instrument collection manual. In some cases, for example the SGRQ,[1] PAM,[2] and PROMIS-anxiety,[3] -depression,[4] -emotional,[5] and –instrumental support index[6] score will be prepared in instrument specific calculators, provided by the instrument's authors, and accounted for any assignments of missing scores based on the availability of item responses. Missing data for other instruments such as PROMIS-social isolation[7] and –informational support index[8], understanding COPD[9], and Morisky measure,[10] will be handled according to the instrument's author's direction.

When no information is available for handling missing item responses on a particular instrument, a rule, allowing no more than 25% of the items for the scale/domain to be missing, was used. If less than 25% of the item responses were missing, the mean of the non-missing item responses was calculated and was used to replace the value of the missing item responses before calculation of the scale/domain score. This approach weights the scale/domain score towards the respondent's mean response and is balanced by requiring a large majority of item responses to be available. If more than 25% of the item responses were missing, the scale/domain score was considered missing.

Statistical Analysis (PCORI Standard IR-1, RC-4)

Statistical summaries and distributions of patient characteristics will be reviewed by study site (JHBMC and HCGH) and by recruitment setting (inpatient and outpatient). Statistical summaries and distributions of patient and clinical characteristics will also be reviewed across study groups. Randomization of the patients to the study groups expects that on average the groups were balanced on characteristics that might affect the study results, such as socio-demographic and health status. Thus, no statistical tests to compare the groups on patient characteristics will be performed. [11]

Exploratory analyses will be performed cross-sectionally at baseline, 3, 6, and 9 months post-discharge for each of the outcomes across the two study groups. This will provide an assessment of the outcomes' distributions, missingness patterns and the need for additional data review and quality assurance.

The main analysis approach for assessing the change in the primary outcome measure from baseline, as well as changes in secondary outcome measures from baseline, will consist of performing analyses of the treatment effect between the two study groups under intention to treat (ITT) adjusted for baseline measure, site, and recruitment setting.

Repeated outcomes in this study will be evaluated using generalized linear mixed random-effects (RE) models. The generalized linear mixed RE model reflects the study's interest in comparisons of change at the individual level, where the changes may be subject-specific and reflective of potentially unmeasured variables. This model also fits well with the approaches related to missing data and heterogeneity of treatment effects discussed below. In particular, this approach will help us handle the missing 9-month data for participants who enrolled later in the study.

The primary repeated outcome (SGRQ) will be evaluated using a linear mixed RE model. Within this model, the primary hypothesis about change in HRQOL from baseline to 6 months, will be evaluated by a hypothesis test of the interaction term between study group and the 6-month time variable.

For secondary outcomes, we will fit appropriate generalized linear mixed RE models based on the type of outcome variable. Continuous measures, such as for HERTH Hope Index or PROMIS support domain scores, will be assessed using linear mixed RE models. Binary outcomes, such as Morisky adherence to medication, will be assessed using logistic mixed RE models. Outcomes that are cumulative counts, such as number of hospitalizations and ED visits, will be assessed using Poisson or negative binomial mixed RE models, as appropriate. Differences in change in outcome from baseline to 3, 6, and 9-months between the study groups will be assessed by including interaction terms between the time variables and study group. We will assess significance by first testing the overall interaction between time and group. If the overall interaction is significant for an outcome measure, we will then estimate and test individual time differences accounting for multiple testing using a Bonferroni correction. Initially models will be adjusted only for baseline measure, site, and recruitment setting. We will also consider adjusting for patient characteristics such as age, gender, presence of caregiver, home oxygen use, and prior hospitalization.

Unadjusted survival analyses using Kaplan-Meier and log rank tests will be performed for *time to death or first COPD-related hospitalization or ED visit*. Statistical significance will be considered for $p < 0.05$.

Complier-Average Causal Effect (CACE) using Instrumental Variable Estimation

CACE: Primary Outcome

Given the nature of the HCP PLUS Peer Support group, it is not possible to guarantee full adherence from all of the patients. As a result, traditional ITT statistical methods might be bias due to the effects from non-adherent participants. To correct for this bias, we would implement an instrumental variable approach to estimate the effect of the intervention on the change in the HRQOL as measured by the SGRQ total score from baseline to 6-months post-enrollment. [12]
One of the requirements for this analysis is to divide the group of patients assigned to the HCP PLUS Peer Support group into adherent and non-adherent participants. For our main analysis, we define as *adherent participants* all those patients who experienced at least 4 or more encounters with their peer mentor either by attending to a get-together, participated in a BREATHE call, or by having a phone conversation with their peer-pal. Phone conversations with peer-pals include both check-in conversations as well as conversations about the COPD related issues discussed at the get togethers. For this analysis, we will instrument patient adherence with the patient's randomized assignment to either the control or the treatment group. Additionally, we will conduct sensitivity analyses by defining adherent participants to be (1) those participants with at least 2 encounters with their peers (get—togethers, BREATHE calls, or phone conversations) and (2) those participants who experienced at least 4 or more encounters with their peers either by attending to a get-together, participated in a BREATHE call, or by having a phone conversation with their BREATHE pal containing discussion of COPD-related issues (determination based on BREATHE pal notes.)

CACE: Secondary Outcomes

In order to analyze the effect of the Peer Support intervention on secondary outcomes such as the level of acute health care utilization (hospitalizations and ED visits), patient-reported outcomes (PROMIS scores), patient's activation measure, and HERTH hope index we will implement a CACE approach to control for the bias produced by not-fully adherent patients.

Just as with the case of our primary outcome, we will use a patient's randomization assignment as an instrument for HCP PLUS Peer Support group adherence. For this analysis we will define as *adherent participants* all those patients who experienced at least four or more encounters with their peer mentor. We will also conduct sensitivity analyses in the same manner as for the primary outcome.

Intervention Implementation Analysis

In addition to assessing the primary and secondary outcomes for patients we intend to investigate which patient characteristics determine participation in the HCP PLUS Peer Support. That is, we will investigate which patient characteristics are related to attendance at BREATHE get togethers, participation in BREATHE calls, and phone interactions with BREATHE pals. As in the CACE analysis, we will define overall participation in the HCP PLUS Peer Support group as experiencing at least 4 or more encounters with a peer mentor either by attending a get-together, participating in a BREATHE call, or having a phone conversation. We will define participation in group support via attendance at 4 or more BREATHE get togethers or BREATHE calls. We will define participation in individualized 1:1 support by 4 or more encounters with a BREATHE pals over the phone. We will use multivariable logistic regression to predict overall participation, as well as participation in group or 1:1 support , from baseline characteristics such as age, gender, education level, distance from patient's home to meeting location, oxygen use, whether patient lives alone, whether patient reports they have a caregiver, self-reported health status, PAM level, and baseline assessments of hope, support, anxiety and depression from Herth Hope Index and PROMIS measures.

Heterogeneity of Treatment Effect (HTE) (PCORI Standard HT-1, HT-2, and HT-3)

HT-1, HT-3:

The goal of the HTE analyses in this study is to consider the difference in treatment effect between the two groups, taking into consideration differences in the groups that are not obviously accounted for in the balance created by the randomization scheme. Patient characteristics such as disease severity or caregivers' presence may show differences in the intervention's effect and thus are important avenues to explore for hypothesis generation. In these hypothesis generating HTE analyses, we will consider the following subgrouping variables for the primary outcome of change in SGRQ from baseline to 6 months: age (4 categories), gender, disease severity (whether they are on continuous home oxygen), baseline PAM score (collapsed into low vs high levels), and caregiver presence (caregiver vs no caregiver). Within the HCP PLUS Peer Support group, we will also consider subgrouping by the propensity for adherence to treatment (collapsed into low vs high levels), with propensity for adherence to treatment as the estimated probability of adherence to treatment from our intervention implementation analysis described above.

HT-2, HT-3:

Subgroup treatment effects will be estimated by including a three-way interaction between the subgroup variable, the study assignment variable, and the 6-month time variable in a generalized linear mixed RE model. We will test for a difference in treatment effect between subgroups by a hypothesis test of the overall three-way interaction in this model. We will report estimates of subgroup treatment effects with corresponding 95% confidence intervals (CIs). For the comparison of propensity for adherence groups within the HCP PLUS Peer Support group, we will include an interaction between the subgroup variable and the 6-month time variable, test this interaction, and estimate subgroup effects with corresponding 95% CIs.

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