PROTOCOL TITLE:

Optimizing self-management COPD treatment through the American Lung Association Helpline

PRINCIPAL INVESTIGATOR:

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VERSION DATE:

2/20/2023

1.0 Purpose of the Study:

Chronic Obstructive Pulmonary Disease (COPD) is an increasingly prevalent and costly chronic health condition, and is the third major cause of morbidity and mortality in the United States. Self-management treatment programs for COPD are shown to improve health-related quality of life and prevent COPD-related hospitalizations. Despite their clinical benefits, these programs are typically multi-component and time- and resource-intensive. To date, no study has been conducted to isolate the role of individual self-management treatment components in contributing to improved COPD outcomes. The proposed research will establish the feasibility of using the Multiphase Optimization Strategy (MOST) framework to optimize COPD self-management treatment delivered by the American Lung Association (ALA) Helpline. Treatment components to be evaluated include duration of self-management education, ground-based walking training, inhaler training, and caregiver support. The primary outcome is health-related quality of life, with secondary outcomes of COPD symptom burden, self-management behaviors, and hospitalization. Specific aims are:

Aim 1: Design a factorial experiment and develop operational procedures. We will design a factorial experiment with the same number of experimental conditions and length of follow-up as the planned optimization trial. In collaboration with the ALA COPD Helpline, we will develop operational procedures (i.e., recruitment, screening, randomization, and database management) for successful implementation.

Aim 2: Establish feasibility and acceptability by pilot testing the study design. We will deliver treatment to three participants per experimental condition (N=48) with good fidelity, and will remotely assess baseline, mediator, and outcome variables. We will conduct qualitative interviews at end-of-treatment with 15-20 participants. Resulting values will provide estimates of recruitment and retention rates, treatment fidelity, acceptability of treatment components, and outcome measure variability to inform a subsequent, fully-powered optimization trial. The primary outcome is health-related quality of life, with secondary outcomes of COPD symptom burden, self-management behaviors, and hospitalization.

2.0 Background / Literature Review / Rationale for the study:

Chronic Obstructive Pulmonary Disease (COPD) is an increasingly prevalent and costly chronic health condition. COPD is a chronic, progressive disease that is the third major cause of morbidity and mortality in the United States.[1] Whereas mortality from most common causes of death such as cardiovascular disease and cancer has declined over the past 40 years, mortality attributable to COPD has doubled.[2] COPD is responsible for more than 2.7 million deaths and 50 billion dollars of healthcare expenditure in the U.S. every year.[3,4]

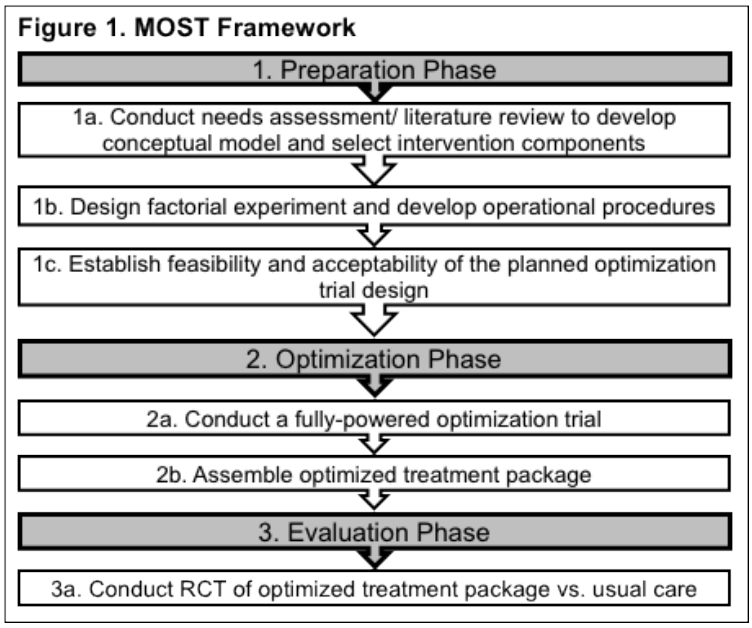
Self-management treatment improves COPD functioning. A recent Delphi process has resulted in the conceptual definition for COPD self-management treatment as structured but personalized and often multi-component, with goals of motivating, engaging, and supporting patients to positively adapt health behaviors and develop skills to better manage their disease.[5] COPD self-management treatment has a dual focus on reducing current symptoms and reducing future exacerbation risk.[6] Programs typically include components focused on COPD education, recognition and treatment of exacerbations, dyspnea management, correct device use, smoking cessation, physical activity, nutrition, social support, and treatment of comorbidities.[7]

Over the past 20 years, numerous randomized clinical trials (RCTs) have shown self-management treatment to have robust effects on improving health-related quality of life in COPD.[6,8-12] Self-management treatment also improves dyspnea,[10,13] decreases emergency department visits,[11,14,15] and prevents up to 40% of COPD-related hospitalizations.[6,8,10,12,14,16,17] Findings on mortality are mixed; two recent high-quality trials have demonstrated decreased mortality risk,[13,18] while a 2017 Cochrane review detected a small, but statistically significant, higher respiratory-related mortality rate in the self-management group as compared to usual care.[6] Authors suggest caution in interpreting this finding, as the overall effect was dominated by two studies,[19,20]

misclassification in cause of death is common, and no effect on all-cause mortality was seen in the overall analysis. Given the overarching evidence of treatment benefit, self-management treatment is proposed in a chronic care model of COPD and recommended in international COPD guidelines.[1,21]

There is a need to optimize COPD self-management treatment. To date, there have been several attempts to characterize the effective elements of COPD self-management treatment; [11,22-24] however, findings have been greatly limited due to program heterogeneity. Jonkman and colleagues (2016) conducted an individual patient data meta-analysis which identified intervention duration as the sole effect modifier.[22] This study design was unable to assess whether negative findings were due to methodological limitations of the meta-analysis, lack of fidelity of intervention delivery, heterogeneous groups of studies being compared, or other sources of variability. Raymond and colleagues (2019) determined that attempts to identify beneficial components were confounded by intervention complexity and heterogeneity, such that the optimal content of COPD self-management treatment cannot be defined from the currently published literature.[23]

Novel experimental approaches could help to address this critical research gap and optimize the effectiveness of multi-component COPD self-management interventions on health-related quality of life. The Multiphase Optimization Strategy (MOST) framework is an innovative, engineering-inspired methodological framework for intervention development (Figure 1) that uses highly efficient randomized experimentation to assess the performance of individual intervention components and their interactions on clinically-relevant outcomes.[25] The MOST framework can be used to systematically identify the most promising intervention components, and interactions of components, that drive the effect of self-management treatment on COPD outcomes. The MOST framework can also identify any treatment component, or combination of components, with unintended harmful effects (i.e., inappropriate management strategies for an exacerbation), [26,27] so that these components can be eliminated from future treatment programs. Thus, MOST is ideally suited to address the significant clinical problem of heterogeneity among self-management programs,[1] and has strong potential to advance the field of self-management treatment for COPD. In the proposed project, we seek to establish the feasibility of using the MOST framework to optimize treatment delivered by the American Lung Association (ALA) Helpline.



3.0 Inclusion and exclusion criteria:

Study eligibility will be determined as follows: Inclusion criteria: Eligible participants will be males and females who are 1) 40 years or older, 2) report a physician diagnosis of COPD, 3) use an inhaler for COPD at least once a week, 4) able to walk at least one block without assistance, 5) able to identify a caregiver, and 6) have access to a connected device (i.e., smart phone, tablet, and/ or computer). Participants will be excluded in the presence of any of the following. Exclusion criteria: 1) cognitive dysfunction impairing ability to provide informed consent and follow study procedures, 2) terminal illness (i.e. less than 6 months life expectancy) that is non-COPD related, 3) living at a chronic care facility (i.e. nursing home, assisted living), or 4) inability to speak and read English.

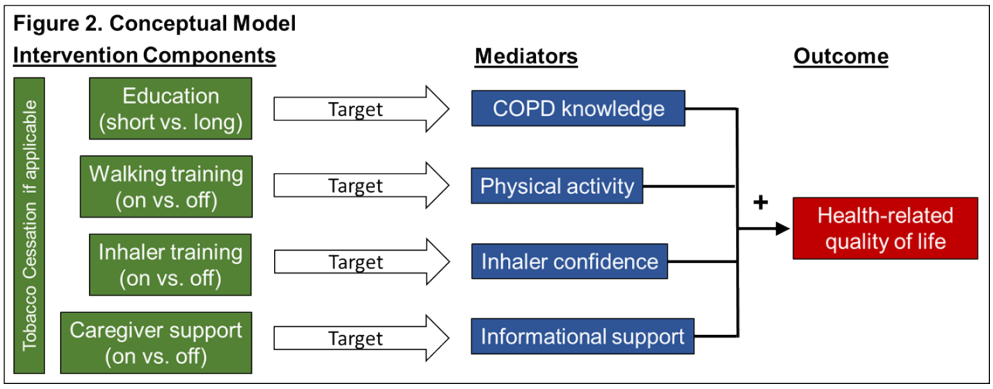
We will not include adults unable to consent, pregnant women, prisoners, or individuals under the age of 18. Socioeconomically disadvantaged persons will be included in this study, but not targeted for recruitment.

4.0 Procedures Involved:

Overall Study Design

In the proposed project, we seek to establish the feasibility of using the Multiphase Optimization Strategy (MOST) framework to optimize treatment delivered by the American Lung Association (ALA) Helpline. MOST is an innovative, engineering-inspired methodological framework for intervention development that uses highly efficient randomized experimentation to assess the performance of individual intervention components and their interactions on clinically-relevant outcomes.

Factorial study design. We will conduct a randomized factorial experiment to examine the effects of four interventions components (Figure 2), in preparation for a full-scale optimization trial. Randomization will be stratified by current smoking status. Each treatment condition corresponds to a factor with two possible levels, resulting in a total 16 experimental conditions (Table 1).



Participants. The randomized factorial experiment will consist of 48 participants. We will partner with the American Lung Association (ALA) Illinois chapter team and recruit participants from the ALA COPD Helpline for this study, following recruitment procedures described below. The PI has collaborated with the ALA-Illinois chapter team since 2015, and the proposed research is a natural extension of this partnership. As the ALA Living Well with COPD programs reaches over 800 callers per year, we believe that accrual targets (4 participants/ month; planned N=48) will be feasible in the grant period.

Procedures. We will conduct a pilot randomized factorial trial in which participants will be randomized to one of two levels for each of the four intervention components. This will result in a total of 16 study conditions, 3 participants per condition (N=48).

Table 1. Study Conditions

Condition	Education	Walking training	Inhaler training	Caregiver support
1	SHORT	ON	ON	ON
2	SHORT	ON	ON	OFF
3	SHORT	ON	OFF	ON
4	SHORT	ON	OFF	OFF
5	SHORT	OFF	ON	ON
6	SHORT	OFF	ON	OFF
7	SHORT	OFF	OFF	ON
8	SHORT	OFF	OFF	OFF
9	LONG	ON	ON	ON
10	LONG	ON	ON	OFF
11	LONG	ON	OFF	ON
12	LONG	ON	OFF	OFF
13	LONG	OFF	ON	ON
14	LONG	OFF	ON	OFF
15	LONG	OFF	OFF	ON
16	LONG	OFF	OFF	OFF

Length of participation. As shown in Figure 4, participants will be enrolled in the study for approximately 4 months (14 weeks).

Pre-Screening and Baseline Assessment. The flow of participants through study procedures is summarized in Figure 3. Following initial recruitment by ALA counselors, potential participants will be contacted by research staff for a full study description and eligibility screening. The pre-screening questionnaire will be administered by phone. Those who remain interested and eligible, will complete informed consent remotely via a secure REDCap link sent by text message or email. Study staff will discuss the consent form while on the phone with the participant following the screening process. If the participant does not have time for this discussion, a second phone call will be arranged.

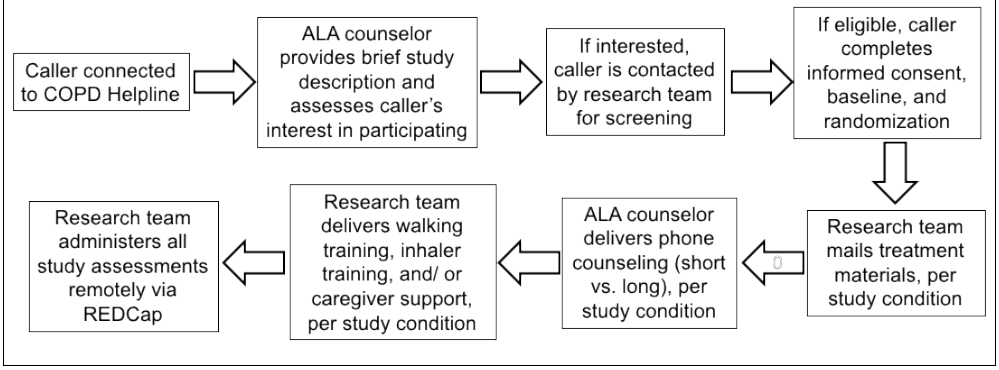
Consenting procedures will follow Rush IRB guidance for the use of electronic informed consent, described below.

Following consent, participants will be sent a baseline survey link by text message or email, or given the option to complete the baseline survey by phone interview format. After baseline survey completion, participants will be randomized to treatment following a randomization scheme programmed in REDCap. Participants will be mailed study materials specific to their treatment condition, consisting of the "Living Well with COPD" booklet and treatment material for up to three other treatment components.

Participants will be assigned to one of 16 possible experimental conditions, consisting of self-management education (either short or long duration) and up to three additional treatment components. The study schedule for each treatment condition is depicted in Figure 4. Self-management education will be delivered by an ALA Helpline counselor who is a certified COPD educator. Inhaler education will be delivered by a trained interventionist (advanced Respiratory Therapy student), overseen by the PI. Ground-based walking training and caregiver support will be delivered by a trained study staff member. All questionnaire assessments will be administered remotely through the REDCap data management system. Study staff will follow up with the participant to ensure all measures are completed, and address any questions or technical issues. Lastly, a subset of 15-20 participants will be invited to participate in a qualitative interview at end-of-treatment.

Baseline Assessment (Week 0). Prior to randomization, participants will complete a questionnaire battery of socio-demographic information, COPD-related measures, potential treatment mediators, and smoking-related measures, if applicable, as described below.

Figure 3. Study Procedures



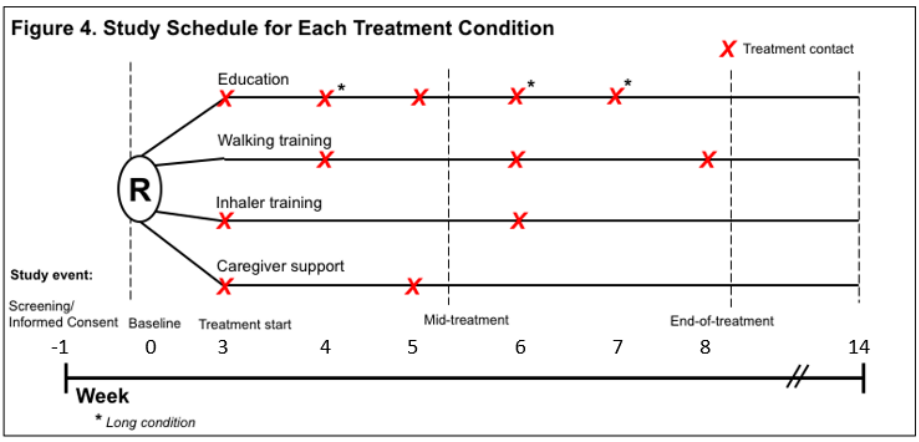
Mid-treatment Assessment (Week 5). Participants will complete a questionnaire battery of potential treatment mediators and adverse events, as described below.

End-of-treatment Assessment (Week 8). Participants will complete a questionnaire battery of COPD-related measures, potential treatment mediators, and smoking-related measures, if applicable, as described below. Participants who were invited to participate in a qualitative interview will complete it at this stage.

90-day follow up (Week 14). Approximately 90 days after treatment start date, participants will complete a final questionnaire battery of COPD-related measures and smoking-related measures, if applicable, as described below.

Intervention components. Our selection of intervention components is based on recent, high-quality meta-analyses[6,10-12,24] and internatio considerations: intervention compo considered for inclusion in an optimized treatment package.[29] Although patient education forms the 'core' of self-management treatment, education alone is insufficient to foster health behavior change.[1] Instead, self-management treatment should be individually tailored and employ structured behavior change techniques.[7]

Figure 4. Study Schedule for Each Treatment Condition



Within multi-component programs, treatment components targeting physical activity are uniquely associated with improved health-related quality of life.[24] Additionally, provision of social support is a critical component of COPD self-management treatment.[30] Receiving positive social support from caregivers is consistently associated with improved health-related quality of life and self-efficacy among individuals with COPD.[31,32] Overall, the four intervention components to be tested in the current study are supported by rigorous scientific evidence, relevant to a range of COPD stages,[28] and can be combined with no conflict or redundancy in an optimized self-management intervention.

Self-management education duration (short vs. long). The self-management education condition is based on the Living Well with COPD program, which has been researched extensively.[9,13,16,33-35] The program consists of a mailed booklet and structured phone counseling delivered by certified COPD educators. Topics include disease information, breathing retraining, action planning, medication use, energy conservation, and following good health habits. The ALA has offered the Living Well with COPD program to over 5700 callers with COPD since 2016.

The duration/ intensity of self-management education programs within the research literature is highly heterogeneous, ranging from a single session[36,37] to 12 or more treatment contacts over up to 24 months.[14,16,38] Although one meta-analysis found longer treatment duration to predict lower hospitalization risk,[22] low-intensity treatments have demonstrated clinically significant effects on health-related quality of life[39,40] and reduced hospitalization.[36,39] Highly intensive treatment programs may also result in substantial treatment burden for individuals with COPD[41] and limited scalability for population health. Thus, identifying optimal parameters of treatment intensity is critical. We will test a 2-session (short) versus 5-session (long) version of the self-management education program, in combination with the mailed booklet. The short condition consists of two calls (30-45 minutes each) to introduce patient education topics and refer to the booklet for further information. The long condition consists of five, weekly calls (30-45 minutes each) following a structured curriculum of patient education topics.

Ground-based walking training (GBWT; on vs. off). GBWT is a well-established, safe, and feasible physical activity program in COPD.[42,43] As walking is the most common form of exercise undertaken in daily life, this modality allows for light to moderate intensity physical activity without the need for specialized equipment or professional supervision. Although long-term results are mixed,[44,45] GBWT is associated with increased daily step count, exercise capacity, and quality of life and at 2- to 3-months.[42,43,46,47] Participants randomized to this condition will be mailed a pedometer (3DFitBud Simple Step Counter) and instructed on its use to establish baseline steps/ day for 7 days. They will then receive a booklet with instructions to establish a walking program and three brief (10-15 minute), bi-weekly calls from a trained staff member to review step count values and engage in setting personal activity goals over the course of 6 weeks,[46] following established exercise guidelines for individuals with COPD.[48] Sessions will be conducted by phone or videoconference via a Zoom meeting hosted on a secure, HIPAA-compliant Rush Zoom account.

Inhaler education (on vs. off). Inhaled medications are commonly prescribed to manage COPD and prevent exacerbations. However, inhaler misuse is common,[49] and errors in use are associated with worse symptoms and increased hospitalizations.[50] Inhaler training with direct observation is shown to improve technique,[51] but often not addressed in routine clinical care, representing a critical unmet need. Participants randomized to this condition will receive two sessions of inhaler technique education using a virtual teach-to-goal (TTG) method,[51,52] in which individuals are observed using their inhaler, provided feedback, and then observed again. Sessions will be conducted by videoconference via a Zoom meeting hosted on a secure, HIPAA-compliant Rush Zoom account.

Caregiver support (on vs. off). Caregivers play a critical role in supporting quality of life among those with COPD, but frequently report unmet needs for support, disease information, and effective management strategies.[58] Participants randomized to this condition will identify an informal caregiver who is involved in their healthcare (i.e., spouse, family member, or friend), who will receive a mailed copy of the Respiratory Health Association's COPD Caregiver's Toolkit, a comprehensive informational resource to support the care of the person living with COPD. Caregivers will receive two brief (10-15 minute) check-in calls from a trained staff member. The structured content of these sessions will include providing an overview of toolkit content,

identifying goals for sections(s) to review and incorporate into caregiving activities, and addressing any questions. Sessions will be conducted by phone or videoconference via a Zoom meeting hosted on a secure, HIPAA-compliant Rush Zoom account.

Treatment fidelity. The ability to deliver each intervention component, and combination of components, to fidelity is a key aspect of study feasibility. Checklists for each treatment condition will be created to describe both the necessary, and proscribed, elements of treatment. Following established procedures,[53] we will use a rigorous database with embedded protocols to guide study activities and specify the order of implementation, such that participants receive all the intervention components to which they are assigned and only the intervention components to which they are assigned. Our study database will also include a scheduling program that tracks when research contacts occur and when visits or calls need to be scheduled based on the participants' condition.

Measures.

Baseline characteristics. Variables assessed at baseline include socio-demographics (i.e., age, gender, race/ ethnicity, employment status, and household income), medical history, and medication use. Health literacy will be assessed with the Calgary Charter on Health Literacy scale.[54] COPD functioning will be assessed with the PROMIS Dyspnea-Activity Motivation scale;[55] comorbid conditions will be assessed with the Charlson Comorbidity Index.[56] For current cigarette smokers, we will assess baseline smoking characteristics with the Smoking History Questionnaire and nicotine dependence with the Heaviness of Smoking Index (HSI)[57] and PROMIS-Nicotine Dependence scale.[58]

Table 2. Measures	**Timepoint Assessed**			
	Baseline	**Mid-treatment**	**End-of-treatment**	**90-day follow-up**
COPD-related measures				
Chronic Respiratory Disease Questionnaire	X		X	X
COPD Assessment Test	X		X	X
Patient Activation Measure-13	X		X	X
Hospitalization history	X		X	X
PROMIS Dyspnea-Activity Motivation	X			
Charlson Comorbidity Index	X			
Medication Use	X			
Calgary Charter on Health Literacy scale	X			
Adverse events	X	X	X	X
Potential treatment mediators				
Bristol COPD Knowledge Questionnaire	X	X	X	
International Physical Activity Questionnaire	X	X	X	
Inhaler Confidence Scale	X	X	X	
PROMIS Informational Support	X	X	X	
Treatment acceptability				
Client Satisfaction Questionnaire			X	
Qualitative Interviews *(subset of 15-20 ppts)*			X	
Smoking-related measures, if applicable				
Smoking History Questionnaire	X			
Heaviness of Smoking Index	X		X	X
PROMIS Nicotine Dependence	X		X	X

Outcomes. The primary outcome of health-related quality of life will be measured by the Chronic Respiratory Disease Questionnaire (CRQ),[59] a 20-item questionnaire yielding a total score and subscale scores for mastery, fatigue, emotional functioning, and dyspnea. The total score ranges from 20-140, with 10 points considered to be a minimal clinically important difference.[60] Secondary outcomes include COPD symptom burden, self-

management behaviors, and hospitalization. COPD symptom burden will be assessed with the COPD Assessment Test (CAT),[61] an 8-item questionnaire measuring the global impact of dyspnea on health status. Self-management behaviors will be assessed with the Patient Activation Measure (PAM-13),[62] a 13-item questionnaire measuring patient knowledge, skill, and confidence for self-management. Self-reported hospitalization history will be assessed by asking participants if they have been hospitalized for their COPD (i.e., respiratory-related hospitalization) or other medical conditions (i.e., all-cause hospitalization) since enrolling in the study. Lastly, we will monitor for adverse events at all assessment timepoints, as described in the Data and Safety Monitoring Plan.

Treatment mediators. COPD knowledge will be assessed with the Bristol COPD Knowledge Questionnaire.[63] Physical activity will be assessed with the International Physical Activity Questionnaire (IPAQ). Inhaler confidence will be assessed with the Inhaler Confidence Scale. Informational support will be assessed with the PROMIS Informational Support scale.[64]

Treatment acceptability. We will assess treatment acceptability with the 8-item Client Satisfaction Questionnaire (CSQ-8), with adequate acceptability indicated by a total score of 24/30 or greater.[65] To complement the CSQ-8, we will conduct qualitative interviews at end-of-treatment with a subset of approximately 15-20 participants, until thematic saturation is reached (i.e., the point at which each subsequent interview provides no new information).[66] Qualitative interview content will focus on perceived benefits of treatment, treatment burden and other negative aspects of treatment, and suggestions for improving COPD self-management treatment. We will use a purposive sampling approach to ensure the sample is balanced by gender, race/ ethnicity, and exposure to each of the four treatment components. Following independent reviews of transcripts by the PI and trained research staff, and identification of *a priori* and in-vivo themes,[67] initial codes will be assigned with content and comparative analysis[68] using QSR NVivo version 11 software.[69]

Analytic Strategy. Three main areas will be examined: 1. Feasibility of recruitment and outcome procedures. Feasibility will be evaluated via enrollment ratios, monthly recruitment rates, retention rates, and data completeness 2. Feasibility and acceptability of the treatment components. Treatment feasibility will be assessed by treatment fidelity ratings. Treatment acceptability will be assessed with the CSQ-8 in the full sample, and qualitative interviews in a subset of participants. 3. Explore the variability and acceptability of trial outcomes and treatment. We will examine the variability of the change in the COPD-related outcomes and treatment mediator measures. We will examine the proportion of hospitalization events over the course of the study, as well as the proportion of participants who endorse clinically meaningful change from baseline to 90-day follow-up on the CRQ and CAT. We will assess all questionnaires for good measurement properties (i.e., good internal consistency and sensitivity to treatment-related change) prior to selection in the planned optimization trial.

5.0 Multiple sites:

N/A

6.0 Incomplete Disclosure or Deception:

N/A

7.0 Recruitment:

Participants will be recruited from the Departments of Internal Medicine, Pulmonary Medicine, and Family Medicine at Rush University Medical Center. We will post study recruitment materials in each clinic, and will ask providers to refer interested and potentially eligible patients to the study team. We will also create an audio hold recording to be played on the Rush on-hold line. Potential participants will be asked to call the

ALA Lung Helpline and ask about the 'Rush COPD Management study;' they may also choose to provide their contact information to receive a phone call from an ALA Lung Helpline counselor.

Study recruitment will be supplemented by partnerships with Rush University organizations such as the Tobacco Oversight Committee and Lung Cancer Screening Program, and community partners who serve individuals with COPD, including the American Lung Association, Respiratory Health Association, and local COPD support groups and Pulmonary Rehabilitation programs. Dr. Mathew will share IRB-approved recruitment materials with community partners through multiple communication channels (i.e., community events, newsletters, e-newsletters, website postings, tweets) to reach potentially eligible individuals with COPD. We will also advertise our study and recruit participants through Researchmatch.org, a nonprofit program funded by the National Institutes of Health (NIH) that allows researchers to connect with people interested in research studies.

All study procedures are conducted remotely, precluding any cost or burden associated with travel to the research center. The ALA Helpline counselors will provide a brief study description and assess the caller's interest in participating at the time of their initial telephone intake. They will share contact information of interested callers through a brief REDCap form. Interested callers will be contacted by the research team for a full study description and eligibility screening. If eligible, callers will complete informed consent remotely via a secure REDCap link sent by text message or email, and will be randomized to treatment.

8.0 Consent Process:

Trained study staff members will obtain electronic consent via REDCap following standardized procedures. Specifically, after completing the phone screener, those who remain interested and eligible for the study will be immediately emailed or texted a link to the appropriate IRB-approved online consent form in REDCap. Study staff will discuss the consent form while on the phone with the participant following the screening process. If the participant does not have time for this discussion, a second phone call will be arranged. Individuals who remain interested will provide an online signature on the REDCap consent form. We will attempt to conduct the signature process in one continuous session with the participant. If this is not possible (e.g., the participant uses a cell phone as their only connected device, and is unable to simultaneously talk on the phone and view the REDCap e-consent), study staff will follow the consent process below to obtain verbal consent. Study staff will then follow up with the participant by email/ text to obtain an electronically signed copy of the consent form as soon as possible after the phone call has ended.

Consenting procedures will follow Rush IRB guidance for the use of electronic informed consent to ensure best practices are followed in remotely obtaining informed consent. Study staff will first verify that: 1) the form the participant received is the currently approved version, 2) all pages of the consent were received, and 3) the participant can read all pages of the consent. Study staff will verify the identity of the participant by asking their date of birth. Study staff will then review all information in the consent form, similarly to how this discussion would be conducted in an in-person format. Participants will be provided with ample time to review the consent and ask any questions they may have. Those who remain interested will provide an online signature on the REDCap consent form. A PDF version of the consents will be saved on the secure network drive and emailed or texted to the participant. Informed consent will be obtained prior to any data collection or study procedures. There is no waiting period between informing the prospective subject of their eligibility and obtaining the consent. Non-English speaking individuals, individuals under the age of 18, cognitively-impaired adults, and adults unable to consent will not be included in the current study.

9.0 Process to Document Consent:

Documentation of the consent process will occur within the REDCap e-consent project (i.e., eConsent form with electronic signature for each study participant, Consent Collection Form, and Consent Process Documentation Form).

10.0 Risks to Participants:

This is a minimal risk study. Study procedures do not involve any medical procedures or medication use; participants will be informed that this is a non-medical study and will not involve any changes to their usual medical care. All study procedures are conducted remotely, precluding any risks associated with in-person study visits. Potential risks include psychological distress and loss of confidentiality. First, participants will be asked to report on their COPD symptoms, health habits such as cigarette smoking and physical activity, and adjustment to disease/ quality of life. As a result, they may experience discomfort or distress from providing self-report of private, potentially embarrassing information. Second, while we will make every effort to protect privacy and keep data confidential, a risk for loss of confidentiality also exists.

Potential study participants will be informed regarding alternative treatments, including the ALA COPD Helpline, which remains available to callers who opt out of the research study. Callers who are ineligible or choose not to participate will be referred back to the ongoing ALA COPD Helpline and Tobacco Quitline services.

11.0 Potential Benefits to Participants:

Participants may not directly benefit from the proposed research, but will contribute to the research literature on improving self-management treatment for individuals with COPD. Study participants may benefit from self-management treatment content focused on understanding COPD, engaging in a healthy lifestyle, and increasing social support. The risk/benefit ratio is seen as highly favorable, as the potential benefits of improved health-related quality of life, COPD symptom burden, and self-management skills greatly outweigh the potential risks.

12.0 Financial Compensation:

Participants will be provided with financial compensation for completing study assessments, with an additional compensation to participants who complete a qualitative interview, as shown in Table 3 below. Participants are only eligible for payment if all study procedures at a given assessment are completed. Payments will be provided in the form of a mailed check, gift card to Amazon or Target, mailed debit card, or reloadable debit card (Greenphire ClinCard). Participants will not be responsible for any costs associated with participating in the research.

Participants will be compensated up to $100 for completing all study procedures, with an additional $20 provided to participants who complete a qualitative interview.

Table 3. Study Compensation	
Study Assessment Timepoint	**Payment**
Baseline Assessment	$20
Mid-Treatment Assessment	$20
End-of-treatment assessment	$20
90-day follow-up assessment	$40
Qualitative interview (optional)	$20
TOTAL	Up to $120

13.0 Provisions to Protect the Privacy Interests of Participants:

The risk of potential loss of confidentiality will be minimized through training and ongoing supervision of study staff as well as storage of all private health information on a secure network drive (detailed in section 14.0 below).

14.0 Confidentiality and Data Management:

Data Acquisition and Maintenance

Data will be collected using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at Rush University. REDCap is a secure, web-based software platform designed to support data capture for research studies. REDCap provides 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

The data manager will be responsible for maintaining the security of the data stored both in REDCap and on the DMC server, and will set permissions on an as needed basis. All data will be stored on the Department of Preventive Medicine's MS SQL server relational database. Rush data network security and availability on DMC servers is supported by Rush Information Services servers. Rush University has two data centers on our Chicago campus at 1700 W. Van Buren St. and 711 S. Paulina St. All servers are located in the locked data centers, with access limited to authorized personnel via a biometrics access system. Data centers each have Sinorix™ 227 and Ecaro-25™ Clean Agent Chemical Fire Suppression Systems, redundant backup diesel generator and uninterruptible power supply (UPS) systems, and redundant chillers for cooling.

The Rush data network is segmented and protected from the internet by a Palo Alto Networks® firewall. Access to the network from the internet requires multi-factor authentication. All network users are required to have a unique login and password. The passwords must be changed every 180 days and must be complex (i.e., must have: a capital letter, small letter, number, special character, and be at least 8 characters in length). Change management policies and procedures are in place to protect the integrity of the systems. A Change Management Review Board meets once each week to review all proposed software and hardware changes. Systems are backed-up nightly and the data is duplicated and sent to an offsite storage facility.

Monitoring of Data Quality

The REDCap database will contain embedded protocols to guide study activities and specify the order of implementation, such that participants receive all the intervention components to which they are assigned and only the intervention components to which they are assigned. Quality assurance checks (i.e., required items, allowable ranges of response values) will be built into each REDCap survey to ensure data accuracy at the time of entry. Erroneous and/or inconsistent values will be flagged and entered into a recurring query report specifically developed for this study. Reports will be generated weekly and distributed to designated study staff for resolution. Once generated, a query will remain part of the weekly report until it is resolved. The PI will receive weekly aggregated reports on study recruitment and follow-up status and study intervention fidelity by treatment component. We will monitor the fidelity to the treatment protocol timeline and percentage of components delivered in each treatment condition. Our study database will also include a scheduling program that tracks when research contacts occur and when visits or calls need to be scheduled based on the participants' condition.

15.0 Data Monitoring Plan to Ensure the Safety of Participants:

Dr. Mathew has developed a data safety and monitoring plan that is commensurate with the risks, size, and complexity of the current study. Potential risks of the self-management treatment are considered minimal.

Monitoring will be provided by the PI, an independent safety officer (ISO), and the Rush University Institutional Review Board (IRB). A detailed data and safety monitoring plan is described below.

Monitoring of Safety Data

Overall framework. The PI is responsible for safety oversight, in coordination with an independent safety officer with relevant expertise in this clinical population (i.e., individuals with COPD). The PI will ensure the study is conducted according to the approved protocol. She will ensure all study staff have completed Collaborative Institutional Training Initiative (CITI) and Good Clinical Practice training, as required by the IRB, and are thoroughly trained on study procedures. The PI will develop standardized procedures for identifying, reviewing, and reporting adverse events (including serious adverse events) and unanticipated problems to the independent safety officer, Rush University IRB, and the appropriate offices at NHLBI, as noted in Table 4.

Adverse events. Adverse events are defined as any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (e.g., abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. During protocol-designated study contacts, which occur at mid-treatment, end-of-treatment, and 90-day follow-up, research staff will ask participants to report all adverse events that have occurred since the previous study contact. However, participants will be advised to report any adverse event to research staff at any time. Adverse events to be assessed include COPD exacerbation, defined as an acute worsening of symptoms of COPD requiring new or increased doses of systemic corticosteroids, antibiotics, and/or emergency treatment or hospitalization. Adverse events will be reported quarterly to the independent safety officer for review, and will also be reported annually for IRB continuing reviews and NIH progress reports.

Serious adverse events. A serious adverse event is defined as follows: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, a congenital anomaly/birth defect, or a medically significant event that may require medical or surgical intervention. Risks of participation will be continually monitored and appropriate measures implemented in cases of unforeseen adverse events. If a serious adverse event occurs, the study PI will notify the independent safety officer and the IRB within 24 hours. The serious adverse event will be reported regardless of whether it appears to be related to study procedures. The PI will consult with the independent safety officer to determine appropriate action, including whether a corrective action plan is needed. The full summary of the SAE and resolution, if applicable, will be reported to the appropriate NHLBI program officials in an expedited manner.

Unanticipated problems. The PI will notify the Rush University IRB and the appropriate NHLBI program officials within five (5) business days of discovering any unanticipated problems involving risks to participants and others.

Table 4. Adverse event reporting time periods.

Event	**Reporting Window**
Adverse Event	≤ 3 months (i.e., in quarterly ISO reports and annual reports to IRB and NHLBI)
Serious Adverse Event	≤ 24 hours
Unanticipated Problem	≤ 5 days

Trial Registration

This project includes an applicable trial which requires registration on ClinicalTrials.gov. The PI will be responsible for compliance of registration and reporting of trial outcomes.

16.0 Data and if applicable, Specimen Banking:

N/A

17.0 Qualifications to Conduct Research and Resources Available:

The primary investigator, Dr. Mathew, is a licensed clinical psychologist with expertise in human laboratory-based and clinical research within the field of smoking cessation. All study staff will be directly supervised by Dr. Mathew and have been trained in human subjects research and current study procedures.

The study interventionist, Amanda Kallinikos, is an advanced standing student in the Rush University Master of Science in Respiratory Care program. She has completed specialized training in COPD self-management and inhaler use, as well as training in human subjects research. She will be directly supervised by Dr. Mathew.

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