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Caregiver-assisted coping skills training for patients with COPD: background, design, and methodological issues for the INSPIRE-II study

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Abstract

Background—Chronic Obstructive Pulmonary Disease (COPD) is a progressive illness characterized by airflow obstruction and dyspnea that afflicts over 12 million people and represents a leading cause of death in the United States. Not surprisingly, COPD is often associated with emotional distress and reduced psychosocial adjustment, which can negatively impact physical functioning and impair quality of life. However, the psychosocial consequences of COPD remain largely untreated. A previous randomized trial from our research team demonstrated that coping skills training (CST) can improve pulmonary-specific quality of life among pulmonary patients awaiting lung transplant (the INSPIRE study). To date, however, no studies have examined the effects of a caregiver-assisted CST intervention in patients with COPD with less severe disease.

Purpose—INSPIRE II is a randomized clinical trial (RCT) funded by the NHLBI to evaluate the effects of telephone-based enhanced CST for patients with COPD and their caregivers compared to standardized medical care (SMC) including COPD education and symptom monitoring on medical outcomes, physical functioning, and quality of life.

Methods—Six hundred COPD patients and their respective caregivers recruited from Duke University and Ohio State University will be evaluated and randomized (in a 1:1 ratio) to enhanced CST (including sessions promoting physical activity, relaxation, cognitive restructuring, communication skills, and problem solving) or to SMC. The primary outcomes include all-cause mortality, COPD-related hospitalizations/ physician visits, and quality of life. These endpoints will be measured through self-report questionnaires, behavioral measures of functional capacity (i.e., accelerometer and six minute walk test) and pulmonary function tests (e.g., FEV_1).

Results—This article reviews prior studies in the area and describes the design of INSPIRE-II. Several key methodological issues are discussed including the delivery of CST over the telephone,

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encouraging physical activity, and inclusion of caregivers as patient coaches to enhance the effectiveness of the intervention.

Limitations—We recognize that SMC does not adequately control for attention, support, and non-specific factors, and that, in theory, non-specific effects of the intervention could account for some, or all, of the observed benefits. However, our fundamental question is whether the telephone intervention produces benefits over-and-above the usual care that patients typically receive. The SMC condition will provide education and additional weekly telephone contact, albeit less than the attention received by the CST group. We recognize that this attention control condition may not provide equivalent patient contact, but it will minimize group differences due to attention. We considered several alternative designs including adding a third usual care only arm as well as an education only control arm. However, these alternatives would require more patients, reduce the power to detect significant effects of our primary medical endpoints, and add a significant additional expense to the cost of the study that would make such an undertaking neither scientifically or financially viable.

Conclusions—We believe that this novel approach to patient care in which caregivers are used to assist in the delivery of coping skills training to patients with COPD has the potential to change the way in which COPD patients are routinely managed in order to reduce distress, enhance quality of life, and potentially improve medical outcomes.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is an obstructive airway disease marked by symptoms of dyspnea, paroxysmal coughing, fatigue, and insomnia [1]. Approximately 12.1 million Americans have been diagnosed with COPD and 70% of these cases represent individuals under the age of 65 [2]. COPD patients who are at an early stage of their disease often experience a progressive worsening of symptoms, while the advanced stages of the disease may be marked by frequent visits to the emergency department or inpatient hospitalizations for acute COPD exacerbations [1]. The expense associated with healthcare utilization for COPD patients in the United States is estimated at $40 billion in annual treatment costs [3]. COPD is a fatal condition for many patients and is the fourth leading cause of preventable death for both men and women in the US, with over 120,000 deaths reported in 2002 [4]. The prognosis of COPD has remained essentially unchanged over the past decade and no new treatments have been approved for the management of COPD during that time [5].

There is no cure for the disease and treatment is primarily focused on symptom management. COPD patients must cope with multiple diseaserelated symptoms and the side-effects of treatment. In addition, COPD patients demonstrate high rates of psychological distress, more than those with other chronic medical conditions [6]. Prevalence rates for depressive symptoms or major depression have been reported to be as high as 80% [7,8], and elevated symptoms of anxiety can exceed 90% [9,10]. Anxiety can be provoked by common symptoms of COPD, such as dyspnea and chronic coughing, and associated public embarrassment. Anxiety worsens COPD symptoms, which in turn lead to heightened anxiety and symptom exacerbation.

Prior studies have demonstrated that psychological distress has a profound impact on quality of life (QoL). General functioning among patients with COPD [9,11,12] may also predict clinical events among COPD patients. For example, patients with anxiety and depressive symptoms experience earlier relapses in their symptoms of lung disease following emergency treatment for COPD exacerbations [13] as well as shorter survival [12-16]. Interestingly, psychological distress, but not pulmonary functioning, has been found to predict exercise capacity for patients with COPD [10] and exercise capacity is the most important predictor of adverse events in COPD patients [14,15].

Despite the deleterious effects of psychological distress on physical and emotional functioning of patients with COPD, these psychological symptoms most commonly remain untreated [7]. Pharmaceutical treatments for anxiety, such as benzodiazepines, can suppress respiratory drive, compromising lung function and worsening hypercarbia in COPD patients [17], while also reducing alertness and social interaction. In addition, patients' concerns and confusion about medications can present additional barriers to effective symptom management [18,19].

Coping skills training in the self-management of COPD

Coping skills training (CST) is based on the notion that cognitive factors such as perceptions, attitudes, beliefs, and expectations can have a significant impact on physical symptoms and disability [18,20,21]. CST utilizes training in relaxation, imagery, calming self-statements, activity pacing, symptom monitoring, and communication to reduce symptoms of anxiety and depression, as well as improve physical functioning [22,23].

The focus of symptom management traditionally has been on the patient [16]; however, studies of caregivers have documented significant stress associated with the caregiver role and the potential benefit of including caregivers in patients' treatments [24,25]. Caregivers of patients with chronic illness face daily challenges associated with caring for the patient and, as a result, often experience disruptions in their own emotional well-being and their physical health [26-28]. Distress among spouses of patients with COPD has been shown to be associated with low levels of physical functioning of patients [29]. However, relatively little is known about the psychosocial functioning of caregivers for patients with COPD. For this reason, the INSPIRE II Study included caregivers in key components of the intervention.

Design and overview

The INSPIRE-II study is a dual-site (Duke and Ohio State University), RCT in which 600 COPD patients and their respective caregivers will be randomly assigned with equal allocation to one of two conditions: (1) Enhanced CST, or (2) standardized care including COPD education and symptom monitoring. The enhanced CST intervention is designed to systematically train patients (and caregivers) in the use of coping skills for symptom management. The present RCT is an extension of our previous trial known as the INSPIRE study (Investigational Study of Psychological Intervention in REcipients of Lung Transplantation), by targeting COPD patients earlier in the disease process, before being considered as candidates for lung transplantation. Moreover, INSPIRE-II intervention is enhanced by involving the caregiver in the CST intervention in which patients are coached by their respective caregivers to master coping skills. Patients and caregivers in the CST condition will receive 14, 30-min telephone sessions focused on training in symptom management strategies over 4 months, while patients and caregivers in the COPD usual care plus education and symptom monitoring control condition will participate in 14 weekly phone calls assessing their health status and providing them with support and COPD education.

Patients and caregivers will be evaluated at baseline, at the conclusion of 4 months of treatment, and at annual follow-up intervals for up to 4 years. Comprehensive assessments before and after treatment will include a battery of psychometric instruments to assess psychosocial functioning and QoL, social support, coping, somatic symptoms, and physical functioning. Behavioral measures of physical activity and communication also will be obtained. In addition, we will track survival and COPD-related physician visits and hospitalizations for a minimum of one year from study entry and document medical expenditures.

Patients

This will be a study of 600 COPD patients and their respective caregivers recruited at Duke and Ohio State University. This sample size is based upon our desire to evaluate the effects of treatment on our two *primary* outcomes: (1) combined death and hospitalizations/COPD-related physician visits and (2) QoL (mental health and physical functioning). Our sample size was chosen to ensure adequate statistical power for the least powerful test, i.e., the time-to-event analysis. We plan to recruit 50% women and 15% ethnic minorities, and anticipate that the average age of participants will be approximately 55 years.

Inclusion criteria—Male or female outpatients ≥21 years of age; a diagnosis of COPD; FEV_1 30-80% of predicted value within 6 months of study enrollment; FEV_1/FVC <70%; capacity to give informed consent and follow study procedures; and having an identified caregiver.

Exclusion criteria—Dementia; psychotic features including delusions or hallucinations; acute suicide or homicide risk; other illness (e.g., cancer) that is likely to cause death within 3 years; unstable angina; congestive heart failure stage III-IV by NYHA classification; or active involvement in pulmonary rehabilitation or a formal exercise program.

Patient recruitment—Ensuring adequate representation of ethnic minorities is challenging as the incidence of emphysema is 20.0 per 1000 in whites but only 9.8 per 1000 in African Americans and 5.8 per 1000 in Hispanics[30]. Our aim is to recruit participants such that at least 15% of our sample will be ethnic minorities.

Patients will be asked to list the people whom they currently rely on for support with activities such as getting to medical appointments and taking medication, as well as for emotional support. The patient-identified primary support person will be designated as the primary caregiver. In most cases this individual will be the patient's spouse or partner; the primary caregivers so identified typically live in the same household and spend at least one hour a week caring for the patient. Written informed consent will be obtained both from caregivers and COPD patients.

Procedures

Assessments will be conducted before and after 16 weeks of treatment and annually for up to 4 years (minimum = 1 year) post-randomization. A measure of event-free survival time also will be obtained. Measures will include assessments of somatic symptoms (fatigue, cough, and dyspnea), depression, anxiety, QoL, coping, communication, self-efficacy for symptom control, quality of the relationship with caregiver, and caregivers' ratings of mood, caregiver strain, caregiver self-efficacy in helping patients manage symptoms of lung disease, quality of relationship with patient, medical outcomes (death and COPD-related physician visits and hospitalizations), and patients' health care utilization.

To our knowledge, this is the first study of CST for COPD patients that includes caregivers and also uses a control condition (Standard medical care plus COPD education and symptom monitoring). Our study is also unique because it will examine the effects of CST not only in patients but also in caregivers. Caregivers who are trained in symptom management strategies may benefit from an increase in self-efficacy about symptom control in addition to improvements in their own mood and level of caregiver strain.

Patients and caregivers will initially complete a pre-treatment evaluation and then will be randomly assigned with equal allocation to one of two conditions: (1) enhanced coping skills training (CST) employing a patient-identified caregiver or (2) standardized medical care

including COPD education and symptom monitoring. Disease severity (defined as requiring the use of supplemental oxygen, which has been prospectively related to mortality in the NETT trial [31]), FEV_1 (30-50% and 51-80% based upon the GOLD criteria), smoking status (non-smoker/quit >4 months ago vs. current smoker/quit<4 months ago), and gender will be used as stratification variables.

Assessments—Patients and their respective caregivers will be assessed at baseline, after 4 months of treatment, and at annual follow-up (Table 1).

Demographic, medical, and pulmonary function information—We will characterize each patient according to pulmonary function, duration of illness, years on disability, level of employment, education, marital status, lifestyle habits such as cigarette smoking history and physical activity, and alcohol use. All patients will have completed a standard pulmonary function test, which measures various properties such as lung volume, ventilation and gas exchange. These procedures are performed in accordance with guidelines established by the American Thoracic Society. Patients are instructed to breathe normally into a spirometer and then to inhale quickly to total lung capacity (TLC) and immediately thereafter perform a rapid and complete forced exhalation to determine the forced vital capacity (FVC). The forced expiratory volume in a specified unit of time is also measured, typically in the first second (FEV_1). The ratio of FEV_1/FVC allows determination of the presence of significant airway obstruction as would occur in COPD or emphysema. The absolute FEV_1 along with other measures of lung volumes, such as the total lung capacity (TLC) are useful in evaluating the severity of obstruction or the presence and severity of any restrictive lung disease such as pulmonary fibrosis. Eligible patients will have FEV_1 values <80% predicted, assessed within 6 months of study enrollment and FEV_1/FVC <70%.

Functional capacity and physical activity—The primary measure of physical function will be a Six Minute Walk Test (6MWT) [32], a self-paced, timed test of the total distance that a patient is able to walk in 6 min. The 6MWT is predictive of morbidity and mortality among patients with COPD [14,15] and is a reliable and sensitive index of change in functional ability following treatment [32]. An exercise physiologist will ensure the test is administered in a reproducible manner, oversee the testing, and monitor the distance completed by the patient during the 6 min allotted for the test. The primary outcome is the total distance walked in 6 min. Additionally, pulse oximetry will be performed to provide a measure of oxygen saturation (SaO_2) during the procedure, adjusting a subject's oxygen to maintain saturations greater than 90%. Although distance achieved at 6 min is the primary measure in the 6MWT, we will also record symptoms and heart rates at rest and at 6 min and record oxygen utilization and desaturations throughout the procedure; for post-treatment testing, we also will obtain symptoms and heart rates at the 6-min distance achieved during baseline testing. In addition, routine daily physical activity will be recorded in 2-min intervals using an accelerometer (Kenz Lifecorder Plus NL-2160; Suzuken Co Ltd., Nagoya, Japan). Data collected with the Lifecorder® activity monitor will be used to evaluate whether the CST intervention results in increased activity patterns during daily life in COPD patients.

Quality of life, psychosocial functioning, and somatic symptoms—Although there is no universal agreement as to how to best measure quality of life, it is generally agreed that a comprehensive QoL assessment should cover a variety of domains including physical functioning, emotional status, social functioning, perceptions of health and well-being, and disease-specific symptoms.

For this study, we propose to borrow from both the generic and the disease-specific measures. Instruments will include the generic Medical Outcomes Survey, Short Form-36 (SF-36) [33], the *Pulmonary-specific Quality of Life Scale* (PQLS), which is a disease-specific quality of life

measure [34] that was used previously in lung transplant patients [35], and *the St. George's Respiratory Questionnaire* [36]. Dyspnea will be assessed by the University of California at San Diego Shortness of Breath Questionnaire [37]. Fatigue will be measured using a modified version of the Brief Fatigue Inventory [38]. Quality of sleep will be measured by the Pittsburgh Quality of Sleep Index[39]. Psychosocial quality of life measures [40-42], including coping [43], social support [44,45], self-efficacy [46], and maladaptive cognitions [47], will also be obtained along with measures of communication between patient and caregiver [48,49].

Measures to be collected from the caregiver at baseline and after 4 months include caregiver's ratings of mood [50], caregiver strain[51-54], caregiver self-efficacy for helping the patient manage symptoms [55], and quality of the relationship with the patient[48,56]. Table 2 provides a listing and brief description of the self-report measures used in INSPIRE-II.

Clinical endpoints—The primary medical endpoint is combined all cause mortality and hospitalizations, emergency department visits, or unscheduled physician office visits because of worsening dyspnea. These criteria have been used in other clinical trials of COPD patients [57,58]. It is estimated that there will be a 30% event rate over our follow-up period in this high risk population of COPD patients, including deaths and COPD-related hospitalizations [14,31,57,59-61].

Interventions

Patients will be randomized to one of two conditions:

Enhanced coping skills training—Patients and caregivers will receive 14, 30-min telephone calls (12 weekly sessions followed by 2 bi-weekly booster sessions) over a 16-week period (A more detailed description of the CST intervention is provided in Appendix A: http://www.duke.edu/web/behavioralmed/inspireappendices.pdf). These sessions will be conducted by a trained clinical health psychologist knowledgeable about lung disease and skilled in CST interventions for both patients and caregivers. All sessions will be audiotaped for purposes of supervision and will be supplemented with written materials, audiotapes, and telephone calls. The primary goals of the CST intervention are: (1) to teach the patients (and caregivers) a variety of coping strategies for increasing physical function and reducing emotional distress, and (2) to teach the caregiver how to help the patient acquire and maintain coping skills over the illness trajectory.

CST can be adapted to address crises and particular problem areas experienced by the patient. For example, if a patient is experiencing panic symptoms, specific intervention strategies for panic can be presented, such as paced breathing, calming self-statements, and identification of panic triggers. In our original INSPIRE study, an informal, qualitative analysis of training session content suggested that a number of patients perceived reductions in distress to be a result of their having had the opportunity to discuss existential and spiritual issues. Involving the caregiver in these discussions can provide an opportunity for the patient and caregiver to address important life issues that they may not be discussing elsewhere.

Standard medical care—Patients and caregivers in the standard care receive their usual medical care plus COPD education and symptom monitoring, including 14 telephone calls providing education about COPD and monitoring their symptoms. Each of these calls will last approximately 15 min and will be conducted by a trained health care educator knowledgeable about COPD and skilled in educational instruction. The health educator will begin each call with a brief medical review of the prior week that will be similar to the review utilized with the CST participants. The medical review will provide an opportunity for patients and

caregivers to discuss the patient's current treatment and symptoms. Caregivers will be encouraged to participate fully in all discussions.

Each of the weekly educational discussions will address a topic relevant for COPD management. Educational topics will include pulmonary physiology, medication usage, maintaining adequate nutritional status, common changes in activities of daily living, and symptom management (e.g., dyspnea, coughing). The educator will follow an outline for each session, and will encourage patients and caregivers to ask questions as they arise. A detailed outline of the educational sessions is provided in Appendix B (http://www.duke.edu/web/behavioralmed/inspireappendices.pdf).

These sessions are designed to provide control participants with useful information about medical aspects of COPD, but will not teach coping strategies or communication skills. Thus, this comparison condition will help to rule out the possibility that gains result merely from contact with the therapist or from the active involvement of the caregiver in the patient's treatment.

Ongoing medical care—All patients will continue to receive their usual medical care. This care includes the provision of educational information about their disease, as well as medical therapy. All patients will be followed by their local pulmonologists who will manage any episodes of escalating or uncontrolled symptoms (i.e., COPD “flares”). Medication use will be documented and controlled in our data analysis, but will not be determined by participation in the trial.

Data management and analysis

Data for each assessment will be collected using machine readable scanning technology, with “bubble fill” format for self-report measures, and customized machine scanning of standardized laboratory-based reports (Cardiff Teleforms v. 10.2, Vista, CA). Additional data used for administrative purposes is stored in a secure Microsoft Access database. The database is located on a secure, encrypted network with access limited to staff with passwords. Data checking is performed at the time of machine-scanning and also at the time of analysis, where consistency and range checks are carried out. Data for analysis will be exported to files amenable for statistical analysis.

Statistical analysis

The primary analytic strategy will be structural equation modeling (SEM) for continuous outcomes, the generalized linear model for count or rate outcomes, and Cox proportional hazards models for time-to-event data. These procedures are available in the most recent versions of MPlus [62], SAS, and R (http://cran.r-project.org), respectively. The predictor variables in each model will be specified a priori, each including a binary treatment group indicator variable, and the baseline measurement of the outcome variable, age, gender, ethnicity, and FEV_1 as the adjustment covariables. In the case of time-to-event models, we also will examine the proportional hazards assumption using the approach outlined in Harrell [63], which examines the correlation between Schoenfeld residuals and the logarithm of time. Patterns of missing data will be characterized using Rubin's criteria (i.e., missing at random, missing completely at random, nonignorable) and managed accordingly using the full information likelihood (FIML) method available in MPlus or multiple imputation procedure in SAS 9.1, depending on the specific context. The predominant contributor to missing data is participant dropout before post-treatment assessment can be completed. Every effort is made to minimize dropout; in cases where it is not possible to prevent a participant from prematurely leaving the study, an attempt will be made to assess the primary outcomes at the time of dropout at the minimum. Another common source of missing data is participant refusal. In order to

reduce missing data from this source, study personnel will review data forms immediately after collection, and follow up with participants regarding missing values. Personnel can clarify whether a data point is missing due to oversight or the participant declining to respond to that item. If due to participant oversight, the participant is asked to complete the missed items. After data collection, sensitivity analyses will be conducted to evaluate the effect of missing data on tests of the primary outcomes, and results interpreted accordingly.

For our primary QoL hypothesis, the effect of treatment on QoL will be examined using SEM as available in the MPlus statistical package. We will adapt the approach recommended by O'Brien [64] for multiple endpoints, constructing separate latent variables to capture the psychological and physical QoL endpoints. We will construct these latent variables for each measurement time point (i.e., pre- and post-treatment). The psychological QoL latent variable will include as indicator variables: BDI, STAI, and the SF-36 mental health subscales, namely, mental health role limitations due to emotional problems, social functioning, and vitality subscales. The indicators for the somatic symptom latent variable will be the SOBQ and PQLS measures, and the SF-36 subscales of physical health, bodily pain, role limitations due to physical problems, and general health perceptions. We will use a binary treatment indicator to predict simultaneously the post-treatment psychological and physical QoL latent variables. The relation between the treatment indicator and the endpoint latent variables will be adjusted for baseline psychological and physical QoL latent variables, site, age, gender, ethnicity, oxygen use, and FEV_1. We will evaluate the treatment effect on a combined endpoint of time to death or first pulmonary-related hospitalization using Cox regression (proportional hazards) models under Harrell's Design library in R. In this model we will evaluate the treatment effect on a combined endpoint of time to death or first pulmonary-related hospitalization, adjusted for site, age at study entry, FEV_1, six minute walk test, oxygen use, gender, and ethnicity. Patients who are alive and who have had no pulmonary-related hospital visits at the time of last follow-up will be treated as censored cases. We also will examine the treatment effect on the number of COPD-related hospitalizations and physician visits. For this outcome, we will use a form of Poisson regression under the generalized linear model in SAS PROC GENMOD.

We will evaluate potential mechanisms by which treatment may have modified outcomes using conventional path modeling techniques [65] in the Mplus software, or the Harrell Design library, depending on the type of analysis. Specifically, we will test whether improved time-to-event status and improvements in quality of life will be mediated by treatment-related changes in functional capacity and improved coping (including enhanced communication with caregivers). These analyses proceed by establishing that (a) the treatment has a meaningful effect on the outcome; (b) the treatment is related to the mediator; (c) the mediator is related to the outcome. After these steps, the analyses proceed according to the type of model appropriate for a given endpoint. For the continuous outcomes the putative mediator is modeled as an intervening variable between the treatment indicator and outcome in the path model, the indirect effect of the treatment via the mediator(s) is evaluated for statistical and practical significance. For the time-to-event models, mediation is evaluated the Sobel test [66], after standardizing the coefficients [67].

Power and sample size—For the two primary QoL outcomes we examined power for a two-sided test using Monte Carlo simulation in MPlus, assuming alpha = 0.025 in order to guard against Type I error, adjustment for covariates, a reliability of about 0.8 on the outcome variables, and a correlation between the mental and physical latent variables of 0.3. Under the above assumptions, we will have a power of 0.95 and be able to detect a treatment group difference of at least 0.3 standard deviations. Among the COPD patients in our previous trial [35], we saw a treatment effect size of 0.4 standard deviations for the SF36 Mental Health subscale, which is associated with power of 0.99 with *N* 600. If we adjust these estimates for a dropout rate of 25% across the entire cohort, using FIML estimation, the power is about 0.90

for an effect size of 0.3 standard deviations. For other continuous variable outcomes, as measured in either patients or caregivers, this sample size also should offer ample power even using a more conservative alpha of .01 in order to protect against Type I Error. The population standard deviation of the BDI, for example, is about 8, based on a large (*N* 1,227) data set of untreated depressed, post-MI patients [68]. A sample size of 600 is associated with a power of 0.98 to detect a 3 point difference on the BDI, and a power of 0.82 to detect an even smaller effect of 2.3 points. Because the sample size for the couples' relationship outcome (QMI) is essentially doubled (both caregivers and patients will be included in this analysis), we clearly will have more than ample power to detect a clinically meaningful difference on this measure and we will be particularly cognizant of the distinction between clinical and statistical significance for this measure.

With respect to the time-to-event analysis under the Cox model, we estimated power using the following assumptions: an alpha of 0.05 using a two-sided test; total accrual time of 2.5 years; median follow-up time of 2.5 years; and an overall event probability of 0.30 in the control group. We estimated that a total sample size of 600 will yield a power of 0.86 to detect at least a 30% reduction in the event probability compared to controls (treatment Hazard Ratio (HR) = 0.66) or 0.80 power to detect at least a 27% reduction in event probability (HR = 0.69). If the event rate is lower, e.g., 25% after 2.5 years, a sample size of 600 will still give us a power of just under 0.80 to detect a reduction of 30% in event probability. For the hospitalization count data, we examined the power to detect treatment effects using a Monte Carlo simulation [69] over a range of dispersion scenarios. These simulations show that with a moderate amount of overdispersion (e.g., dispersion parameter, $k = 9$), assuming a control group mean =0.5, SD = 1, and two-sided test at alpha =0.05, we will have power greater than 0.80 to detect a 25% reduction in the mean number of events.

Challenges

There are several unique challenges associated with implementing a partner-assisted psychological and behavioral intervention in patients with COPD. First, when working with chronically ill patients, participation in coping skills training may be limited by exacerbations in the patient's illness or by resistance on the part of the patient, caregiver, or both, to see the relevance and potential benefits of treatment. Our approach is designed to address this obstacle by providing patients with a model for understanding the relationship between attitudes and behaviors and physical symptoms, and by teaching patients techniques and strategies, such as relaxation and cognitive reappraisal, that enable patients to gain greater control over their health and by teaching caregivers to coach the patient to participate in treatment despite their physical limitations.

Traditional skills training or psychosocial interventions require patients to travel to centers for face-to-face sessions. This requirement presents a significant barrier to patients who live far away and are too ill to travel to receive treatment as is the case for many COPD patients. Therefore, we chose to deliver our intervention by telephone, to overcome this obstacle, a departure from traditional mental health approaches to treatment. Most COPD patients would be unwilling or unable to participate in traditional face-to-face psychotherapy. The strategy we employ with CST tends to “de-stigmatize” the treatment by emphasizing our approach of building on patients' existing coping skills and by including the caregiver in the process. Delivering the treatment via the telephone is also likely to reduce patients' anxieties about treatment. However, a challenge associated with telephone-based interventions is the more limited opportunity to ensure that patients and caregivers are practicing skills effectively. To ensure mastery of skills, patients will practice various exercises during telephone sessions, with their caregiver serving as an in-session coach. The interventionist will provide live feedback to both the caregiver and the patient, to ensure that the skills are being practiced effectively.

The inclusion of caregivers in the coping skills training protocol is an additional innovative feature of INSPIRE II, which poses yet another challenge regarding recruitment and retention of caregivers who will participate in the weekly telephone-based intervention with the patient. Baucom *et al.* [70] have identified three different types of couple-based interventions that can be used when one person is the identified patient. The three approaches form a continuum of increasing attention to the couple's relationship in treating the individual's condition. We will employ a “partner-assisted” intervention wherein the partner acts as a surrogate therapist, coaching the individual to complete homework assignments and providing support. In addition, the interventionist provides both members of the dyad with psychoeducation about the nature of the maladaptive coping strategies (e.g., anxiety-avoidance) and more adaptive approaches to coping, including using physical activity, activity-rest cycling, goal setting, relaxation, and active problem solving. In this approach, little attention is paid to couple functioning that is unrelated to the patient's symptoms (unlike marital counseling, for example). In essence, this caregiver-assisted approach will train the caregiver to serve as a coach to the patient; caregiver participation in behaviors such as physical activity, activity-rest cycling, goal setting, and relaxation will be used to expose caregivers to the skills that patients are learning so as to enhance acquisition and mastery of these skills. We believe that one potential benefit is that caregivers are likely to use learned coping skills to manage and reduce their own distress.

Our decision to include caregivers was influenced by literature regarding the vital role that caregivers of patients with COPD often assume in assisting patients to manage and monitor their symptoms, their medical regimen, and communicating with healthcare providers [71, 72]. Often caregivers perform these types of activities while also confronting significant personal sacrifice, such as loss of income and increased emotional distress [27,71,73,74]. Not surprisingly, studies show that as caregiver burden increases, emotional well-being of the caregiver appears to decline [75,76]. This finding suggests that as the patient requires increasing support from the caregiver, the caregiver may have greater difficulty in meeting the needs of the patient. Patients with COPD often experience limitations in their ability to function in social settings and maintain their social roles, resulting in feelings of isolation [77,78]. The caregiver provides a critical role in providing social contact for the patient during a time when patients may be withdrawing from other social networks [71]. In addition to these subjective benefits, involvement of caregivers has been identified as a primary factor in determining whether patients will remain at home or move to an inpatient facility as a result of their illness [79,80]. Thus, involving caregivers in coping skills training for COPD patients may enhance the effectiveness of this intervention for the patient and also benefit caregivers by reducing their distress, improving their coping, and increasing their feelings of satisfaction in having contributed to the patient's care and well-being.

There are several reasons that involving caregivers in this enhanced CST intervention may be helpful both to COPD patients and their caregivers. First, the caregiver's involvement in CST can lead to a greater understanding of disease and treatment-related symptoms and the role that coping skills can play in reducing symptom distress, physical disability, and psychological disability. Training the caregiver will facilitate communication between the patient and caregiver regarding symptoms and symptom distress, potentially resulting in more efficacious treatment. Second, caregivers can learn how to prompt and positively reinforce patients' efforts to cope with symptoms of COPD. By training caregivers along with patients in multiple cognitive behavioral coping skills (e.g., training in relaxation, imagery, calming self-statements, activity pacing, symptom monitoring, and communication skills), patients are more likely to receive support for applying their coping skills to manage a variety of symptoms that may occur. Third, a caregiver's prompting and reinforcement may be especially useful in helping the patient overcome obstacles to applying coping skills to symptoms such as breathlessness, pain, fatigue, or wheezing and coughing. Fourth, caregivers may facilitate greater adherence to prescribed medical therapies, including recommendations for physical

activity. Fifth, involving caregivers in such training may enhance caregivers' sense of self-efficacy in managing the patient's symptoms and reduce the emotional distress associated with caregiving. By including caregivers in treatment we will employ a “partner-assisted” model in which the caregiver will help “coach” the patient to learn and apply a variety of coping skills.

Because of the prognostic significance of higher levels of functional ability in COPD patients as evidenced by studies using the 6 Minute Walk Test [84], along with data documenting the psychological benefits of exercise [22,81], it was important for us to devise effective strategies to increase patients' physical activity and potentially improve their functional capacity. Our approach encourages patients to increase safe physical activities with encouragement and support from their identified caregivers. Both aerobic exercises (e.g., walking) and toning and strengthening exercises are suggested based upon patients' pulmonary function, 6MWT performance, presence of medical comorbidities as assessed by the Charlson index [82] and self-reported current activity patterns. Simple exercises are illustrated in Appendix C (http://www.duke.edu/web/behavioralmed/inspireappendices.pdf).

Another challenge for this trial will be to provide guidance for home-based activity that is both safe and effective. Adherence will also be an important issue, and we will evaluate exercise adherence by patient self-report as well as by taking advantage of advances in technology that allow us to objectively quantitate activity during routine activities of daily life. Routine daily physical activity will be recorded in 2-min intervals using an accelerometer (Kenz Lifecorder Plus NL-2160; Suzuken Co Ltd., Nagoya, Japan) worn on the hip for 2 consecutive days. The Lifecorder® activity monitor is a small, lightweight device that utilizes a solid-state medical grade sensor and digital filtering to filter out motion and vibration in order to monitor and record the intensity and duration of a person's activity. The Lifecorder® activity monitor is a calibrated accelerometer that has a 60 day memory storage apparatus, housed in a casing that, in size and shape, resembles a pager. The Lifecorder® interfaces with a PC via a USB cord. The Physical Activity Analysis Software® can be used to program the recording unit, download data into storage, and engage a scoring algorithm. Because this monitor is unobtrusive, study participants will wear the monitor for 2 days at baseline, before randomization, and for 2 days immediately following completion of the intervention phase of the study. Average daily step counts, average daily activity minutes, total calorie expenditure and average daily activity level based on the intensity of physical activity are the measures which will be used to measure physical activity levels of the participants. Data collected with the Lifecorder® activity monitor will be used to evaluate whether the CST intervention results in increased activity patterns in COPD patients. In addition, patients will complete the CHAMPS Activities Questionnaire [83], which was designed as a comprehensive self-report measure of exercise activity for use among sedentary older adults.

A final challenge concerns the training, supervision, implementation, and ongoing quality control of the CST (and SMC) intervention, which is further complicated by the dual site study design. Two clinical centers were required in order to recruit the requisite number of patients and also increase the generalizability of our findings. To ensure uniformity of treatment across the sites, CST therapists and Standard Medical Care health educators will undergo extensive training regarding the implementation of each of the standardized sessions of their respective protocols, including frequent group training attended by therapists from both sites (including conference calls). A detailed treatment outline will be used and sessions will be audiotaped and reviewed during regularly scheduled therapist supervision. Treatment adherence and therapist competence will be documented throughout the trial.

Summary

Given the significant symptom burden associated with COPD, and the impact of resulting psychological distress on physical functioning and exercise capacity, there is a great need for treatments that reduce the psychological symptoms of patients. The INSPIRE-II study is designed to reduce distress among COPD patients and to evaluate the impact of reduced distress on quality of life and medical endpoints. Inclusion of caregivers in this treatment is designed to allow for ongoing coaching support for patients, while also reducing caregiver strain, a common problem among caregivers of chronicallyill patients. The INSPIRE-II study promises to provide important information about the impact of improving coping skills and physical activity on survival, COPD-related physician visits and hospitalizations, and quality of life. If the intervention is shown to be effective, this study will provide a new model for manualized treatment for this under-served population of COPD patients and their caregivers.

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Table 1

Assessment schedule for INSPIRE-II

Measure	Baseline	16 weeks	1 year	Annual follow-up
Demographic/Medical Characteristics	X	X	X	X
6 min Walk, Accelerometry	X	X		
Coping and Social Support Measures	X	X	X	
Psychological QOL Questionnaires	X	X	X	X
Physical QOL Questionnaires	X	X	X	X
Communication Assessments	X	X		
Caregiver Assessments	X	X		
Clinical Endpoints		X	X	X
Health Care Utilization Cost		X	X	X

Table 2

Description of measures in INSPIRE-II

	Measure Name and number of items	Description of measure
Measures of Physical Quality of Life	Medical Outcomes Survey, Short Form-36(SF-36; 36 items)	Our primary measure of quality of life in 8 domains, including mental health & physical functioning scales, which will be the primary psychosocial endpoints for the study
	Pulmonary-Specific Quality of Life Scale (PQLS; 25 items)	A disease-specific measure of quality of life
	St. George's Respiratory Questionnaire (SCRQ; 50 items)	A disease-specific measure of the impact of mild to severe airway disease on overall health, daily life, and perceived well-being.
	University of California at San Diego Shortness of Breath Questionnaire (SOBQ; 24-items)	Assesses shortness of breath on a 6 point scale (0 to 5) at various levels of exertion.
	Brief Fatigue Inventory (BFI; 9 items)	Measure levels of current, worst, and usual fatigue and interference due to fatigue
	Pittsburgh Sleep Quality Index (PSQI; 11 items)	Measures sleep quality and disturbances
Measures of Psychosocial Quality of Life	Beck Depression Inventory-II (BDI-II; 21 items)	Measures severity of affective, cognitive, motivational, and physiologic areas of depressive symptomatology
	State-Trait Anxiety Inventory (STAI; 20 items)	Two inventories measuring state & trait anxiety
	Perceived Stress Scale (PSS; 10 items)	Measures the degree to which individuals feel that events in their lives are unpredictable and uncontrollable
	Brief COPE Inventory (COPE; 28 items)	Measures functional and dysfunctional coping styles, including problem-focused coping, and emotion-focused coping
	Perceived Social Support Scale (PSSS; 12 items)	This scale was developed at Duke to measure perceived social support from family, friends, and significant other
	COPD Self-Efficacy Scale (CSES; 34 items)	Assesses patients' confidence in their ability to manage major symptoms of lung disease.
	Dysfunctional Attitude Scale (DAS; 40-items)	Assesses maladaptive cognitions (irrational beliefs & faulty assumptions)
Measures of Communication	Modified Quality of Marriage Index (QMI; 6 items)	Items are reworded to assess the quality of the relationship between the patient and caregiver
	Modified Marital Satisfaction Inventory-Revised Problem Solving Communication Subscale (MSI-R-PSC; 19 items)	Measures how patient and caregiver address differences, problems, and sensitive issues
	Modified Marital Satisfaction Inventory-Revised Affective Communication Subscale (MSI-R-AFC; 13 items)	Measures perceived support, affection, understanding, and disclosure of feelings between patient and caregiver
Caregiver Measures	Profile of Mood States-SF (POMS-SF; 30 items)	Assesses caregiver mood, using positive & negative adjectives
	Caregiver Strain Index (CSI; 13 items)	Assesses a variety of stressors commonly experienced by caregivers
	Self-efficacy Scale-Caregiver-Revised (14 items)	This modified version of a patient measure assesses caregivers' confidence in their ability to help the patient manage COPD symptoms
	Modified Quality of Marriage Index (QMI; 6 items)	Assesses the quality of the caregiver-patient relationship
	Caregiver Subjective and Objective Burden Scale (SCOB; 22 items)	Assesses the subjective burden experienced by examining how caregivers' activities have changed as a result of caring for another person
	Miller Social Intimacy Scale (MSIS; 16 items)	Assesses perceived closeness in a mature relationship

	Measure Name and number of items	Description of measure
	Caregiver Benefit Index (CBI; 15 items)	Examines whether a caregiver experiences benefits such as personal growth from helping the patient, spending time with the patient
	Caregiver Assistance for Instrumental Activities of Daily Living (CA-IADL's; 25 items)	Assesses how much assistance a caregiver provides, via helping with fundamental self-care activities