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The psychological challenges of respiratory disease

Edited by
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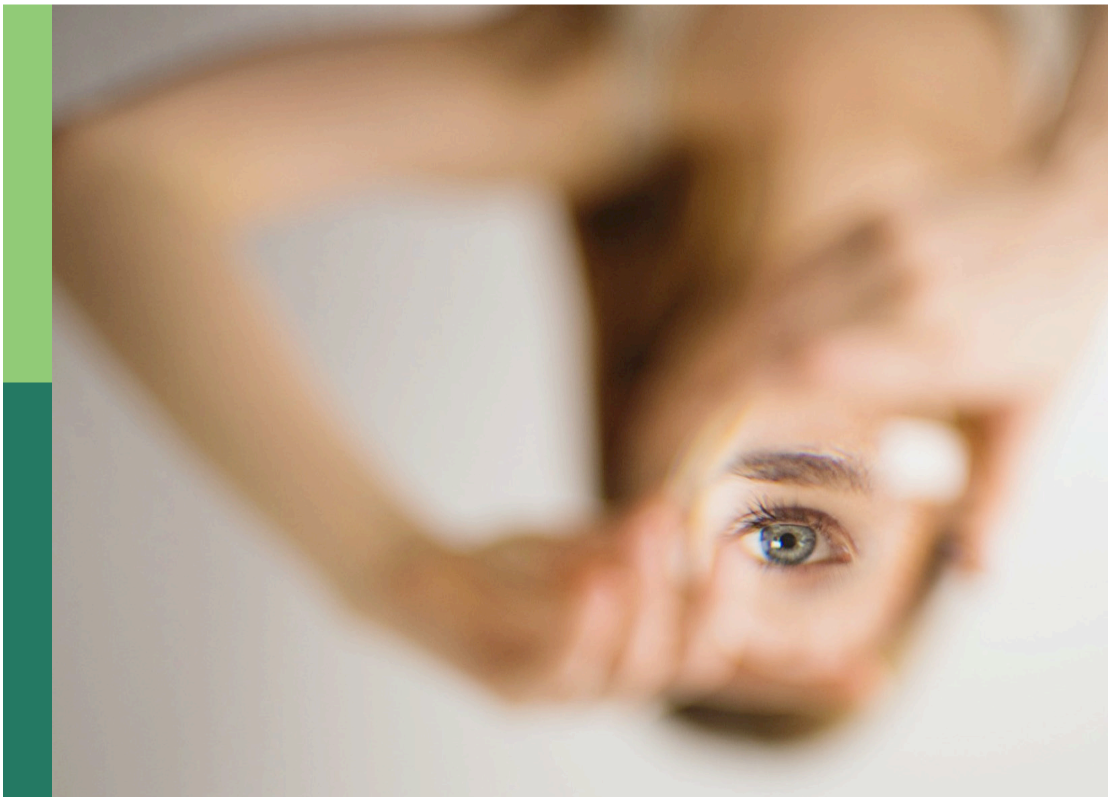

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The psychological challenges of respiratory disease

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Editorial: The psychological challenges of respiratory disease

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Editorial on the Research Topic
The psychological challenges of respiratory disease

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1. Introduction

Over the last few decades, there has been a growing body of literature on the influence that psychological factors can have on chronic respiratory diseases and how these, in turn, might have major implications on the psychological distress and quality of life of those affected. Over time, a strong association between increased symptoms of anxiety and depression and chronic respiratory diseases such as Chronic Obstructive Pulmonary Disease (COPD) (Vieira et al., 2011; Ohayon, 2014; Volpato et al., 2023), asthma (Verkleij et al., 2013, 2017), Primary Ciliary Dyskinesia (PCD) (Verkleij et al., 2021a), or Cystic Fibrosis (CF) (Quittner et al., 2016; Verkleij et al., 2018) has been documented Similarly, a strong relationship has been found between certain respiratory symptoms such as dyspnoea, wheezing or nocturnal problems and the onset of anxiety and depression (Leander et al., 2014). Nevertheless, many patients with chronic respiratory diseases do not meet all the diagnostic criteria for mental illness, but still experience high levels of some of their symptoms (e.g., worry, decreased mood, and loss of interest), difficulties in managing their lifestyle (e.g., disturbed sleep and lack of appetite), and other emotional reactions to their illness (e.g., shame, guilt, loneliness, and lower self-esteem) (Verkleij et al., 2018; Jerpseth et al., 2021; Noij et al., 2023; Volpato et al., 2023). In addition, going along with polypharmacy (Ierodiakonou et al., 2021; Woolford et al., 2021), quitting smoking, using Long-Term Oxygen Therapy (LTOT) and/or Non-Invasive Ventilation (NIV) (Mehrtash et al., 2019; Pierucci et al., 2022) require changes in habits and behavior that may, in turn, contribute to the presence of distress and emotional reactions, with consequent effects on self-perception, adherence and clinical outcomes (Jerpseth et al., 2018; McCormick et al., 2022).

However, it is important to note that, on the one hand, the literature on the psychological implications of respiratory health is often controversial and with little clinical applicability, and on the other hand, there is still too little awareness of these issues on the part of both health professionals and the general population.

The main aim of this Research Topic is to present the most recent advances in research on the psychological factors involved in respiratory diseases, as well as their implications in the health management process.

This opening essay outlines the contributions and ways in which they help us better understand the psychological challenges faced by people with a chronic respiratory disease. Unanswered questions will be highlighted to encourage direction to the focus of new research in the future.

The nine original research articles in this Research Topic address three main themes related to psychological challenges in respiratory disease:

- What are the psychological and cognitive factors involved in the use of medications/devices/medical visits and daily activities?
- What are possible innovative psychological treatments for respiratory diseases?
- Which tools can help identify and prevent mental health symptoms in respiratory diseases?

1.1. Active or not active?

A substantial body of studies now demonstrates that pulmonary rehabilitation is effective in reducing respiratory symptoms by providing both educational and self-management components to improve exercise capacity, clinical outcomes, quality of life, and understanding of the disease, as well as involvement and adherence to proposed treatments (Hayton et al., 2013; McCarthy et al., 2015; Volpato et al., 2021). Among the psychological factors recently studied in the respiratory disease world are motivation and the Patient Activation Measure (PAM), which provides insight into a person's readiness and role in the care process (Greene and Hibbard, 2012). As demonstrated by Peters et al., a topic as relevant as it is affecting respiratory diseases such as COPD or asthma, a prerequisite to be able to raise the impact of self-management interventions. These constructs are even more important when thought about adaptation to proposed therapies and interventions such as, for example, NIV or Continuous Positive Airway Pressure (CPAP) (Rapelli, Pietrabissa, Angeli, Bastoni et al.; Rapelli, Pietrabissa, Angeli, Manzoni et al.). Exactly for greater engagement in their care process, Friedman et al. involved patients with CF in the structuring of their Cognitive Behavioral Therapy (CF-CBT), which allowed them to denote among the most stressful factors disease management, disease uncertainty, and financial issues (Verkleij et al., 2021b).

1.2. When new meets existing

In light of the recent psychological and cognitive factors studied, there is an urgent need to propose multidisciplinary interventions, including innovative approaches such as Acceptance and Commitment Therapy, studied by Giusti et al., or hypnosis (Anlló et al.) as synergistic components with others, especially in the improvement of anxiety and depression's symptoms. Add to this the importance of considering an albeit useful change of setting, as is the case in the study by Gazzi et al., making use of telepsychology and remote interventions, which can also facilitate caregiver participation.

1.3. Toward innovative perspectives and tools

In recent years, moreover, the use of different instruments to detect often non-specific psychological and cognitive factors has become apparent, which is why it is important to converge toward the application of measurement tools that differentiate general symptoms of anxiety or depression from those typically found in various populations with respiratory diseases, as in the study of Farver-Vestergaard et al.. Add to this new challenges such as those posed by the COVID-19 pandemic and the use of safety measures that have changed the way we live, as in the case of the use of humidifier disinfectants (Lee et al.).

2. Conclusions

Although the intake and delineation of psychological interventions for respiratory diseases is a complex task, requiring integration and process, all papers in this Research Topic highlight new methods and strategies that can be employed to identify psychological and cognitive factors, as well as their treatment, paying attention to the specificity of the conditions. This allows clinicians and scientists to progressively develop cutting-edge interventions that are attentive to personalization and not only to classificatory diagnosis but also to the management of experiences that are not necessarily to be considered mental illnesses.

Author contributions

This Research Topic on psychological factors in respiratory diseases was initially proposed and set up and this editorial introduction was led by EV. All the editors worked collaboratively to decide which papers were accepted or rejected, and each manuscript was subject to review by the panel of editors as well as peer reviewers. All the editorial team contributed their thoughts and revisions to help craft the published document.

Acknowledgments

We would like to thank very much those colleagues who have contributed to investigating the role of psychological factors in chronic respiratory diseases by taking part in this Research Topic and those who continue to study in this field.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; CF, Cystic Fibrosis; PCD, Primary Ciliary Dyskinesia; LTOT, Long-Term Oxygen Therapy; NIV, Non-Invasive Ventilation; PAM, Patient Activation Measure; CPAP, Continuous Positive Airway Pressure; CF-CBT, Cystic Fibrosis-Cognitive Behavioral Therapy.

Publisher's note

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ORIGINAL RESEARCH
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The Effects of an Acceptance and Commitment-Informed Interdisciplinary Rehabilitation Program for Chronic Airway Diseases on Health Status and Psychological Symptoms

Emanuele Maria Giusti[1], Barbara Papazian[2], Chiara Manna[3], Valentina Giussani [4], Milena Perotti[4], Francesca Castelli[4], Silvia Battaglia[4], Pietro Galli[4], Agnese Rossi[4], Valentina Re[4], Karine Goulene[4], Gianluca Castelnuovo[1,3] and Marco Stramba-Badiale[4]*

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Background: Chronic airway diseases are prevalent and costly conditions. Interdisciplinary rehabilitation programs that include Acceptance and Commitment-based (ACT) components could be important to tackle the vicious circle linking progression of the disease, inactivity, and psychopathological symptoms.

Methods: A retrospective evaluation of routinely collected data of an interdisciplinary rehabilitation program was performed. The program included group sessions including patient education, breathing exercise, occupational therapy and an ACT-based psychological treatment, and individual sessions of physical therapy. Demographic data, clinical characteristics of the patients and the values of outcome variables (health status, quality of life, anxiety, and depression) before treatment, at discharge, at 3 months, and at 6 months were extracted from medical records. Multiple imputation was employed to address missing data. Linear mixed models were employed to assess changes over time. Multivariable logistic regression was performed to assess predictors of a minimum clinically important change of health status from baseline to the 6-months follow-up.

Results: Data from 31 patients with chronic obstructive pulmonary disease (COPD) and 12 patients with bronchiectasis were extracted. Health status improved from baseline to discharge to the 3 months follow-up, but not to the 6 months follow-up. Anxiety and depression improved across all the time points. Quality of life did not improve over time. Having a worse health status at baseline and fewer depressive symptoms were significantly associated with achieving a minimum clinically important change of health

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status at 6 months. The effects of the interdisciplinary program were not different for patients with COPD or with bronchiectasis.

Discussion: Interdisciplinary programs including ACT-based components are promising treatments for the rehabilitation of patients with chronic airway diseases.

Keywords: chronic obstructive pulmonary disease (COPD), bronchiectasis, rehabilitation, acceptance and commitment based therapy, interdisciplinary program

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) and bronchiectasis are chronic airway diseases, mainly characterized by airflow limitation, frequent lung inflammation, presence of mucus and dyspnea (Celli et al., 2004). COPD is now the third leading cause of mortality worldwide, and the sixth leading cause of disability (Vos et al., 2020). COPD prevalence is estimated to be 13.1% worldwide, while in Europe is 12.4% (Blanco et al., 2019). Bronchiectasis has a lower prevalence, which is estimated to range from 1 in 176 to 1 in 1,492 in European countries (Chalmers et al., 2017). However, mortality at 1-year follow-up after suffering an exacerbation of bronchiectasis is between 20 and 30%, which is higher if COPD is comorbid (Finklea et al., 2010; Goeminne et al., 2014).

These conditions have a multifactorial genesis which includes genetic, environmental (e.g., exposure to pollution) and behavioral factors, in particular cigarette smoking. Although they mainly affect respiratory traits, they also cause considerable consequences on other health domains, reducing patients' quality of life (Athanazio, 2012). Furthermore, patients who suffer from these diseases are forced to frequent hospitalizations, causing direct costs to the healthcare systems.

People suffering from airways diseases also experience psychological symptoms, such as anxiety and depression. Previous researches showed a high prevalence of psychological distress in COPD patients (Kunik et al., 2005): authors reported that 40% of COPD patients suffer from anxiety (Willgoss and Yohannes, 2013) and that female patients seem to experience greater anxiety and depression than men (Di Marco et al., 2006). Psychological distress is consequently associated with a disproportionate increase in health care utilization rates and costs: previous studies showed that COPD patients suffering from anxiety are more likely to be hospitalized and have an increased mortality risk rate (Dalal et al., 2011; Panagioti et al., 2014).

It is also known that physiological and psychological factors interact with each other, making patients' prognosis worse (Barnes et al., 2015). These factors also interact with sociodemographic characteristics, so it becomes essential to assess their potential predictive value on the treatment's response (De Rooij et al., 2013).

Because of their multifactorial genesis, these illnesses require a multidisciplinary approach for treatment. For this purpose, guidelines recommend an integrated approach that includes exercise training, self-management education, psychosocial interventions, breathing exercise, and occupational therapy (Gloeckl et al., 2013; GOLD, 2020; Wingårdh et al., 2020). These interventions are developed to reduce symptoms, optimize functional status, increase participation, and reduce health care costs through stabilizing or reversing systemic manifestations of the disease. These interventions have shown to significantly reduce the number of hospitalization and in improving patients' prognosis, exercise capacity, and quality of life (Kruis et al., 2013; Poot et al., 2021). Nonetheless, these changes are often below the threshold for identifying a minimum clinically important difference, and, following a thorough review of the existing evidence, scholars have called for an improvement of these programs (Poot et al., 2021). This could be achieved if these programs are developed from an interdisciplinary rather than a multidisciplinary perspective, i.e., the different treatments are not simply juxtaposed with each other but are guided by a common framework (Giusti et al., 2017; Liang et al., 2019).

Moreover, to address the psychological issues associated with COPD and bronchiectasis, it could be useful to include an Acceptance and Commitment Therapy (ACT)-based program as a component of the interdisciplinary program. ACT-based programs are psychological interventions focused on modifying patients' psychological flexibility, i.e., the ability to contact the present moment more fully and to change or persist in behavior when doing so serves valued ends (Hayes et al., 2006). Psychological flexibility can be evaluated assessing the six interrelated processes, or dimensions, that constitute it, namely acceptance, self as a context, cognitive defusion, contact with the present moment, values and committed action. Previous studies showed that ACT-based treatments are effective in improving both rehabilitation outcomes and patients' quality of life scores (Graham et al., 2016).

Therefore, the primary purpose of this research was to propose and evaluate the presence of changes in clinical and psychological variables following the participation to an interdisciplinary treatment which includes an ACT-based group component for patients with COPD and bronchiectasis. A second purpose was to identify the sociodemographic, psychological, and physiological predictors of the treatment's response.

MATERIALS AND METHODS

We performed a non-controlled study based on the analysis of routinely-collected archival data. We extracted routinely collected data from medical records of patients with COPD or bronchiectasis who were enrolled in an interdisciplinary rehabilitation program at the Rehabilitation Medicine Unit of the IRCCS Istituto Auxologico Italiano. Data were extracted from records of patients meeting the following inclusion criteria: (1) being enrolled in the interdisciplinary rehabilitation program, (2) having a medical diagnosis of COPD or bronchiectasis. We did not consider the records of patients who discontinued the program before the third session. We extracted data from medical visits, physiotherapists' and psychologists' records, which include information about the pre-rehabilitation demographic and clinical characteristics of the patients and the rehabilitation outcome variables. Outcome variables are collected before the start of the rehabilitation program, at the end of the program, at 3 months from the start of the rehabilitation program via phone calls, and at 6 months from the start of the rehabilitation program during routine follow-up visits. Since this study was a retrospective chart review of medical data and all patient identifiers were removed from the data before analysis, the ethical review and approval was not required. All the patients had signed a consent form regarding the use of their clinical data.

Characteristics of the Interdisciplinary Rehabilitation Program

The interdisciplinary rehabilitation program administered at the IRCCS Istituto Auxologico Italiano was a twelve-sessions intensive program lasting 4 weeks. Physiotherapy sessions were individual, whereas the other components are administered in groups of 4–6 patients. Its components were:

- Exercise sessions. Patients underwent 12 exercise sessions of 1 h each. During the first session, patients underwent an initial functional assessment, which was performed by the referring physiotherapist by administering the COPD Assessment Test (CAT), the Borg scale, the 6-Minutes Walking Test (6MWT), and the modified Medical Research Council questionnaire (mMRC). The results of this assessment were used to adapt the content and intensity of the exercise program to the characteristics of each patient. The exercise sessions combined endurance training, resistance training and airway clearance training. Endurance training included treadmill walking, free walking, stationary cycling, stair climbing, and arm ergometer training. Exercises were performed using variable resistance and their intensity ranged from moderate (5 or 6/10 on a CR10 Borg scale) to vigorous (7 or 8/10 on a CR10 Borg scale). Resistance training was generally performed at low intensity and included weight training, leg press, and elastic band training. Airway clearance training was performed using devices such as Slow Expiration With Glottis Opened in Lateral Posture, positive expiratory pressure, temporary positive expiratory pressure, and expiratory flow accelerator. The choice of the airway clearance device was based on the patient's clinical conditions, learning ability, and treatment compliance.
- Educational sessions. The first educational sessions is administered at the beginning of the program by a pulmonologist. Topics covered are clinical characteristics of airway diseases, their diagnosis, prognosis and treatment. A second educational session is administered by a physiatrist and covers the rationale and benefits of exercise treatment, modalities to perform exercises at home. Both sessions are co-led by a psychologist to explain psychosocial aspects related to chronic airway diseases, facilitate group discussions about the topics covered by the sessions and address potential barriers to behavior change.
- Breathing exercise. Six group sessions of breathing exercises, derived from yoga practices, are administered by licensed speech therapists. These sessions are administered to improve breath awareness and empower the patient in modifying the tendency to exert efforts to breathe, ultimately enhancing ventilatory mechanics.
- Occupational therapy. The occupational therapy component of the interdisciplinary program is administered in four sessions. These sessions are focused on teaching strategies to improve patients' autonomy in performing basic and instrumental activities of daily life. The objectives of the treatments are tailored based on an initial evaluation of the functional limitations associated with the disease, which are assessed using the St. George Respiratory Questionnaire (see "Measurement Instrument" section). The occupational therapy program includes both educational and practical sessions aimed at providing guidance about the proper technique for the use of inhalers and adaptive equipment (e.g., sock sliders, long shoehorns) and at developing strategies to reduce shortness of breath (e.g., positioning of pillows, making pauses during basic, and instrumental activities of daily life).
- Acceptance and Commitment Therapy-based group sessions: according to the ACT principles, psychological inflexibility, in the form of the unwillingness to experience unpleasant emotions, thoughts, and bodily experiences (e.g., dyspnea), could be a core process leading to difficulties in adapting to chronic airway diseases, since it might impair motivation regarding persisting in exercise, maintain a healthy diet, and/or quit smoking. This might lead to a vicious circle linking the worsening of the disease, inactivity, and depression. The ACT-based treatment had the aim to reduce this variable. The first session was devoted to teaching defusion techniques (i.e., distancing from negative or catastrophic thoughts). The second session was devoted to discussing techniques to contact the present moment. The third session involves the exploration and identification of values. The final session is devoted to the topic of valued action and to discuss doubts and barriers to change. All the sessions were conducted using experiential exercises, metaphors and mindfulness meditation.

Patients were also provided further medical counseling at request. The organization of the program is represented in **Figure 1**.

Measurement Instruments

The following information was collected from the medical records:

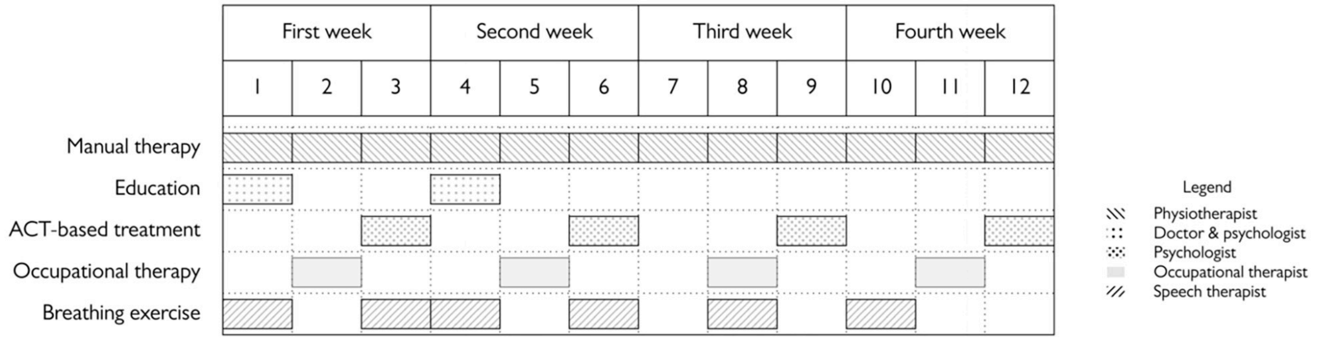

FIGURE 1 | Components of the interdisciplinary program.

- Demographic (sex, age, occupation, education, and civil status) and clinical (smoke status, Body Mass Index, systolic and diastolic blood pressure, resting heart rate, GOLD classification for COPD patients, and presence of comorbidities) data.
- Spirometry results. We extracted Forced Vital Capacity (FVC), FVC in percentage predicted (FVC%), Forced Expiratory Volume in one second (FEV1), FEV1 in percentage predicted (FEV1%), the FEV/FVC% and the percentage predicted ratio FEV/FVC data (FEV/FVC% pred). Predicted values were calculated using GLI equations (Quanjer et al., 2012).
- Six-Minutes Walking Test (6MWT) data (Enright, 2003). The 6MWT is a measure of exercise tolerance for COPD patients. Patients are asked to walk as far as possible in 6 mins, with the possibility to stop or slow down when necessary. During the test physiological factors, such as oxygen saturation, blood pressure and heart frequency rate, are also recorded. The 6MWT was expressed in meters and as a percentage of the predicted normal value for age and gender, according to Enright equation *(*Enright and Sherrill, 1998*)*.
- COPD Assessment Test (CAT) data. The CAT is a self-report instrument that assesses chronic airway diseases symptoms and their impact on the patient's daily life. It is composed of eight items where patients are asked to answer on a 5-point scale. Answers are focused on symptoms such as cough, mucus, daily-life limitations, quality of sleep and energy. Scores range from 0 to 40, corresponding, respectively to the best and the worst health status. Originally developed to assess COPD symptoms, the CAT has been shown to reliably and validly measure the impact of bronchiectasis and other chronic airway diseases (Agnelo Silva de Castro et al., 2015). The Italian version of the CAT has received extensive validation which confirmed its consistency and sensitivity (Dal Negro et al., 2014). The Cronbach's α of the CAT in our sample was 0.81.
- St. George Respiratory Questionnaire (Jones et al., 1991). The SGRQ is a self-report questionnaire investigating three respiratory-specific domains, namely symptoms (i.e., frequency and severity of respiratory symptoms such as breathlessness, coughing, and wheezing), activity (i.e., activities that cause or are limited by breathlessness) and impacts (social and psychological disturbances due to the disease). A total score can also be calculated. Total and subscale scores range from 0 to 100, with higher scores demonstrating greater impairment. The SGRQ was validated for the use with Italian patients (Carone et al., 1999).
- Modified Medical Research Council Dyspnea Scale (mMRC) (Bestall et al., 1999). The mMRC is a self-report dyspnea scale consisting of five items measuring the degree of breathlessness upon daily activities. The mMRC is scored on a range of 0 (no dyspnea or only with strenuous exertion) to 4 (dyspnea at rest).
- European Quality of life Instrument (EQ-5D) data (The EuroQol Group, 1990). The EQ-5D is a brief self-report instrument that assesses the health-related quality of life (HRQOL). It is composed of five questions, assessing five different quality of life domains: mobility, self-care, daily activities, pain, and anxiety/depression. The Italian version of the EQ-5D showed acceptable internal consistency and construct validity (Savoia et al., 2006). The EQ-5D scores were corrected using Italian norms (Scalone et al., 2013). The Cronbach's α of the EQ-5D in our sample was 0.90.
- European Quality of life Instrument Visual Analog Scale (EQ-5D – VAS). The EQ-5D – VAS is a visual analogue scale spanning from 0 to 100, where patients have to indicate their actual perceived health status (The EuroQol Group, 1990).
- Patient Health Questionnaire (PHQ-9) data (Kroenke et al., 2001; Mazzotti et al., 2003). The PHQ-9 is a self-report instrument that assesses depressive symptoms. It is composed of nine items, based on the DSM-5 criteria to diagnose major depression. Answers were asked on a Likert scale ranging from 0 to 3, where 0 indicates "not at all" and 3 "nearly every day". The PHQ-9 scores range from 0 to 27, with higher levels indicating higher depression severity. The scores of the Italian version of the PHQ-9 were found to be unidimensional and to have an adequate internal consistency (Shevlin et al., 2021). The Cronbach's α of the PHQ-9 in our sample was 0.75.

- Generalized Anxiety Questionnaire (GAD-7) data (Spitzer et al., 2006). The GAD-7 is a self-report instrument that assesses anxiety symptoms. It is composed of seven items based on the DSM- IV criteria for the diagnosis of Generalized Anxiety Disorder. Answers range on three points Likert scale, where 0 indicates "not all sure" and 3 indicates "nearly every day". GAD-7 scores range from 0 to 21, with higher values indicating higher anxiety levels. The Italian version of the GAD-7 showed adequate internal consistency and was found to be unidimensional (Shevlin et al., 2021). The Cronbach's α of the GAD-7 in our sample was 0.82.
- Acceptance and Action Questionnaire (AAQ-II) data (Bond et al., 2011; Pennato et al., 2013). The AAQ-II is a self-report instrument aimed to assess psychological inflexibility. It is composed of seven items where patients are asked to answer on a 7-point Likert scale (from 1 = never true to 7 = always true). Higher scores indicate higher psychological inflexibility. The Italian version of the AAQ-II showed adequate internal consistency and good structural and construct validity (Pennato et al., 2013). The Cronbach's α of the AAQ-II in our sample was 0.79.

Statistical Analysis

Categorical variables are described using counts and percentages, continuous variables are described as medians and interquartile ranges (IQR). The internal consistency of the self-reported questionnaires was assessed by calculating their Cronbach's α coefficient.

As a first step of our analysis, we inspected missing data mechanisms. Little's MCAR test was performed to assess if missing data were Missing Completely At Random. Then, the associations between missing data and sex, categorical variables (education, work, and clinical diagnosis) and continuous variables were assessed using *t*-tests, ANOVAs and correlations, as appropriate. The presence of Missing At Random mechanisms were identified when *t*-tests and ANOVAs were significant or when correlations were >0.30. Since data were judged to follow a MAR mechanism, we decided to perform a multiple imputation procedure (20 datasets, 100 iterations). This approach was chosen since, contrarily to listwise deletion, it reduces bias in parameter estimates and standard errors while maintaining the original relationships among variables (van Ginkel et al., 2020). Quality of imputed data was ascertained comparing distributions of imputed datasets with the one with complete data. Multiple imputed datasets were then employed to perform the subsequent analyses.

Secondly, we checked for differences in demographic, clinical and psychological variables between patients with COPD and patients with bronchiectasis. These differences were assessed using Fisher's exact tests, chi-square tests or Mann-Whitney tests, as appropriate.

Thirdly, we investigated the presence of changes over time in the outcome variables. Changes in psychological flexibility scores, SGRQ scores and in 6MWT results were assessed performing a separate Wilcoxon signed-rank test for each variable. Changes in general and specific quality of life, anxiety and depression were assessed using a separate linear mixed model for each variable using time (discharge vs baseline, 3 months vs baseline, and 6 months vs baseline) and diagnosis (COPD vs bronchiectasis) as fixed effects. All the models were estimated using a Restricted Maximum Likelihood estimator.

Finally, we investigated the predictors of a minimum clinically important difference at 6 months. This analysis was performed in two steps. Firstly, we performed separate bivariate logistic regressions testing the association of demographic (sex, age, and education), clinical (smoke status, BMI, presence of an exacerbation of the condition in the month before the start of the treatment, history of tumor, diabetes, history of cardiovascular diseases, and other lung diseases), spirometry (FVC and FEV1 values at the baseline), 6MWT (walked distance in meters at baseline), health status-related (baseline scores on the EQ-5D) and psychological (anxiety, depression and psychological flexibility at baseline, change in psychological flexibility from baseline to discharge) data with presence of a minimum clinically important difference at 6 months. Then, variables which were significant in bivariate analyses were included in a final multivariable logistic regression model.

The significance threshold was set at 0.05. Missing data analysis was performed using the R (version 3.6.0) package *mice* (van Buuren and Groothuis-Oudshoorn, 2011), Cronbach's α was calculated using the R package *psych* (Revelle, 2019), linear mixed models were analyzed using the R package *lme4* (Bates et al., 2015).

RESULTS

We extracted data from 43 patients who participated in the interdisciplinary program. Descriptive statistics and missing data percentages are reported in **Table 1**. Patients with bronchiectasis were more likely to be women, to have osteoporosis, to have higher FEV1%, FEV1/FVC, and FEV1/FVC% at the spirometry performed at baseline, a higher SPO2% at the baseline 6MWT and lower mMRC scores compared to patients with COPD.

Missing Data Analysis

Little's MCAR test was significant [$\chi^2_{(243)} = 16,907$, $p < 0.01$]. Post and follow-up scores of the mMRC and follow-up scores of the 6MWT were missing for $>50\%$ of the patients, therefore these variables were excluded from further analysis. Analysis of variables associated with missing data revealed that meters covered during the baseline 6MWT were associated with missingness at 3 months and that baseline diastolic blood pressure and meters covered during the baseline 6MWT were associated with missingness at 6 months. Based on the results of this analysis, missing data were considered to be Missing At Random. The multiple imputation procedure converged and imputed datasets were employed for the subsequent analyses.

Analysis of Change

Both the meters in the 6MWT ($U = 60$, $p < 0.01$), the SGRQ total ($U = 628$, $p < 0.01$) and subscales (Symptoms $U = 480.5$, $p < 0.01$; Activities $U = 417.5$, $p < 0.01$; Impact $U = 584$, $p < 0.01$)

TABLE 1 | Demographic and clinical characteristics of the sample.

		Total (*n* = 43)		**COPD (*n* = 31)**	**Bronchiectasis (*n* = 12)**	
Variable	**Level**	***N* (%), Median [IQR]**	**Missing (%)**	***N* (%), Median [IQR]**	***N* (%), Median [IQR]**	***p***
Demographic data						
Female sex	Female	22 (51.2)	0 (0%)	12 (38.7)	10 (83.3)	0.02
Occupation	Unemployed	7 (16.3)	0 (0%)	4 (12.9)	3 (25.0)	
	Worker	6 (14.0)	0 (0%)	5 (16.1)	1 (8.3)	
	Retired	30 (69.8)	0 (0%)	22 (71.0)	8 (66.7)	0.56
Education	Elementary	4 (9.3)	0 (0%)	3 (9.7)	1 (8.3)	
	Middle	11 (25.6)	0 (0%)	9 (29.0)	2 (16.7)	
	High	19 (44.2)	0 (0%)	12 (38.7)	7 (58.3)	
	Degree	9 (20.9)	0 (0%)	7 (22.6)	2 (16.7)	0.7
Civil status	Unmarried	5 (11.6)	0 (0%)	3 (9.7)	2 (16.7)	
	Married	28 (65.1)	0 (0%)	21 (67.7)	7 (58.3)	
	Divorced	5 (11.6)	0 (0%)	4 (12.9)	1 (8.3)	
	Widow	5 (11.6)	0 (0%)	3 (9.7)	2 (16.7)	0.8
Age		74 [69, 77]	0 (0%)	74 [69.0, 76.5]	75.5 [69.8, 77.0]	0.48
Smoke		5 (11.6)	0 (0%)	5 (16.1)	0 (0.0)	0.34
Clinical data and comorbidities						
BMI		24.9 [21.2, 27.2]	0 (0%)	25 [21.2, 27.7]	23 [21.3, 24.7]	0.3
SBP		120 [120, 130]	0 (0%)	120 [120, 130]	120 [110, 130]	0.5
DBP		80 [70, 80]	0 (0%)	80 [70, 80]	75 [70, 80]	0.35
RHR		71 [64.0, 76.5]	0 (0%)	70 [62, 76]	71.5 [67.0, 77.2]	0.34
GOLD classification	A	3 (11.5)	5 (12%)			
	B	11 (42.3)				
	C	4 (15.4)				
	D	8 (30.8)				
Hypertension		18 (41.9)	0 (0%)	15 (48.4)	3 (25.0)	0.29
Tumor		15 (34.9)	0 (0%)	11 (35.5)	4 (33.3)	1
Diabetes		8 (18.6)	0 (0%)	7 (22.6)	1 (8.3)	0.52
CVD		15 (34.9)	0 (0%)	12 (38.7)	3 (25.0)	0.62
Osteoporosis		4 (9.3)	0 (0%)	0 (0.0)	4 (33.3)	0.01
Dyslipidemia		6 (14.0)	0 (0%)	4 (12.9)	2 (16.7)	1
Other lung disease		8 (18.6)	0 (0%)	8 (25.8)	0 (0.0)	0.13
Spirometry results						
FVC		2.3 [1.9, 2.8]	7 (16)	2.4 [1.8, 3.0]	2.2 [2.0, 2.4]	0.63
FVC%		77 [66.8, 87.4]	7 (16)	75 [64, 84]	86 [77.0, 88.2]	0.1
FEV1		1.6 [1.1, 1.9]	7 (16)	1.5 [0.9, 1.9]	1.7 [1.6, 1.9]	0.19
FEV1%		71 [53.8, 86.0]	7 (16)	59 [42, 75]	87 [78.5, 90.0]	<0.01
FEV1/FVC%		66.8 [53.7, 78.1]	8 (19)	63 [50.9, 72.3]	78.1 [75.0, 80.3]	0.01
FEV1/FVC (% pred.)		86 [70.2, 100.0]	11 (26)	77.7 [64.2, 92.0]	100.5 [99.2, 104.5]	<0.01
Six-Minutes Walking Test results						
Borg scale pre		3 [2, 4]	1 (2)	3 [2.0, 4.8]	2 [0.8, 3.2]	0.08
Borg scale post		3 [1.8, 4.0]	3 (7)	3 [2, 4]	2 [1.5, 4.0]	0.57
SPO2% - pre		89 [86, 92]	2 (5)	87 [85, 92]	91 [90.5, 93.2]	0.02
SPO2% - post		91 [89.0, 93.2]	3 (7)	90 [89, 93]	93 [90.0, 95.5]	0.15
Meters - pre		385 [237.0, 439.5]	1 (2)	340 [200.0, 433.5]	410 [388.8, 440.0]	0.09
Meters - post		430 [352.5, 480.0]	3 (7)	410 [300, 480]	460 [442.5, 497.5]	0.1
Predicted% - pre		77.5 [54.8, 91.5]	1 (2)	68.5 [39.8, 89.8]	86 [73.5, 97.2]	0.08
Predicted% - post		87.5 [68, 100]	3 (7)	84 [61, 99]	96 [90.5, 101.5]	0.12
Health status and quality of life						
mMRC Pre	0	5 (26.3)	24 (56)	5 (33.3)	0 (0.0)	0.01
	1	6 (31.6)		2 (13.3)	4 (100.0)	
	2	3 (15.8)		3 (20.0)	0 (0.0)	
	3	5 (26.3)		5 (33.3)	0 (0.0)	
CAT pre		14 [8, 17]	1 (2)	15 [8.5, 17.0]	13 [7.0, 17.5]	0.57
CAT post		8 [4, 15]	2 (5)	13 [4, 16]	6 [0.0, 8.5]	0.15

(Continued)

TABLE 1 | (Continued)

		Total (*n* = 43)		**COPD (*n* = 31)**	**Bronchiectasis (*n* = 12)**	
Variable	**Level**	***N* (%), Median [IQR]**	**Missing (%)**	***N* (%), Median [IQR]**	***N* (%), Median [IQR]**	***p***
CAT 3 months		8.5 [5, 13]	7 (16)	9.5 [5.2, 13.8]	7.5 [5.5, 9.8]	0.48
CAT 6 months		12 [9, 15]	10 (23)	12.5 [9.2, 15.8]	8 [6.5, 13.5]	0.19
SGRQ symptoms pre		42 [25.2, 64.2]	5 (12)	44.5 [25.3, 65.5]	35.3 [22.6, 56.0]	0.39
SGRQ symptoms post		28.1 [17.7, 44.0]	6 (14)	28.1 [16.4, 42.0]	32.1 [21.3, 44.6]	0.4
SGRQ activities pre		59.8 [52.2, 66.2]	3 (7)	59.8 [53.5, 66.3]	59.3 [40.7, 66.2]	0.71
SGRQ activities post		53.6 [41.5, 66.2]	7 (16)	53.6 [44.7, 66.7]	53.6 [18.4, 60.2]	0.24
SGRQ impact pre		33.7 [15.9, 45.5]	3 (7)	34.1 [15.2, 45.7]	32.7 [27.4, 41.1]	0.94
SGRQ impact post		23 [9.2, 36.9]	7 (16)	24.2 [10.8, 39.5]	9.5 [9.1, 27.5]	0.18
SGRQ total pre		41 [30.3, 52.0]	3 (7)	42 [27.5, 54.5]	38.9 [32.5, 43.2]	0.67
SGRQ total post		30.6 [21.5, 45.4]	7 (16)	37.6 [21.4, 45.7]	25.4 [23.9, 27.2]	0.27
EQ-5D pre		0.8 [0.8, 0.9]	1 (2)	0.8 [0.8, 0.9]	0.8 [0.8, 0.9]	0.77
EQ-5D post		0.9 [0.8, 0.9]	7 (16)	0.8 [0.8, 0.9]	0.9 [0.8, 0.9]	0.7
EQ-5D 3 months		0.9 [0.8, 1.0]	7 (16)	0.8 [0.8, 1.0]	0.9 [0.8, 0.9]	0.51
EQ-5D 6 months		0.9 [0.8, 0.9]	9 (21)	0.8 [0.7, 0.9]	0.9 [0.8, 0.9]	0.43
EQ-5D – VAS pre		60 [50, 70]	2 (5)	60 [50, 70]	60 [55, 70]	0.73
EQ-5D – VAS post		70 [60, 75]	7 (16)	70 [60, 75]	70 [66.0, 73.8]	0.64
EQ-5D – VAS 3 months		68.5 [50, 75]	7 (16)	60 [50, 75]	70 [60, 80]	0.16
EQ-5D – VAS 6 months		65 [50, 75]	9 (21)	65 [47.5, 72.5]	65 [55, 75]	0.55
Psychological variables						
AAQ-II Pre		12 [10, 18]	2 (5)	12 [9.2, 15.0]	18 [11, 21]	0.38
AAQ-II Post		13 [9.2, 19.2]	9 (21)	11 [9, 17]	14 [11.5, 22.2]	0.18
PHQ-9 Pre		7 [5, 10]	2 (5)	7 [4.2, 9.0]	9 [6.0, 12.5]	0.33
PHQ-9 Post		5 [3, 7]	7 (16)	4.5 [3, 7]	7 [4.5, 9.2]	0.12
PHQ-9 3 months		5 [2, 8]	6 (14)	6 [3.5, 8.5]	5 [2, 5]	0.43
PHQ-9 6 months		3.5 [2, 6]	9 (21)	4 [2, 8]	3 [1.5, 3.5]	0.07
GAD-7 Pre		5 [3.2, 8.0]	1 (2)	5 [3, 8]	6 [5, 9]	0.25
GAD-7 Post		4.5 [3, 6]	7 (16)	4 [3, 5]	6 [5.0, 8.2]	0.04
GAD-7 3 months		3 [1, 6]	7 (16)	3 [1, 5]	6 [2, 7]	0.22
GAD-7 6 months		2 [1.2, 7.8]	9 (21)	2 [1.5, 6.5]	3 [1.5, 7.5]	0.82

Categorical variables are described using frequencies and percentages, continuous variables using medians and Interquartile Ranges (IQR). p Values are calculated based on Fisher tests, chi square tests of Mann Whitney tests, as appropriate.

IQR, interquartile range; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; RHR, resting heart rate; CVD, cardiovascular disease; FVC, forced vital capacity; FVC%, percentage predicted FVC; FEV1, forced expiratory volume; FEV1%, percentage predicted FEV1; FEV1/FVC%, percentage predicted FEV1/FVC; CAT, COPD Assessment Test; SGRQ, St George Respiratory Questionnaire; AAQ-II, Acceptance and Action Questionnaire – II; PHQ, Patient Health Questionnaire - 9-item version; GAD, Generalized Anxiety Disorder Scale - 7-item version.

scores and the AAQ scores ($U = 265.5$, $p < 0.01$) improved from baseline to discharge. The results of the multilevel model are reported in **Table 2**. Improvement in CAT scores and in the EQ-5D – VAS was present at discharge and at 3 months, but not at 6 months. The model which analyzed changes in the EQ-5D was non-significant, showing an absence of changes over time. Conversely, both PHQ-7 and GAD-7 showed lower levels of anxiety and depression at discharge, at 3 months and at 6 months compared to baseline. The fixed effect of diagnosis (COPD vs bronchiectasis) was not significant in any model. **Figure 2** displays the changes in outcome variables over time.

Predictors of Improvement

24 patients ($n = 43$, 55.8%), 22 ($n = 35$, 62.9%) and 17 ($n = 32$, 53.1%) patients had a minimum clinically important difference in their health status, as measured by the CAT, at discharge, at 3 months and at 6 months, respectively. Age, baseline health status, smoke status, depression levels and the difference between baseline and discharge levels of psychological inflexibility were associated with a minimum clinically important difference in CAT scores in univariate analyses. In the multivariable model, reaching a minimum clinically important difference at 6 months was predicted by baseline health status, with which had a positive association, and by baseline depression, with which had a negative association (**Table 3**).

DISCUSSION

This study aimed to preliminarily assess the effects of an interdisciplinary ACT-based treatment for chronic airway diseases by analyzing changes in clinical and psychological variables in participants who attended to it, and to identify predictors of response to the treatment. The results show that patients' health status improved over time and psychopathological symptoms decreased over time, and that

TABLE 2 | Results of the mixed linear models testing the differences in the main outcomes over time.

	CAT		**EQ-5D**		**EQ-5D VAS**		**PHQ-9**		**GAD-7**	
	B	**95% CI**	***B***	**95% CI**	***B***	**95% CI**	***B***	**95% CI**	***B***	**95% CI**
Intercept	14.24	11.89–16.60*	0.82	0.76–0.87*	58.02	52.70–63.33*	7.65	6.37–8.93*	6.12	4.68–7.56*
Time										
Post	−3.69	−6.03 to −1.35*	0.03	−0.02 to 0.07	7.9	2.01–13.79*	−1.59	−2.99 to −0.18*	−0.84	−2.19 to 0.51
Follow-up 3 months	−4.09	−6.49 to −1.69*	0.04	−0.01 to 0.09	6.05	1.51–10.59*	−1.92	−3.37 to −0.46*	−2.15	−3.52 to −0.08*
Follow-up 6 months	−0.7	−3.19 to 1.78	−0.01	−0.06 to 0.05	1.85	−4.10 to 7.79	−2.73	−4.21 to −1.24*	−1.95	−3.34 to −0.56*
Diagnosis										
COPD vs Bronchiectasis	−2.48	−6.11 to 1.16	0.01	−0.06 to 0.08	4.2	−3.66 to 12.07	0.02	−1.84 to 1.87	0.91	−1.43 to 3.26

Estimates are unstandardized coefficients.
*CI, confidence interval; CAT, COPD Assessment Test; PHQ-9, Patient Health Questionnaire – 9-item version; GAD-7, Generalized Anxiety Disorder Questionnaire – 7-item version. *significant result.*

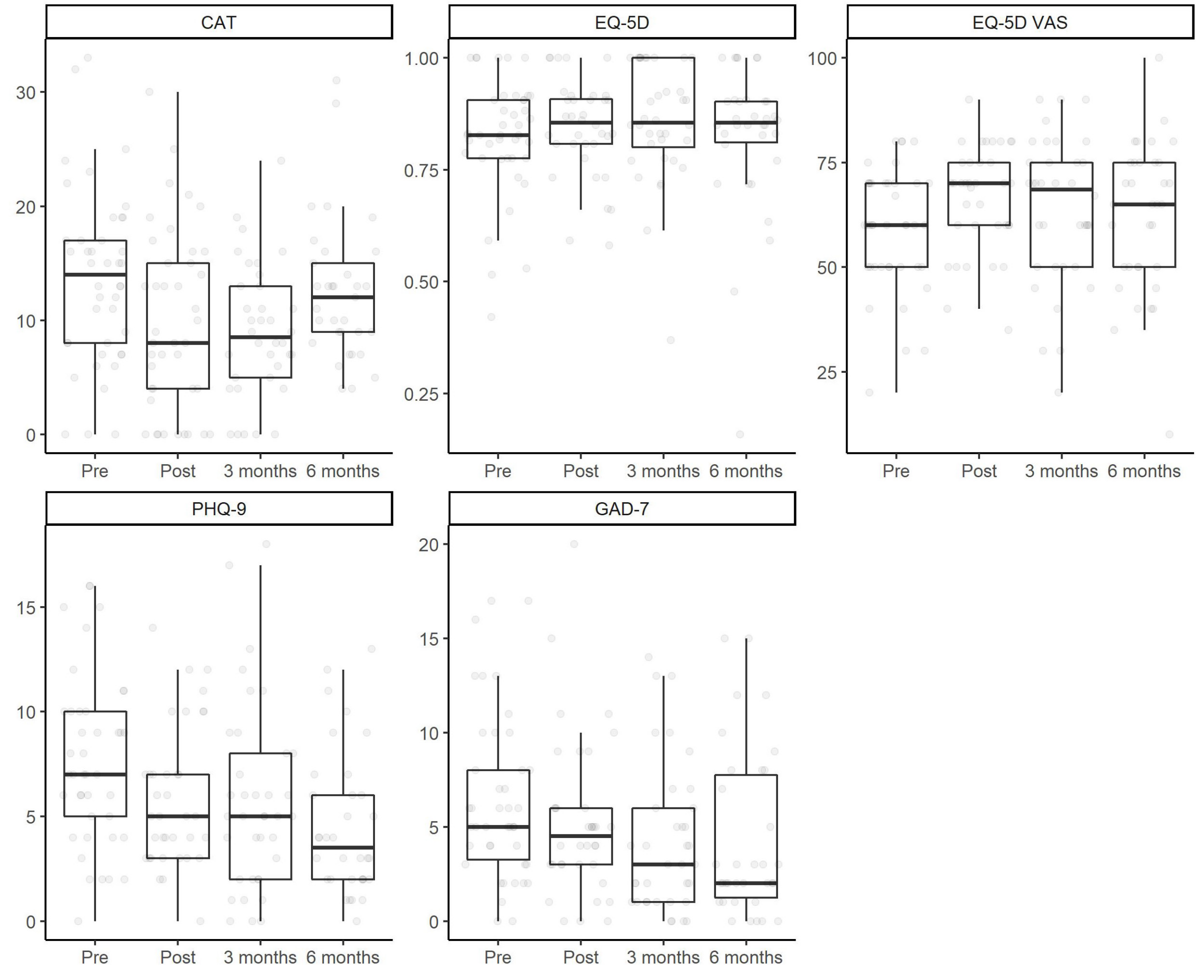

FIGURE 2 | Changes over time in outcome variables.

baseline health status and depression were associated with achieving a minimum clinically important difference in health status at 6 months.

The potential role of ACT-based components included in interdisciplinary rehabilitation programs for patients with chronic airway diseases has been suggested before

TABLE 3 | Multivariable logistic model including potential predictors of minimum clinically important difference in health status from baseline to the 6-months evaluation.

	OR	95% CI
(Intercept)	0.01	0–5.1
Age	1.01	0.01–1.18
Smoke status	0.82	0.62–1.12
CAT – baseline	1.43	1.08–1.89
PHQ – baseline	0.69	0.43–0.95
AAQ at discharge – AAQ at baseline	–0.35	0.29
F value		2.41
Degrees of freedom		5, 5,534.78
P		0.04

OR, odds ratio; CI, confidence interval; CAT, COPD Assessment Test; PHQ, Patient Health Questionnaire; AAQ, Acceptance and Action Questionnaire.

(Fernandes-James et al., 2019). ACT-based components have shown to be effective in improving the adaptation to several chronic conditions (Graham et al., 2016), and seem suitable to tackle the vicious circle linking inactivity, disease progression and psychopathological symptoms which is central for the adaptation to the disease (Hartman et al., 2013; Ramon et al., 2018). This is because ACT-based components address psychological inflexibility, which is an important factor explaining the engagement in pulmonary rehabilitation (Fernandes-James et al., 2019). Nonetheless, no study has ever addressed their efficacy. Our results, albeit of a preliminary nature, suggest that they can be an important component of interdisciplinary programs. As a note of caution, we comment that the ACT component worked in synergy with the other components and that, as a result, its specific effect is not separable from the one of the other components of the interdisciplinary program. Since interdisciplinary programs are developed by collaboration between different health professionals, the effects of their components are not entirely distinguishable.

The participation to the interdisciplinary program investigated in this study was concomitant with an improvement in patients' health status from baseline to discharge and at 3 months, and in a reduction in psychopathological symptoms up to 6 months. Given the absence of a control group, these results should be interpreted with caution. Nevertheless, since COPD and bronchiectasis are chronic and progressive diseases, the improvement of health status in the short and medium term is of considerable clinical importance (GOLD, 2020). Similarly, improvement of anxious-depressive symptoms is crucial for optimal management of the disease (Zareifopoulos et al., 2019). Notably, the changes in health status and psychopathological symptoms did not differ between patients with COPD and patients with bronchiectasis, suggesting that both categories of patients may benefit from this treatment.

Having a worse health status at baseline was associated with more marked improvements. This suggests that interdisciplinary programs such as the one investigated in this study are particularly suitable for patients with more severe initial symptoms, as they are likely to achieve greater improvement in the long term. In contrast, higher levels of depression at the start of the program were associated with less improvement. This may be explained by the fact that depression, in general, has a negative impact on motivation for treatment and life changes needed to cope with respiratory diseases, in terms of abstinence from smoking, increased activities and being adherent to pharmacological and nonpharmacological prescriptions (Volpato et al., 2021).

The main limitation of this study is the absence of a control group. Since this study is a retrospective review of chart data, these results should be only used as the basis for further studies on the effects of ACT-based interdisciplinary treatments. In addition, the presence of missing data made it impossible to assess differences in aerobic capacity and endurance measured by the 6MWT. Missing data was substantial also for other variables, but their effect was controlled using the multiple imputation procedure.

In conclusion, this retrospective study shows that intensive interdisciplinary rehabilitation programs including an ACT-based component are promising treatments that can be employed to improve the health and psychological status of patients suffering from chronic airway diseases.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusion of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

EG conceived the study, performed the statistical analyses, and participated in the drafting of the manuscript. BP conceived the study, aided in interpreting the results, participated in the drafting of the manuscript, and conceived the study. CM participated in the drafting of the manuscript. VG, FC, SB, PG, AR, VR, KG, and GC reviewed and edited the manuscript. MP extracted the data from the medical records. MS-B was in charge of overall direction and reviewed and edited the manuscript. All authors provided critical feedback and helped to shape the research, analysis and manuscript, and approved the submitted version.

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Anxiety and Depression in Chronic Obstructive Pulmonary Disease: Perspectives on the Use of Hypnosis

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Chronic Obstructive Pulmonary Disease (COPD) is a highly prevalent and debilitating respiratory condition, characterized by chronic airflow limitation, breathlessness, and other persistent respiratory symptoms. Critically, patients suffering from COPD often find themselves trapped in a vicious comorbidity cycle: while breathlessness and increased respiratory rate are known inducers of anxiety, the latter have been shown in turn to exacerbate breathlessness and chest discomfort. Hypnosis holds great potential for the simultaneous complementary management of anxiety and breathlessness in COPD. It is an inexpensive psychological intervention tailored to the patient's own experience, convenient in terms of logistics and implementation. In this short qualitative review, we present hypnosis' structural, cognitive, and neural fundamentals, and assess existing instances of hypnosis use in the treatment of anxiety, depression, and respiratory disease. We then discuss its potential as a tool for improving health-related quality of life and the self-management of COPD within (and beyond) pulmonary rehabilitation.

Keywords: COPD, anxiety, depression, hypnosis, breathlessness, comorbidity, self-management, complementary care

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) causes persistent and progressive respiratory symptoms, including breathlessness, sputum, and suboptimal oxygenation (GOLD Report, 2022). Aside from a daunting mortality rate [3.23 million deaths in 2019 according to the WHO (2020) report on noncommunicable diseases], COPD hinders patients' health-related quality of life (HRQoL) by reducing mobility, increasing fatigue levels, and propitiating psychological comorbidities such as anxiety, depression, and suicidality (Kellner et al., 1992; Hegerl and Mergl, 2014; Pumar et al., 2014). The 2022 edition of the Global Initiative for Obstructive Lung Disease report (GOLD) observes that treating psychological comorbidities is critical in COPD, as evidence shows that the alleviation of anxiety and depression symptoms also improves respiratory disease prognosis. In particular, the complementary use of cognitive behavioral therapy and mind–body interventions such as mindfulness-based therapy have been found to reliably reduce anxiety and depression in COPD, diminish fatigue, and improve lung function and exercise capacity (Farver-Vestergaard et al., 2015).

Evidence shows that hypnosis is a fast, cost-effective intervention for the treatment of anxiety and depression, both as stand-alone therapy and as a part of larger therapeutic strategies (Hammond, 2010; Cafarella et al., 2012; Milling et al., 2019; Valentine et al., 2019). On the grounds of its implementational and therapeutic advantages, it is worth discussing its incorporation to the treatment of breathlessness-related anxiety and depression in COPD. In the present work, we succinctly introduce hypnosis' structure, its cognitive building blocks, and its basic neural correlates. We then reflect upon how hypnosis could contribute to the treatment of transient and chronic anxiety and depression in COPD, and its compatibility with pulmonary rehabilitation and self-management strategies.

COPD, PSYCHOLOGICAL COMORBIDITIES, AND QUALITY OF LIFE

At the current juncture, COPD is a chronic, incurable condition. This makes improving patients' symptoms and HRQoL a chief priority in the management of the disease (Engström et al., 2001). Because of its handicapping nature, COPD progression affects all subjective and objective dimensions of HRQoL in an incremental fashion (Afroz et al., 2020). On the physical level, it restricts general physical function and breathing mechanics, leading to increased levels of fatigue and reduced autonomy. On the psychological level, it fosters negative affects, increases emotional burden and negative coping. On the social level, it restricts the patient's capability to work and generally impacts interpersonal relations and autonomy.

While multiple comorbidities are associated with COPD, anxiety and depression have been reliably identified as some of the most important predictors of poor HRQoL and treatment adherence (Dalal et al., 2011; Willgoss and Yohannes, 2013; Yohannes and Alexopoulos, 2014). Timely diagnosing anxiety and depression in COPD have proven particularly challenging due to symptom overlapping and an unclear etiological association between conditions (Pumar et al., 2014). However, identification and treatment of these psychological comorbidities are paramount: evidence shows that anxiety, depression, and suicidality are not only highly prevalent among the COPD population (Kunik et al., 2005; Stage et al., 2006; Sampaio et al., 2019), but also are accurate predictors of poorer health status, of increased risk of exacerbation, and of higher emergency admissions (Blakemore et al., 2019). Studies exploring HRQoL in stable and severe COPD cohorts have found clear associations between anxiety and depression levels, and poorer quality of life (Cully et al., 2006; Eisner et al., 2010). This is unsurprising, given the vicious bidirectional nature of the relationship between COPD and these psychological comorbidities (Atlantis et al., 2013). On the one hand, breathlessness, chest tightness, and increased respiratory rate are known inducers of anxiety (Kellner et al., 1992; Tselebis et al., 2016), and the psychosocial adversity caused by COPD can easily lead to depression (Alexopoulos, 2005). On the other hand, anxiety and depression are common culprits for the acute worsening of chronic breathlessness, chest pain, fatigue, and other prominent COPD symptoms (Atlantis et al., 2013; Simon et al., 2013).

Interestingly, clinical and biological markers of COPD appear to be less important determinants of depression than actual feelings of breathlessness and subjective appreciation of HRQoL (Hanania et al., 2011). At the same time, the impact of anxiety and depression on HRQoL in COPD appears to be decorrelated from bronchiectasis and objective lung function (Engström et al., 2001; Ekici et al., 2015). Overall, these findings suggest that improvements of HRQoL in COPD may depend on therapeutic strategies that concentrate on patients' subjective and experiential correlates of the disease, or at the very least takes them seriously into account.

HYPNOSIS FUNDAMENTALS

To the effects of the present review, it is more convenient to privilege a procedural definition of hypnosis rather than to navigate the long-standing theoretical debates on the nature of the phenomenon (Terhune, 2014; Terhune et al., 2017). During a standard hypnotic intervention, customarily a trained professional (e.g., a researcher, a medical doctor, and a therapist) delivers a suggestion (e.g., motor, cognitive, and affective) to a receptor (e.g., the participant of a research protocol and a patient). Usually, this suggestion is preceded by an induction phase composed of relaxation and attention exercises, aimed at producing experiential and motivational changes that serve the purpose of enhancing the receptor's permeability to suggestion (Woody and Sadler, 2016). Much like placebo interventions, hypnotic interventions work best when practiced within a socio-cultural context that increases the receptor's motivation and compliance (e.g., a lab and a hospital; Lynn and Sherman, 2000).

When performed under these conditions, hypnosis elicits a hypnotic response, which consists of the inhibition/facilitation of all sorts of motor, sensory, cognitive, or affective responses. For example, an inhibitory motor suggestion can successfully induce paralysis and set off neurophysiological patterns different from simulated paralysis (Cojan et al., 2009). On the other hand, a facilitatory perceptual suggestion can effectively trigger hallucinatory content for susceptible individuals (Woody and Szechtman, 2011) or the onset of positive feelings (Gaunitz et al., 1975). **Figure 1** below presents a short summary with examples of tested hypnotic suggestions, sorted by type, the function they target, and the hypnotic response they are known to produce.

While there is no definitive answer on what are the cognitive mechanisms behind hypnotic responses, reasonable consensus has been reached that they rely primarily on cognitive control and the top-down modulation of perception (Terhune et al., 2017). Perception is built simultaneously by bottom-up sensory information, and top-down conceptual information stemming from prior world-knowledge and expectations (De Lange et al., 2018). Crucially, it has been shown that, when purposefully managed, top-down influences can drastically shape perception (Carrasco et al., 2004; Balcetis and Dunning, 2006, 2010). Hypnosis would thus be a particularly powerful technique for

	FUNCTION			
TYPE	Motor	Perceptual	Cognitive	Affective
Inhibition	**Arm paralysis** (Roelofs, 2002)	**Analgesia** (Facco, 2011)	**Agnosia** (Barnier, 2010)	**Numbing** (Anllo, 2021)
Facilitation	**Arm levitation** (Cardeña, 2012)	**Color hallucination** (Kallio, 2016)	**Age regression** (Nash, 1983)	**Posthypnotic happiness** (Gaunitz, 1975)

FIGURE 1 | Examples of hypnotic suggestions. Hypnotic and posthypnotic suggestions can either inhibit or facilitate a vast array of motor, perceptual, cognitive, and affective responses. Examples are provided together with studies evaluating their implementation and phenomenology.

the maximization of the top-down influence in the building of perceptual experience: instead of accessing the usual perceptual priors triggered by standard contextual information, hypnotized individuals rely on the hypnotic mental representations and expectations conveyed to them through hypnotic suggestion and use them to consolidate an alternate perceptual experience instead (Brown and Oakley, 2004).

Concerning hypnosis' neural substrates, much remains to be uncovered. Yet, several studies coincide in pointing out common brain correlates to hypnotic responding, such as (1) reduced activity in the dorsal Anterior Cingulate Cortex, (2) increased functional connectivity between the dorsolateral prefrontal cortex and the insula in the Salience Network (Jiang et al., 2017), and (3) reduced connectivity between the Executive Control Network and the Default-Mode Network (Jiang et al., 2017; Landry et al., 2017). At the neurophysiological level, Jensen et al. (2015) have proposed that the changes detected in theta oscillations during hypnosis may act as facilitators of hypnotic responding.

Hypnosis has long been used with diverse therapeutic purposes, such as introducing and reinforcing better adaptive behavioral patterns (e.g., to diminish compulsory acting), thinking patterns (e.g., to counteract depressive ruminations), and emotional response (e.g., to induce calmness in the aftermath of trauma; Barabasz et al., 2010). Furthermore, hypnosis is of great use for re-orienting attention away from aversive stimuli, which has warranted it a particularly popular place in acute, chronic, and perioperative pain management therapies (Patterson and Jensen, 2003; Patterson et al., 2006; Patterson, 2010). It can yield positive results when utilized as stand-alone therapy but is most effective when implemented as a therapeutic complement to an already established psychological treatment or medical procedure (Ramondo et al., 2021). Oftentimes, practitioners wonder whether a hypnotic intervention's efficacy will be conditioned to the patients' hypnotic suggestibility. While, indeed, hypnotizability is the main predictor of successful hypnotic responding in experimental hypnosis (Barnier et al., 2021), suggestions posed in the context of medical treatments are generally easy to follow and do not demand a particularly high susceptibility (e.g., relaxation, searching for positive memories, and evoking mental imagery). Further, existing evidence has indicated that the success of hypnosis in the clinical milieu depends primarily on patient motivation and expectation (Barber, 1980), even when treating psychological conditions as complex as anxiety and depression (Yapko, 2001).

Finally, evidence shows that the technique is safe, and the risks associated with it (e.g., evoking bad memories and emotional abreactions) are negligible (Lynn et al., 1996). Peer-reviewed research on hypnosis safety suggests that the occurrence of "negative" sensations following hypnosis is rare, and decorrelated from suggestibility, which indicates hypnosis may not be at the source of these feelings to begin with (Brentar et al., 1992; Lynn et al., 1996).

HYPNOSIS AND THE COMPLEMENTARY MANAGEMENT OF MOOD AND RESPIRATORY DISORDERS

Over the past 30 years, efforts to assess the efficacy of hypnosis as a therapeutic tool for the treatment of anxiety and depression in a controlled manner have progressively mounted, with favorable results. While less numerous, promising studies on the use of hypnosis in respiratory medicine have also shown that the technique can flexibly target key respiratory symptoms present in COPD.

A recent comprehensive meta-analysis including 13 randomly controlled trials (RCT) has assessed the efficacy of hypnosis for treating depression symptoms (Milling et al., 2019). Results show that hypnosis samples presented a mean significant improvement superior to controls, both at treatment end (effect size of improvement $d = 0.71$) and follow-up ($d = 0.52$). Such an impact places hypnosis within the same range of efficacy of other forms of treatment such as cognitive behavioral therapy ($d = 0.67$) and short-term psychodynamic therapy ($d = 0.69$; Cuijpers et al., 2011). Studies posterior to this meta-analysis continued to confirm this trend. For example, Fuhr et al. (2021) have shown no difference in mean reduction of depressive symptoms between hypnosis and cognitive behavioral therapy after 16–20 sessions, nor at the 6-month and 12-month follow-ups. In a study comparing hypnosis to meditation and progressive muscle relaxation in children with primary headaches, all three methods were shown to reliably reduce depression symptoms after 9 months of treatment (Jong et al., 2019). Aravena et al. (2020) also showed a significant decrease of depressive symptomatology after audio-recorded hypnosis sessions in patients with fibromyalgia.

The evaluation of evidence concerning the use of hypnosis for the management of anxiety is also positive overall. In a novel meta-analysis, Valentine et al. (2019) analyzed 17 RCT and found a mean significant improvement of anxiety against controls at treatment end ($d = 0.79$; $d = 1.12$ when contrasted against no-contact controls) and during follow-up ($d = 0.99$). Of note, hypnosis was at least as effective as cognitive behavioral therapy ($d = 0.82$) and better than mindfulness meditation ($d = 0.39$; Mitte, 2005; Blanck et al., 2018). Here as well, newer studies on the efficacy of hypnosis for treating anxiety symptoms as either stand-alone or complementary therapy indicate intervention effectiveness. To name a few, Roberts et al. (2021)

have shown support for the use of hypnosis to reduce symptoms of anxiety among postmenopausal women. Roberts et al. (2021) indicate that hypnosis is a suitable adjunct in Crohn's disease and may improve general psychosocial QoL, including anxiety.

Concerning the use of hypnosis specifically targeted at respiratory diseases, evidence has been somewhat scarce, but equally promising. Hypnosis-based psychodynamic treatments were proven effective for reducing anxiety and depression in amyotrophic lateral sclerosis patients with impaired respiratory function (Kleinbub et al., 2015). Further examples include hypnosis for improving breathlessness in pediatric medicine (McBride et al., 2014), asthma (Brown, 2007), and palliative care (Brugnoli, 2016; Montgomery et al., 2017). While no meta-analysis has been conducted to date, the observed main benefits of incorporating hypnosis to the management of respiratory conditions include relief of anxiety related to ventilation problems, alleviation of discomfort, and improvements in breathing regulation (Anbar, 2012).

In the specific case of COPD, hypnosis has been used almost exclusively as a relaxation technique (Cafarella et al., 2012). To our knowledge, there is only one RCT evaluating the use of hypnosis to manage anxiety and breathlessness in COPD that implements a relaxation control (Anlló et al., 2020). This crossover study has shown that a 15-min scripted hypnotic intervention positively impacted respiratory rate, pulsated oxygen saturation, Borg scores, and anxiety (as assessed by State–Trait Anxiety Inventory – 6 items version).

Interestingly, as of 2022, many new trials assessing the impact of hypnotic interventions on depression and anxiety symptoms are currently in progress, which shows that the technique continues to accrue interest in the medical community (e.g., Anlló et al., 2021a; Grégoire et al., 2022; Fernandes et al., *ongoing* NCT04010825). In particular, at least two of these ongoing trials are targeting the use of hypnosis specifically for the psychological and emotional correlates of COPD (Anlló et al., 2021b; Fernandes et al., *ongoing* NCT04010825).

DISCUSSION

While hard to disentangle, it is important to understand the separate roles of each of the building blocks of hypnosis as an intervention. Treating the technique as a monolithic interventional battery hinders our understanding of its real potential in respiratory medicine. For example, when implemented in respiratory medicine, and particularly in COPD, hypnosis has been mostly used as a form of "relaxation therapy" (Cafarella et al., 2012; Tselebis et al., 2016). Certainly, hypnotic inductions often include relaxation exercises (Batty et al., 2006), and of course, the implementation of hypnosis and other forms of guided mental imagery as a form of relaxation is beneficial in and of itself (Hammond, 2010; Volpato et al., 2015, 2022). However, as explained above, hypnotic effects depend primarily on the contents of suggestions (**Figure 1**), which are fundamentally independent from hypnosis' relaxation component (Cardeña et al., 2012). Thus, a different use of hypnosis, where the emphasis is shifted toward tailoring suggestions to generate sensory and experiential changes that modify the subjective experience of patients (Elkins, 2017), could represent significant progress in the complementary management of the physical and psychological symptoms of respiratory disease. For instance, Anlló et al. (2020) hypothesized that these perceptual modulations could be implemented to optimize breathing mechanics and reduce anxiety by suggesting a feeling of "air effortlessly entering the lungs." There, a 15-min scripted hypnotic intervention positively impacted transient anxiety in mild and severe COPD patients (23.8% after hypnosis versus only 3% after the "relaxation and attention" control). Crucially, it also improved respiratory rate, arterial oxygen saturation, and Borg scores. We think it is plausible that this across-the-board effect may respond to the endogenously generated sensory feedback produced by the hypnotic suggestion. While promising, more evidence is needed to support this conclusion.

Wide consensus exists concerning the fundamental importance of Pulmonary Rehabilitation Programs (PRPs) for improving the clinical outcomes and behavioral patterns of COPD patients (GOLD Report, 2022). Comprehensive PRPs frequently supplement physical activity with short psychological therapy plans and self-management strategies. These have been shown to improve the psychological symptoms associated with COPD and decrease the risk of exacerbation regardless of disease severity (Coventry et al., 2013; Gordon et al., 2019). Beyond its proven clinical impact, hypnosis could greatly help with the logistic and implementational limitations that encumber PRPs (Ranjan et al., 2021). Hypnosis does not need hefty material or technological investments, its implementation is fast, and patients can obtain clinically significant relief even after short sessions (Anlló et al., 2020). Further, recent efforts assessing the feasibility of online PRPs have produced encouraging results (Beatty and Lambert, 2013; Ranjan et al., 2021). Given how hypnosis is also effective when administered through recordings and online, this renders it a suitable complement to this approach (Flynn, 2019). Additionally, most implementations of hypnosis eventually transition into self-hypnosis (Barabasz et al., 2010), which makes it a potentially useful technique for the self-management of COPD symptoms (Lenferink et al., 2017).

Given this array of advantages, we propose that an understanding of how the effects of hypnosis and self-hypnosis interact with COPD-related breathlessness, anxiety, and depression is worth considering. In particular, in patients who manifest a strong preference for drug-free approaches or have a mitigated response to pharmacological strategies. It could also be advantageous for patients who present an inability to exercise or to relax by their own means. Of course, further research in the form of new RTCs is needed before hypnosis can be endorsed conclusively for the complementary management of anxiety and depression in COPD: we still know little about hypnosis' effectiveness across levels of disease severity, its interaction with lung function, its interaction with antidepressants, and patients' willingness to adhere to a hypnosis-based treatment. However, given the existing evidence and current challenges in the treatment of COPD, we conclude that the effort of answering these questions is clearly justified.

AUTHOR CONTRIBUTIONS

HA, FL, and BH conceived the outline of the article and determined which were the important aspects to be covered in this mini-review. HA wrote the manuscript under the supervision of BH. HA and BH conducted the qualitative literature search. FL provided additional feedback and evaluated the feasibility of the review. All authors reviewed the manuscript, contributed with hands-on amendments and critical feedback, and validated the final draft.

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Disease-Specific Anxiety in Chronic Obstructive Pulmonary Disease: Translation and Initial Validation of a Questionnaire

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Background: Commonly applied measures of symptoms of anxiety are not sensitive to disease-specific anxiety in patients with chronic obstructive pulmonary disease (COPD). There is a need for validated instruments measuring COPD-specific anxiety. Therefore, we translated the COPD-Anxiety Questionnaire (CAF) into Danish (CAF-R-DK) and performed an initial validation of the psychometric properties in a sample of patients with COPD.

Materials and Methods: Translation procedures followed the World Health Organization guidelines. Participants with COPD completed questionnaires measuring COPD-specific anxiety (CAF-R-DK), general psychological distress (Hospital Anxiety and Depression Scale) as well as variables related to COPD (COPD Assessment Test; modified Medical Research Council dyspnea scale), quality of life (the 12-item Short Form survey, SF12), and socio-demography.

Results: A total of 260 patients with COPD (mean age: 65.0, 69% female) completed questionnaires. The Danish version of CAF-R-DK demonstrated acceptable Cronbach's α values that were comparable with those of the original CAF. As expected, the CAF-R-DK showed positive correlations with convergent constructs (CAT; HADS) and negative correlations with discriminant constructs (SF-12). However, the results for specific subdomains of the CAF-R-DK indicated inconsistency in the underlying concept of disease-specific anxiety, which was also suggested based on the subsequent confirmatory and exploratory factor analyzes.

Conclusion: The CAF could serve as an important supplement to generic psychological distress screening of patients with COPD in somatic health care settings, and the questionnaire is now available in Danish. Translation into other languages is needed with the purpose of obtaining data for further testing the psychometric properties of the questionnaire.

Keywords: disease-specific fear, respiratory illness/disease, psychological distress, assessment, measurement, Danish translation

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INTRODUCTION

Living with breathlessness, reduced mobility, and uncertainty related to chronic obstructive pulmonary disease (COPD) is associated with high levels of anxiety for many patients (Willgoss and Yohannes, 2013; von Leupoldt, 2017). Anxiety is a natural psychophysiological response to a perceived threat, which for most patients occur as passing emotional states in relation to external events (e.g., exacerbations of symptoms, hospitalization, or receiving messages with negative contents related to health and/or treatment options) or internal events (e.g., bodily sensations or intrusive thoughts or memories). However, for a considerable proportion of patients with COPD, symptoms of anxiety are persistent over a longer period of time and can be associated with behavioral avoidance of activities that are expected to trigger dyspnea (Holas et al., 2017; Stoeckel et al., 2018; Hanania and O'Donnell, 2019). Hence, symptoms of anxiety can aggravate daily functioning and quality of life, and are related to increased healthcare utilization, morbidity, and mortality in COPD (Eisner et al., 2010).

General symptoms of anxiety can be assessed with questionnaires such as the Beck Anxiety Inventory (BAI) (Fydrich et al., 1992), the General Anxiety Disorder-7 (GAD-7) (Spitzer et al., 2006), and the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983). In COPD, the HADS is most commonly applied (Smid et al., 2017b; Larsen et al., 2021), and was initially developed for use in somatic disease populations to avoid ceiling effects due to overlap between physical symptoms from the somatic disease and the psychological condition, respectively. Routine screening for general symptoms of anxiety and depression are important with the purpose of detecting potential psychological comorbidities in COPD, but the existing instruments has been criticized for suboptimal screening accuracy against diagnostic interviews (Baker et al., 2018). Moreover, recent studies differentiates general from disease-specific symptoms of anxiety in COPD, and stress the importance of assessing both aspects in COPD care (von Leupoldt and Janssens, 2016; Reijnders et al., 2019). Reijnders et al. (2019) showed that greater reductions in COPD-specific anxiety were associated with greater improvements in exercise capacity, quality of life, and health status as well as a more pronounced decrease in depression over the course of a pulmonary rehabilitation program – independent of general anxiety levels. Moreover, Keil et al. (2014) showed that COPD-specific anxiety contributed independently to disease-specific disability after statistically controlling for disease severity, sociodemographic variables, and general anxiety.

While several instruments measuring general symptoms of anxiety exist, fewer disease-specific anxiety measures are available for use in respiratory disease populations. The Anxiety Inventory for Respiratory Disease (Willgoss et al., 2013) was developed according to the same principles as the HADS, where somatic symptoms are excluded. This increases the specificity of the questionnaire, which means that the risk of identifying false positive cases is lowered, but at the same time it reduces the sensitivity, which leads to an increased risk of overseeing true positive cases (Trevethan, 2017; Baker et al., 2018). The Interpretation of Breathing Problems Questionnaire (Sutton et al., 1999) and the Breathlessness Catastrophizing Questionnaire (Solomon et al., 2015) are examples of questionnaires designed to measure dyspnea-related anxiety in respiratory illness, and they are therefore not sensitive toward other aspects of COPD-specific anxiety.

The COPD-Anxiety Questionnaire (CAF) was developed in Germany in 2011 to assess COPD-specific anxiety (Kühl et al., 2011). The original, German-language scale consists of 27 general items and 8 conditional items for patients with a partner and/or who receive oxygen treatment. The items cover the five subdomains of Fear of dyspnea (FD), Fear of physical activity (FPA, Fear of progression (FP), Fear of social exclusion (FSE), and Sleep-related worries (SRW). A shorted, 20-item version (CAF-R) was validated in 2014 (Keil et al., 2014). While questionnaires assessing general symptoms of anxiety have long been available in multiple languages, measurement instruments of disease-specific anxiety were developed relatively recently, and have therefore not yet been translated and validated more broadly.

On this background, the present study aimed to translate the CAF-R into Danish, and to validate the Danish version of the questionnaire (CAF-R-DK) in a sample of patients with COPD, including an initial evaluation of different response formats, i.e., electronic and paper-version.

MATERIALS AND METHODS

The translation and initial validation strategy was based on the World Health Organization's (WHO) guidelines for the process of translation and adaptation of instruments[1] and is described in detail below.

Translation Procedures

The initial translation of the CAF from German into Danish language was performed by the second author (SRR) who is a nurse with considerable experience within respiratory medicine. The translator is knowledgeable of the German-speaking culture and her mother tongue is Danish. The initial translation was based on a conceptual rather than literal approach, aiming at the conceptual equivalent of a given word or phrase rather than a word-by-word translation. Use of technical terms, colloquialism, idioms, or vernacular terms was avoided. Back-translation was performed by two independent native German translators, who had no prior knowledge of the questionnaire. Discrepancies were discussed until an agreement was reached.

An expert panel of researchers from different relevant disciplines (i.e., psychology, respiratory medicine, pulmonary rehabilitation) discussed the Danish translation of the CAF-R. Relevant adjustments of the CAF-R-DK were made on the basis of the suggestions from the panel.

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[1] https://cdn.who.int/media/docs/default-source/publishing-policies/whoqol-100-guidelines/translation-methodology.pdf?sfvrsn=74cdb8f5_2

Pre-Testing and Cognitive Interviewing

Five pre-test respondents with a diagnosis of COPD were recruited from the pulmonary outpatient clinic at the Department of Medicine, Lillebaelt Hospital, Vejle, Denmark. Each respondent completed the questionnaire individually and immediately thereafter participated in a debriefing asking (1) whether they could repeat the question in their own words, (2) what came to their mind when they heard a particular phrase or term, and (3) explain how they choose their answer. The questions were repeated for each item in the questionnaire. Hereafter, the cognitive interviewing was based on understanding potential conflicts in verbal answers and questionnaire-answers with the purpose of reaching consistency. Relevant adjustments of the CAF-R-DK were made on the basis of the interview material to ensure face validity.

Questionnaires

A questionnaire package was distributed electronically via the webpage and social media platforms of the Danish Lung Association. Furthermore, a paper-version of the questionnaire package was distributed among COPD outpatients at the Department of Medicine, Lillebaelt Hospital, Vejle, Denmark. The questionnaire package consisted of the following questionnaires.

The Danish version of the COPD-Anxiety Questionnaire 20-item version (CAF-R-DK) (Keil et al., 2014) was applied to measure COPD-specific anxiety. The questionnaire consists of 20 item each rated on a Likert scale from 0 = "never" to 4 = "always." The items cover the domains of Fear of dyspnea ("When I become short of breath, I get scared"), Fear of physical activity ("I avoid physical exertion"), Fear of progression ("I fear that someday I will become a burden for others because of my illness"), Fear of social exclusion ("I feel left alone with my illness"), and Sleep-related worries ("I wake up at night because of my breathing"). The original CAF-questionnaire has good internal consistency, with Cronbach's α of domain scales ranging from α = 0.78 (SRW) to α = 0.87 (FSE, FP) (Keil et al., 2014). The Danish version of the questionnaire can be obtained from the authors upon request.

The COPD Assessment Test (CAT) (Jones et al., 2009) was included with the purpose of measuring COPD-specific disability, or health status, and consists of 8 items that are rated on a semantic differential scale from 0 (e.g., "I am not limited doing any activities at home") to 5 (e.g., "I am very limited doing activities at home"). The CAT is commonly applied in COPD research and clinical practice and shows good psychometric properties, e.g., Cronbach's α = 0.88 (Jones et al., 2009, 2011; Kon et al., 2014; Smid et al., 2017a).

The modified Medical Research Council dyspnea scale (mMRC) (Williams, 2017) was applied to measure the degree of dyspnea on a Likert scale from 0 = "I only get breathless with strenuous exercise" to 4 = "I am too breathless to leave the house or I am breathless when getting dressed." The scale is recommended for baseline assessment of dyspnea in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines (GOLD, 2017).

The Hospital Anxiety and Depression Scale (HADS) was used to measure symptoms of anxiety and depression. The scale consists of 14 items, including 7 for symptoms of depression (e.g., "I feel as if I am slowed down") and 7 for general symptoms of anxiety (e.g., "I feel tense or 'wound up"). Items are rated on a semantic differential scale from 0 (e.g., "Not at all") to 3 (e.g., "Most of the time"). The scale is commonly used as a screening tool in COPD, with a Cronbach's α of 0.87 (Baker et al., 2018).

The 12-item Short Form survey (SF-12) (Ware et al., 1996) was applied to measure quality of life by addressing different aspects of emotional states and daily activities (e.g., "Have you felt down-hearted and blue?"; "Have you accomplished less than you would like as a result of your physical health?"). Total scores for the physical components score (PCS) and the mental component score (MCS), respectively, are calculated based on population norms (score range from 0–100), with higher scores indicating better health. The SF-12 demonstrates good sensitivity to change and discriminative values in grades of COPD (Menn et al., 2010).

Analysis

All analyzes were performed using Stata 17 software (StataCorp. 2021. *Stata Statistical Software: Release 17*. College Station, TX, United States: StataCorp. LLC). For all analyzes, p-values of $\leq$ 0.05 were considered statistically significant. Correlation coefficients of 0.20, 0.40, 0.60, and 0.80 were considered weak, moderate, strong, and very strong, respectively. Missing data were imputed by mean substitution, except from the SF-12, where missing data were handled according to the scoring descriptions (Ware et al., 1995) (the full description can be found in **Supplementary Material 1**). For the CAF-R-DK, missing data on individual items were explored with the purpose of identifying whether particular items in the CAF-R-DK indicated problems in understanding the content (Primdahl et al., 2021).

Convergent validity was tested with Spearman's rank correlation coefficients. We expected positive correlations with all convergent variables (i.e., CAT, HADS-Anxiety, and HADS-Depression) and negative correlations with discriminant variables (i.e., SF-12 PCS and SF-12 MCS). Reliability was assessed by computing Cronbach's α. A confirmatory factor analysis was conducted to evaluate whether the factor structure of the CAF-R-DK corresponded to the original CAF-R. If a less than acceptable fit was obtained, a supplementary exploratory factor analysis was performed to evaluate the number of latent variables/subdomains of the CAF-R-DK, and whether individual items belonged to subdomains other than those hypothesized by the original CAF-R. Bartlett's test of sphericity (Bartlett, 1951) and Kaiser-Meyer-Olkin (KMO) sampling adequacy (Kaiser, 1974) were calculated to ensure that factor analysis was appropriate.

RESULTS

In the period from May to September 2020 a total of 260 participants completed the questionnaire package. Respondents for electronic and paper-based completion were recruited in parallel. A total number of 333 individuals opened the link to the online questionnaire, resulting in 238 (71.5%) completed electronic responses. The remaining responses (n = 22) were paper-based. See **Table 1** for an overview of participant characteristics.

Reliability and Construct Validity

Correlation coefficients of all validity and reliability analyzes can be found in **Table 2**. The CAF-R-DK total score and all individual domain scores showed acceptable to excellent reliability with Cronbach's α ranging from 0.77 to 0.89. All convergent and discriminant construct showed the expected direction of the correlations (positive correlations for convergent constructs versus negative correlations for discriminant constructs). Correlations with convergent constructs were all moderate to strong (r = 0.39–0.69). The discriminant construct of SF-12 PCS was weakly correlated with the CAF, compared to the SF-12 MCS (PCS r = −0.04 to −0.30; MCS r = −0.43 to −0.67).

Internal Consistency

The p-value for Bartlett's test of sphericity was < 0.001 and the KMO measure of sampling adequacy was 0.907, which were both sufficient for conducting factor analysis (Bartlett, 1951; Kaiser, 1974).

A confirmatory factor analysis was conducted to test whether the structure of the CAF-R-DK corresponded to the original version of the questionnaire. The root mean square error of approximation was 0.087 (CIs: 0.077–0.097; p = 0.000), the Comparative Fit Index was 0.911, and the Tucker-Lewis index was 0.894, which altogether indicate a less than acceptable fit (Fan et al., 1999).

Hence, a polychoric exploratory factor analysis with oblique rotation was conducted with the purpose of exploring whether the number of latent variables in the CAF-R-DK was different from those identified in the original version of questionnaire, or whether the individual items loaded on different latent variables than described. Horn's parallel analysis (Dinno, 2009), together with a scree plot, was conducted with the purpose of assessing the number of latent variables, and the existence of five factors in the questionnaire was confirmed (see graph in **Supplementary Material 2**). **Table 3** shows the factor loadings for each individual item in the CAF-R-DK. For factors 2–5, the loading of the individual items of the CAF-R-DK were comparable to those of the original questionnaire. However, items originally belonging to the subscales of Fear of dyspnea (e.g., "When I get short of breath I am afraid that I will suffocate"), Fear of physical activity (i.e., "I plan the route in detail before I go for a walk"), and Fear of progression (i.e., "I am afraid that my breathing problems will become worse") all loaded on the same factor (factor 1) in the present dataset.

Missing Values

An overview of missing values per item can be found in **Table 3**. Number of missing values for each item in the CAF-R-DK varied from 16 (6.2%) on Item 8 ("I avoid activities that make me sweat") to 21 (8.1%) on Item 18 ("I fear that I will eventually become dependent of care from others because of my illness"). Compared to electronic questionnaire responses, paper-based responses had a very low number of missing items, with only one participant missing one item (Item 1).

DISCUSSION

It has been proposed that many patients with COPD are living with unrecognized symptoms of anxiety due to the poor availability of instruments measuring disease-specific anxiety in this population (Yohannes and Lavoie, 2013; Breland et al., 2015; Larsen et al., 2021). The COPD Anxiety Questionnaire (CAF) is an example of a COPD-specific anxiety instrument that has been developed in German language, but is still not available in multiple languages. For the purpose of the present study, we translated the short version of the CAF (CAF-R) into Danish (CAF-R-DK) and performed an initial validation of its psychometric properties in a sample of 260 patients with COPD across all degrees of obstructive lung function impairment (mild, moderate, severe, and very severe).

The results of the present study indicated that the CAF-R-DK showed acceptable to excellent reliability with Cronbach's α scores of subscales ranging from 0.77 to 0.89, which are also comparable with reliability scores of the original questionnaire (Cronbach's α of subscales: 0.78–0.87 (Keil et al., 2014).

With respect to construct validity, the CAF-R-DK showed positive correlations with converging constructs [COPD-symptoms level (CAT), general symptoms of anxiety (HADS-Anxiety), symptoms of depression (HADS-Depression)] and negative correlations with discriminant constructs [physical quality of life (SF-12 PCS), mental quality of life (SF-12 MCS)], as expected. Concerning the individual converging constructs, the total score of the CAF-R-DK showed higher correlations with the HADS-depression scale (r = 0.69), compared to the HADS-anxiety scale (r = 0.62). This is surprising, as the construct of disease-specific anxiety was expected to correlate relatively more with general symptoms of anxiety, compared with symptoms of depression. A possible explanation could be that the correlation with symptoms of depression are driven by the specific CAF-subdomains Fear of social exclusion (r = 0.57) and Fear of physical activity (r = 0.59), which include items such as "I feel let alone with my illness" and "I avoid all kinds of physical activity". Such items could be interpreted as expressions of hopelessness and lethargy, respectively, which are characteristic of depressive states (Osler, 2021). Moreover, the converging construct of COPD symptoms, measured with the CAT, also showed a relatively higher correlation (r = 0.67) with the CAF-R-DK total score, than the HADS-Anxiety. This was especially the case for the CAF-subdomains of Fear of physical activity (r = 0.60) and Sleep-related worries (r = 0.62), the latter consisting of items such as "The sound of my breathing or coughing wake me up at night". The wording of such items could be more indicative of physical symptom level than of anxious symptom interpretation, which may explain the higher correlation of the CAF-R-DK with COPD symptom level than with general symptoms of anxiety. On the other hand, when inspecting correlations of the CAF-R-DK with the discriminant constructs of physical and mental quality of life, all subdomains of the CAF-R-DK showed considerably stronger correlations with the mental component score of the SF-12 ($r = -0.67$), compared with the physical component score ($r = -0.18$). This finding supports CAF-R-DK as measuring the predominantly psychological, not physical, construct of disease-specific anxiety. Taken together, the present study results indicate that disease-specific anxiety in COPD can be understood as a psychophysiological construct, including and correlating strongly with physical symptoms and sensations (O'Donnell et al., 2007; Ora et al., 2010; Hanania and O'Donnell, 2019). However, the results could also be indicative of relatively poor construct validity and wording of individual items in the CAF, which should be kept in mind when applying the questionnaire and interpreting its results in future studies and clinical practice. As the present study did not perform a direct comparison between the original version and the Danish translation of the questionnaire, it is unknown whether these findings are true only for the CAF-R-DK, or whether they could be extrapolated to the CAF more generally. However, the developers of the original version of the CAF (Kühl et al., 2011) appear to have collected relatively limited data for the conceptualization of disease-specific anxiety prior to designing the questionnaire, i.e., five patient interviews and items from the Cardiac Anxiety Questionnaire (Eifert et al., 2000), which may have compromised the construct validity of the questionnaire. In addition to cardiac-related anxiety, the construct of disease-specific anxiety in COPD may also share features with anxiety in asthma, measured with the Asthma-Related Anxiety Scale (Bruzzese et al., 2011). Moreover, in other to determine the specific characteristics of anxiety in COPD in the future, a mapping of shared and distinctive features of anxiety in COPD, asthma, cardiac disease, multiple sclerosis and other diseases that are characterized by chronic impairment and a high risk of acute symptom worsening (i.e., exacerbations; attacks) is needed (Murray et al., 2005).

Furthermore, concerning the internal consistency of the CAF-R-DK, the initial confirmatory factor analysis of the structure of the original version of the questionnaire did not result in a good fit to the data in the present study. In the subsequent exploratory factor analysis, the five-factor structure of the questionnaire was confirmed, but individual items that belonged to the Fear of physical activity (i.e., "I plan the route in detail before I go for a walk") and Fear of disease progression (i.e., "I am afraid that my breathing problems will become worse") subscales in the original version of the questionnaire loaded on the Fear of dyspnea scale (e.g., "When I get short of breath I am afraid that

TABLE 1 | Participant characteristics.

Total sample (*n* = 260)	**Mean**	**SD**	***N***	**%**
Age	65.0	9.0		
Female gender			179	68.8
Obstruction (FEV1% pred.)				
Mild (>80%)			8	3.1
Moderate (50–80%)			62	23.8
Severe (30–50%)			85	32.7
Very severe (<30%)			89	34.2
Smoking status				
Current smoker			36	13.8
Previous smoker			196	75.4
Never smoker			9	3.5
Living alone (vs. living with a partner)			115	44.2
LTOT users			39	15.0
mMRC dyspnea	2.3	1.1		
CAT total	19.6	7.2		
HADS total	14.0	7.9		
SF-12 PCS	30.0	7.2		
SF-12 MCS	43.9	12.8		
CAF-R-DK-total	39.7	15.4		
CAF-R-DK-FSE	8.0	3.9		
CAF-R-DK-FD	9.1	4.4		
CAF-R-DK-FPA	10.2	5.2		
CAF-R-DK-FP	10.2	4.1		
CAF-R-DK-SRW	2.2	1.8		

CAF-R, COPD anxiety questionnaire revised; CAT, COPD assessment test; FEV1% pred, forced expiratory volume in 1 second,% of predicted value; FD, fear of dyspnea; FP, fear of progression; FPA, fear of physical activity; FSE, fear of social exclusion; HADS, hospital anxiety and depression scale, range 0–42, higher score means more psychological distress; LTOT, long term oxygen therapy; mMRC, modified medical research council dyspnea scale, range 0–4, higher score means more dyspnea; SF-12, 12-item short form survey; PCS, physical component score; MCS, mental component score, range 0–100; higher score means; SRW, sleep-related worries.

TABLE 2 | Validity and reliability of the chronic obstructive pulmonary disease-anxiety questionnaire revised – Danish version (CAF-R-DK).

	CAF-R-DK FSE	CAF-R-DK FD	CAF-R-DK FPA	CAF-R-DK FP	CAF-R-DK SRW	CAF-R-DK-total
Validity (convergent constructs)						
CAT	0.44	0.56	0.60	0.46	0.62	0.67
HADS-Anx	0.46	0.60	0.43	0.55	0.43	0.62
HADS-Dep	0.57	0.53	0.59	0.55	0.39	0.69
Validity (discriminant constructs)						
SF-12 PCS	−0.12	−0.07	−0.30	−0.11	−0.04	−0.18
SF-12 MCS	−0.52	−0.55	−0.53	−0.56	−0.43	−0.67
Reliability (internal consistency)						
Cronbach's α	0.87	0.85	0.89	0.87	0.77	-

CAF-R-DK, COPD anxiety questionnaire revised – Danish version; CAT, COPD assessment test; FD, fear of dyspnea; FP, fear of progression; FPA, fear of physical activity; FSE, fear of social exclusion; HADS, hospital anxiety and depression scale; SF-12, 12-item short form survey; PCS, physical component score; MCS, mental component score; SRW, sleep-related worries.

TABLE 3 | Factor loadings of items from the chronic obstructive pulmonary disease-anxiety questionnaire revised – Danish version (CAF-R-DK).

Item	Subscale in original questionnaire	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Missing n (%)
1	SRW	−0.0078	0.0014	0.0133	0.0643	**0.7767**	19 (7.3)
2	FPA	0.0144	**0.8965**	−0.0285	−0.1335	0.0825	17 (6.5)
3	FSE	0.0958	0.0121	**0.8594**	−0.1324	−0.0404	17 (6.5)
4	FD	**0.8300**	−0.0087	−0.0599	−0.0802	0.2312	18 (6.9)
5	FPA	**0.3667**	**0.3667**	−0.0910	0.1400	0.1109	18 (6.9)
6	FP	0.0836	0.0914	−0.0287	**0.7065**	0.0862	19 (7.3)
7	FSE	−0.0976	0.2109	**0.6512**	0.0692	0.0286	16 (6.2)
8	FPA	−0.0432	**0.8412**	0.0974	0.0363	0.0421	16 (6.2)
9	FD	**0.4163**	−0.0644	0.1889	−0.1005	0.3174	17 (6.5)
10	FP	**0.5491**	0.1275	0.1424	0.2417	−0.3232	17 (6.5)
11	FD	**0.4736**	0.0039	0.1642	0.0477	0.1246	19 (7.3)
12	FSE	−0.0990	−0.0564	**0.8428**	0.1408	0.0944	17 (6.5)
13	FD	**0.8351**	−0.0254	0.0315	0.0809	0.0369	19 (7.3)
14	FSE	0.0850	0.0116	**0.8162**	0.1009	−0.0651	19 (7.3)
15	FPA	0.0242	**0.9205**	0.0668	−0.0362	−0.0712	20 (7.7)
16	SRW	−0.0597	0.0793	−0.0285	0.0459	**0.8131**	19 (7.3)
17	FP	−0.0061	−0.0846	0.0736	**0.9066**	0.1077	20 (7.7)
18	FP	0.0625	−0.0233	0.0207	**0.9034**	−0.0212	21 (8.1)
19	FPA	0.0087	**0.9276**	−0.0652	0.0551	0.0290	20 (7.7)
20	FD	**0.8509**	0.0664	−0.0017	0.1383	−0.1764	20 (7.7)

CAF-R, COPD anxiety questionnaire revised; CAT, COPD assessment test; FD, fear of dyspnea; FP, fear of progression; FPA, fear of physical activity; FSE, fear of social exclusion; SRW, sleep-related worries.Notes: The highest factor loading for each item on the CAF-R-DK, thus identifying a factor, is marked in bold.

I will suffocate") in the present study. The results do not allow for any conclusions as to whether these differences stem from language- or cultural differences between the German and Danish version of the questionnaire or whether they are resulting from a suboptimal scale construction of the original version of the CAF. However, researchers and clinicians should be aware that it can be difficult to differentiate certain latent variables of disease-specific anxiety, and there may be significant overlap between the experience of fear of dyspnea, fear of physical activity, and fear of disease progression.

When inspecting the number of missing answers for the items in CAF-R-DK, there was a relatively high proportion of missing values across all items (6.2–8.1%). As 16 respondents (6.2%) missed the entire CAF-R-DK, the missing responses are less likely to be a result of poor understanding of individual items. Missing values were predominantly observed for the electronic responses, while only one participant missed one item in the paper-based responses. This may speak to an increased feasibility of the paper-version of the CAF-R, but it also stands in contrast to other studies, showing a higher number of missing in paper-based responses (Palen et al., 2008; Shih and Fan, 2009), and the feasibility of electronic vs. paper-based questionnaire formats appears to depend on the specific respondent population (Shih and Fan, 2009). Hence, the relatively high missing rates in the electronic responses of the present study should not prevent researchers from using the electronic format in future studies. However, "forced responding" in the electronic version of the CAF could be considered (Nayak and Narayan, 2019).

Clinical Implications

The results of the present study expand the availability of instruments for the assessment of disease-specific anxiety in COPD, which is relevant for psychological screening in routine care, e.g., rehabilitation clinics, general practice, and outpatient hospital visits. In a study by Hardy et al. (2014), primary care nurses were trained in following a systematic psychological screening and intervention pathway during the annual review of 35 patients with COPD. The results of their evaluation showed that 75% of the patients felt pleased about being asked questions regarding depression and anxiety, while the remaining patients reported that they had no particular feelings. Moreover, 91% reported that they felt more motivated to manage their symptoms after the screening and consultation with the nurse. On the other hand, screening and assessment of anxiety in clinical practice can be obstructed by certain barriers among healthcare professionals. In an editorial, Heslop-Marshall and Burns (2019) present three important barriers: (1) Clinicians may not recognize the scale of the problem, assuming that the symptoms of anxiety is a natural part of the 'psychological makeup' of the patient with COPD; (2) Clinicians may consider psychological symptoms to be outside their professional remit; (3) Access to appropriate therapy and availability of trained therapists are scarce, and clinicians may therefore consider identification of psychological symptoms pointless. The results of the present study do not allow for conclusions it terms of (barriers to) the practical use of the CAF-R-DK, and it is therefore important to address such barriers in future research with the purpose of achieving and optimal implementation of psychological screening procedures in clinical practice.

Moreover, when applying instruments such as the CAF, clinicians should be aware that a high CAF-score is not necessarily equal to high level of general symptoms of anxiety or to the presence of a mental *disorder*, e.g., panic disorder, generalized anxiety disorder, social phobia, and post-traumatic stress disorder, for all of which a high prevalence rate has been demonstrated in COPD (Yohannes et al., 2010; Willgoss and Yohannes, 2013; Ouellette and Lavoie, 2017). Disease-specific anxiety and accompanying, maladaptive avoidance or safety behaviors could potentially increase the *risk* of developing an anxiety disorder, but future studies, including diagnostic interviews, are needed to confirm the relationship between disease-specific anxiety and the development of anxiety disorders and other mental disorders in COPD.

Strengths and Limitations

The present study has several strengths. First, owing to the electronic participation option, the study is based on a large sample of patients with COPD with all degrees of obstructive lung function impairment (mild, moderate, severe, and very severe), including a considerable proportion of long-term oxygen therapy users (15%) who can be difficult to reach for research purposes. Second, the translation of the CAF-R into Danish is based on a comprehensive and systematic approach, which ensures a high-quality version of the questionnaire ready for application in the Nordic countries. Third, taking a comprehensive approach to measurement, the questionnaire package of the present study includes several relevant scales that allows for assessment of associations with both convergent and discriminant constructs.

However, a number of limitations should also be noted. First, the questionnaire format, i.e., electronically versus paper-based, were applied in two different recruitment setups, i.e., patient organization versus outpatient clinic, and a direct comparison of the response formats could therefore not be performed. Studies using random assignment to electronic versus paper versions of the questionnaire are needed to test whether the response format impacts the validity of the questionnaire. Second, due to recruitment anonymity for online respondents, and with the purpose of limiting participation burden for patients in the present study, the single measurement design did not allow for assessment of test-retest reliability of the questionnaire. A more comprehensive testing of the psychometric properties of the CAF-R-DK is needed to confirm longitudinal, predictive validity and reliability. Third, while the CAF is currently the only existing instrument measuring COPD-specific anxiety beyond fear of dyspnea, the quality of the questionnaire can be criticized: (a) The initial conceptualization of the construct of COPD-specific anxiety was based on five patient interviews (Kühl et al., 2011), which can be considered as a relatively restricted database (de Vet et al., 2011). (b) The developers of the questionnaire (Kühl et al., 2011) claim that the wording of the items was based on the Cardiac Anxiety Questionnaire (Eifert et al., 2000). But very few similarities between the wording of the two questionnaires can be found, and several items of the CAF does not adhere to suggested standards for item wording (e.g., avoiding negative wording; items should be specific) (de Vet et al., 2011). (c) The questionnaire has not been translated into English, leading to relatively limited application and testing of the questionnaire worldwide. Lastly, due to the experiential nature of the construct of anxiety, it is not possible to validate the scale against a "gold standard," objective measurement method, which prevents the analyzes of predictive validity as well as the determination of a clinically significant cut-point. Future studies could benefit from performing a direct comparison between CAF scores and diagnostic interviewing by a mental health specialist.

CONCLUSION

A Danish version of the COPD-Anxiety Questionnaire (CAF-R-DK) is now available for the assessment of disease-specific anxiety in Danish-speaking patients with COPD. The CAF should not be used as an alternative to screening for symptoms of anxiety in general, but can be applied as an important supplement to the Hospital Anxiety and Depression Scale (HADS) (as an example) with the purpose of identifying relevant areas of disease-specific anxiety that might act as barriers for outcomes of rehabilitation programs. There might be general inconsistencies in the construct validity of the CAF-R-DK and/or the CAF in general. In the future, there is a need for translation of the questionnaire into other languages with the purpose of obtaining clinical and research-based data on the psychometric properties and practical application of the CAF. Moreover, there is a need for studies that aim to test measures of disease-specific anxiety against general anxiety questionnaires and diagnostic interviews in COPD.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

IF-V had a leading role in the conception and design of the present study as well as in the data analysis and drafting of the present manuscript. SR-R had a leading role in data acquisition. ST contributed to the statistical analysis. SR-R, ST, CFC, OH, and AL contributed to the conception and interpretation of data for the work and to revising the contents of the present manuscript. All authors provided approval for publication of the content of the present manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2022.907939/full#supplementary-material

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Feasibility of telepsychology support for patients with advanced cardiorespiratory diseases and their caregivers

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Objective: The aim of this study was to test the feasibility of telepsychology support for patients with severe cardiorespiratory disease and their caregivers. A secondary objective was to explore pre-post relationships between patients' and caregivers' clinical measures.

Methods: A telehealth program incorporating telepsychology support, i.e., an "on-demand" phone service with a psychologist, was provided to consecutive cardiorespiratory patients at discharge from inpatient rehabilitation and to their caregivers. At the start and end of the 1-year program, participants were interviewed "face-to-face," and their anxiety/depression level, patients' quality of life (MRF-28, SF-36, and MQOL), and caregivers' ($n = 18$) family strain (FSQ) and needs (CNA) were assessed: we analyzed the correlations and evaluated customer satisfaction.

Results: Of 80 eligible individuals, 40 took part in this study: 22 patients (FVC $= 39 \pm 14\%$; EF $= 39 \pm 13\%$) and 18 caregivers. Eleven (28%, 6 patients and 5 caregivers) requested tele-psychological support, resulting in 51 consultations focused on anxiety, difficulty in patient management, worry about the patient's emotional state, and need for emotional support; 3 participants underwent a tailored psychotherapy program. All participants expressed high satisfaction with the service. At enrolment, anxiety was less evident in patients (73% men) than in caregivers, while depressive symptoms were more evident (6.5 ± 3.1), and correlated with MRF-28 and MQOL. Caregivers' (94% women) FSQ showed a "strongly recommended" need for support; at enrolment, high levels of anxiety/depression were correlated with high FSQ (for both, $p < 0.05$); depressive symptoms correlated negatively with age ($p = 0.025$) and positively with emotional needs ($p = 0.025$); anxiety was positively correlated with education level ($p = 0.048$). At follow-up, patients' perception of support ($n = 13/22$) tended to increase ($p = 0.089$), while caregivers' strain ($n = 10/18$) tended to decline (to within the "range of attention"). At enrolment, caregivers' anxiety/depression and strain correlated with patients' quality of life (for both; $p < 0.05$). At follow-up, caregivers' strain correlated with patients' quality of life ($p = 0.028$) and cognitive performance ($p = 0.048$).

Conclusion: Telepsychology support associated with a telehealth service is feasible and satisfying for both participants and psychological management. A suitable support program can benefit both patients and caregivers, particularly those at higher risk of depressive symptoms (younger caregivers) and anxiety (all caregivers).

KEYWORDS

COPD, cardiorespiratory, rehabilitation, heart failure, telepsychology

Introduction

In recent years, there has been an increased focus on the management of cardiorespiratory diseases from a palliative point of view. Patients with advanced Chronic Obstructive Pulmonary Disease (COPD) and Chronic Heart Failure (CHF) require a specific dedicated approach due to their frequently impaired health status (Janssen et al., 2011) and uncertain prognosis with variable disease progression over time. Previous studies suggest that the health status of these patients may be even more impaired than that of patients with incurable cancer (Gore et al., 2000; O'Leary et al., 2009). Early identification of the clinical correlates of impaired health status can allow clinicians to modulate the therapeutic plan to stabilize the disease-specific health status and intervene more effectively through a better understanding of patients' needs (Gardiner et al., 2010; Gardener et al., 2018).

In a previous study (Vitacca et al., 2019), we showed the efficacy of a post-discharge telenursing program that offered patients with advanced COPD and CHF the availability of a specialist second opinion. It helped to satisfy patients' need to understand and manage better their symptoms and medication, reduce hospitalizations, support a healthy lifestyle, and enable prompt intervention where necessary. Access to the service and navigating it was easy, and patients could discuss end-of-life planning. Nevertheless, several signs emerged of diminished health status (general and disease-specific) in these patients. They included important psychological features such as anxiety, depression, and the ability to cope with feelings/worry and to try to live positively with the disease, think about the future, and support the family's needs (Gardener et al., 2018). It is well-known that symptoms of anxiety, depression, and care dependency are correlates of general and disease-specific health status in advanced COPD and CHF (Yohannes, 2007; Janssen et al., 2011; von Leupoldt and Kenn, 2013), and the psychological aspect plays an important role in the course and management of disease, not only for patients but also for their caregivers. Functional and emotional impairment has significant consequences for patients and their families: dependency on caregivers may lead to frustration, depression, and social isolation, increasing the burden on caregivers and their psychological sufferance (Fitzsimons et al., 2007).

For this reason, primary aim of this study was to test the feasibility of a model of telepsychology support offered on-demand to patients with advanced COPD and CHF and their caregivers. As a secondary aim, we wished to explore the changes at follow-up in all participants and in the patient-caregiver relationship through scales administered pre-post intervention by the psychologist assessing the self-reported quality of life, anxiety and depression symptoms, caregiver strain, and needs.

Methods

Study design

This was a prospective longitudinal study on the feasibility of a telemedicine service making psychologist support available for adult patients with severe cardiorespiratory at an advanced stage of disease following discharge from the hospital. The psychologist support service approached the "Nuove Reti Sanitarie" telehealth program managed by the Maugeri Center for Telehealth and Telecare (MCTT) (Scalvini et al., 2018). Patients were consecutively enrolled in the program following their discharge from the Rehabilitation Unit of the Istituti Clinici Scientifici Maugeri, IRCCS, Institute of Lumezzane (BS), Italy, where they had undergone a period of standard rehabilitation between October 2017 and May 2019. A previous report on the MCTT service focused on monitoring palliative care and including a few patients with COPD as a life-limiting disease showed its feasibility (Vitacca et al., 2019).

Eligibility criteria: Patients and caregivers

Clinical criteria for patients' eligibility for the "Nuove Reti Sanitarie" telehealth program were as follows:

1. Patients with cardiac problems, NYHA class II-IV, heart failure or ventricular dysfunction, and ejection fraction <50% and at least one admission to the hospital in the previous 6 months;
2. Patients with respiratory problems, GOLD III-IV, and on long-term therapy with oxygen for at least 3 months.

Exclusion criteria were as follows: patients unable to be discharged home from the hospital; refusal to participate; and cognitive decline (MMSE <20).

At the time of the patient's admission to the program, the psychologist contacted their caregivers and proposed to them the same service of psychological support "on-demand." Therefore, based on whether they agreed or declined, the study participants could be patients with their caregivers, or patients (or caregivers) separately. This study was approved by the institutional Ethics Committee (CE2108, 11 July 2017). All participants gave their signed informed consent to participate in the study.

Intervention

At discharge from the hospital, patients were enrolled in "Nuove Reti Sanitarie," which is a 6-month tele-assistance multidisciplinary support program designed to clinically follow patients at home and monitor their clinical problems, through telephone consultations managed by a nurse tutor. Patients can call the nurse if in clinical need (the service is available 24/7). Details on the tele-assistance are reported elsewhere (Scalvini et al., 2018; Vitacca et al., 2019). To better manage the patient, the MCTT program envisages the psychologist's collaboration with the nurse tutor and, if necessary, the clinician. The nurse tutor can also call on the psychologist to intervene in managing the patient's problems. Moreover, GPs are aware of the MCTT service and can be contacted by the psychologist, in particularly serious cases. Besides the patients, the psychologist also considers the patient's caregiver as a frail individual needing support when the patient is discharged home.

In this study, featuring the addition of telepsychology support directly to the participants for 1 year, at the time of the patient's discharge, the psychologist conducted an in-hospital "face-to-face" interview only with those patients/caregivers who adhered to the project. The aim was to collect clinical information and explain the modality of interaction with the telepsychology service. Tests assessing anxiety, depression, and quality of life were also administered. If warranted, the psychologist could suggest a tailored support program (clinical intervention).

Once at home, all participants could, if they needed any psychological help, call the psychologist. The psychologist was available to receive calls at all times (24/7). Such "on-demand" calls were independent of the scheduled phone calls performed by the nurse tutor in MCTT. The phone appointment was agreed on according to the psychologist's full availability and the patient's or caregiver's preferences. To reduce the sense of isolation and increase the perceived support, caregivers were also offered the possibility to join a monthly help group, in order to share experiences with others in a similar situation.

The duration of the psychology service was 1 year from the start (T0) for both patients and caregivers. All participants were reassessed at the end of the program (T1) in the hospital by the same psychologist using the same tools/assessments performed at T0.

Feasibility

We evaluated the feasibility of the service in terms of participants' satisfaction. Customer satisfaction was assessed at the end of the program. We recorded the percentage of patients who agreed to do the program and their satisfaction, at the end of the program, with the service overall and with the psychologist's support (score 1= poor; 2= scarce; 3= good, and 4 = great).

Outcome measures for patients and caregivers

The following questionnaires were administered to the patients:

- *Mini-Mental State Examination (MMSE)* (Folstein et al., 1975): a 30-item questionnaire to assess the cognitive status, with a score of <24 identifying cognitive deficit.
- *Anxiety-Depression Short Scale (AD-R)* (Moroni et al., 2006): to evaluate the presence of anxiety/depression symptoms, especially in people with cardiorespiratory diseases. It consists of 15 items testing depression (cutoff >7 for men and >9 for women) and 10 items testing anxiety (cutoff >22 for men, >25 for women): the higher the score in both dimensions, the greater the presence of significant symptoms.
- *Short Form Health Status (SF-36)* (Ware et al., 1993): a 36-item patient-reported survey of patient global health divided into eight domains, namely, physical functioning, physical role limitations, bodily pain, general health, vitality, social functioning, emotional role limitations, and mental health. For each domain, scores range from 0 (worst) to 100 (best); a physical and mental component summary is provided and scores range from 0 (worst) to 100 (best).
- *The Maugeri Respiratory Failure questionnaire (MRF-28)* (Vidotto et al., 2007): a 28-item disease-specific measure of health-related quality of life for patients with chronic respiratory failure; the higher the score, the more compromised the QoL. Two indexes can be found: disability perception and impairment in daily activities.
- *McGill Quality of Life, Italian version (MQOL-It)* (Sguazzin et al., 2010): a 16-item questionnaire to assess the quality of life in palliative care; items are rated on a numeral scale from 0 to 10, with a verbal anchor at the beginning

and end of each visual scale. It has 5 domains, namely, physical symptoms, psychological wellbeing, existential area, support, and comparison with the health status of the previous year, and each domain scored from 0 (worst) to 10 (best) with a total score (0–10), which is the mean of the 5 subscales.

The following tests were administered to caregivers:

- *Anxiety-Depression Short Scale (AD-R):* as for patients (Moroni et al., 2006).
- *Family Strain Questionnaire-SF (FSQ-SF)* (Rossi Ferrario et al., 2001; Vidotto et al., 2010): a tool to assess the severity of burden in family caregivers; it consists of 30 dichotomous items, the higher the score, the more severe the strain.
- *Caregiver Needs Assessment (CNA)* (Moroni et al., 2008): to assess caregiver perceived needs related to assistance; it consists of 17 items referring to emotional needs, functional needs, cognitive-behavioral aspects, relational aspects, social needs, and spiritual ones. Each item is scored on a 4-point Likert scale from 0 (no need) to 3 (much need), giving a maximum total score of 51; two component summaries can be calculated: information/communication needs and need for emotional and social support.

Statistics

Data were analyzed using Graph Pad-Prism software (version 8 for Windows, GraphPad Software, La Jolla California USA, www.graphpad.com) and expressed as mean ± standard deviation (SD). The normality of data was tested using the Shapiro-Wilk test. A paired T-test was performed to evaluate pre-post measures in both patients and caregivers with reevaluation at follow-up. Correlation analysis was conducted using the Pearson's test. Values of $p < 0.05$ were considered significant.

Results

Feasibility

In this feasibility study, our team implemented the MCTT service with a telepsychology format, dependent on the MCTT for the patient's clinical care but independent as regards the management of the calls between the psychologist and participants. Telepsychology support was proposed to 80 individuals (patients and caregivers): 40 accepted and were eligible (50%); the 40 who declined did not give a reason (Figure 1).

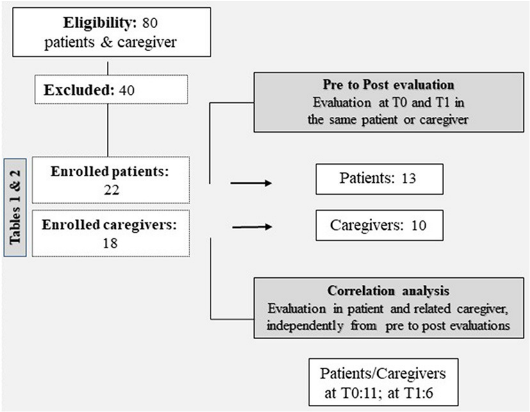

FIGURE 1
Flowchart of this study.

Among the 40 participants who agreed to take part in the program, 22 were patients (Table 1) and 18 caregivers (Table 2); the vast majority (98%) came from the province of Brescia.

All patients had a visit with the psychologist during their in-hospital stay. At the time of patients' enrolment in the program (T0), their caregivers underwent a psychological interview. The psychological tests showed 2 out of 18 caregivers to be "at risk," but they declined the psychologist's offer of a structured psychological program and opted instead for telepsychology support (in which they could call her during the year if in need).

The 18 caregivers who completed the psychology assessment were all relatives of the patient, without home help, and living with the patient, except for two. Out of 18, 11 caregivers participated in this study together with the patient, while 7 caregivers took part alone without the patient.

During the study period, 51 psychological consultations took place through phone call with 11 participants (28% of total participants), of whom 6 were patients and 5 were caregivers. The reasons for requesting a psychological consultation varied, but the interventions focused mainly on the following:

- Anxiety attacks.
- Depressive symptoms.
- Emotional problems/demoralization (fear of worsening).
- Relational problems.
- Difficulties in the patients' management.
- Discussing end-of-life topics.
- Fear of loss and grief.
- Help in the reorganization of daily activities.
- Support after re-exacerbation.

"Face-to-face" psychological support was provided to one patient, both during hospitalization and after enrolment in the program, with improvement. For 3 of the 6 patients who

TABLE 1 Clinical characteristics and evaluations in patients at admission (T0) to the telepsychology service.

Patients at T0 ($n = 22$)	Mean ± sd
Gender, M/F	16/6
Age, years	71.6 ± 5.8
Education, years	7.1 ± 2.0
MMSE, score	27.0 ± 1.9
CIRS, score	1.9 ± 0.4
FEV1*, % pred	39.3 ± 14.5
EF**%	39.4 ± 13.2
Oxygen therapy, y/n	17/5
Anxiety scale, score	16.5 ± 3.4
Percentile	34.3 ± 22.6
Depression scale, score	6.5 ± 3.1
Percentile	70.9 ± 22.8
SF-36 ISF index, score	29.1 ± 6.6
Physical activity	38.2 ± 27.0
Physical limitation	9.1 ± 22.6
Physical pain	61.7 ± 27.1
Health	28.9 ± 18.2
SF-36 ISM index, score	44.9 ± 10.2
Vitality	49.3 ± 17.1
Social activity	53.2 ± 22.2
Emotional limitation	49.9 ± 42.1
Mental health	61.1 ± 18.5
Total MRF-28, score	12.9 ± 0.6.8
MRF-28-AQ	6.3 ± 3.8
MRF-28-DP	6.7 ± 3.6
MRF-28%	49.7 ± 25.1
Global MQOL, score	7.5 ± 1.4
Physical symptoms	7.3 ± 2.0
Psychological wellbeing	6.8 ± 1.8
Esistential area	7.2 ± 1.9
Support	8.1 ± 1.8

MMSE, Mini-Mental State Examination; CIRS, Cumulative Illness Rating Scale; FEV1, forced expiratory volume in 1 second; EF, Ejection fraction; SF-36, Short Form Health Status; MRF-28, Maugeri Respiratory Failure questionnaire; MQOL, McGill's Quality of Life questionnaire. *Data available in 17 COPD patients (main diagnosis), **available in 5 cardiac patients (main diagnosis).

6/22 Patients were cardiorespiratory patients, having both diseases.

TABLE 2 Clinical characteristics and evaluations in caregivers at admission (T0) to the telepsychology service.

Caregivers at T0 ($n = 18$)	
Gender (M/F), number	1/17
Age, years	64.9 ± 11.01
Education, years	8.7 ± 4.4
Anxiety scale, score	18.9 ± 7.1
Percentile	41.2 ± 31.8
Depression scale, score	3.7 ± 2.7
Percentile	39.2 ± 24.4
Total CNA, score	30.0 ± 10.5
CNA-emotion	13.2 ± 6.8
CNA-information	16.8 ± 4.9
FSQ, score	14.6 ± 7.7

CNA, Caregiver Needs Assessment; FSQ, Family Strain Questionnaire.

contacted the psychologist, a significant decrease in anxiety (a total reduction of anxiety attacks and improvements in the anxiety score at the end of the program) and depression level was reported. For one caregiver, a psychotherapy program took place "face to face" due to privacy problems at home, with great. Only 3 of the caregivers had previous experience with a psychologist: one for cognitive impairment of a relative, one for a daughter, and one for a son (reporting a negative experience).

Unfortunately, the monthly caregiver help group did not get underway due to a limited number of participants. The main reason was not lack of interest (several manifested interest) but the distance from the hospital and the lack of help with the patient's assistance.

All participants expressed a high level of satisfaction with the service of the Telehealth and Telecare program (MCTT) reporting it to be very useful in reducing the sense of abandonment and providing a sense of security and ease of utilization. All participants who had contact with the psychologist reported satisfaction with her service. All participants, both those who contacted the psychologist and those who did not, described the psychology service as important and useful and said they would recommend it.

Patients and caregivers: Changes from enrolment to follow-up

Clinical and anthropometric characteristics of the 22 patients at T0 are reported in Table 1. Patients were mainly men (73%) and aged 63–87 years (Table 1).

The mean anxiety percentile was 34.3 ± 22.6, which is on average high but in the range of normality; only one patient had pathological values, and two were borderline. The mean depressive symptom percentile score was 70.9 ± 22.8, and 7 patients (5 out 7 were men) had scores above the significance level. The SF36 ISF index (physical index) mean score was 29.1 ± 6.6, while ISM (mental index) was 44.91 ± 10.19, showing a better mental health quality of life than a physical one, but both were below 50, i.e., below the norm. The MRF-28 mean score was 12.9 ± 0.6.8, and the MQOL mean total score was 7.5 ± 1.4, with psychological wellbeing as the lowest subscore. At T0, depression was positively related to MRF-28 score ($r = 0.7557$, $p = 0.007$), in particular to the perceived disability index ($r = 0.9329$, $p = <0.0001$); MQOL was negatively correlated with depression ($r = -0.8680$, $p = <0.001$), i.e., the lower the perceived quality of life, the higher the level of depression. MQOL was also negatively related to MRF-28, in particular to the perception of disability index ($r = -0.7766$, $p = <0.001$). Almost all patients reported worrying about their illness worsening and limitations in activities, with a reactive state of demoralization and fear of symptoms; many patients ($n = 12$) reported more social isolation.

The clinical and anthropometric characteristics of the 18 caregivers at T0 are reported in Table 2.

Caregivers were mainly women (94%) and spouses, aged on average 65 years. The mean anxiety percentile was 41.2 ± 31.8 (i.e., in the range of normality), although 5 had pathological values. Caregiver anxiety positively correlated with education level ($r = 0.606$, $p = 0.048$). The mean depressive symptom percentile score was 39.2 ± 24.4, which is in the range of normality; only one participant had a pathological value. Depression symptoms were correlated with age ($r = -0.665$; $p = 0.025$) suggesting that younger caregivers experienced more depressive symptoms and anxiety ($r = 0.713$, $p = 0.014$). Depression was positively correlated with the emotional section of the Caregiver Needs Assessment ($r = 0.666$; $p = 0.025$): the more depressive symptoms were present, the more emotive needs caregivers experienced. Almost all caregivers reported worries about illness worsening and possible difficulties in the patient's clinical and emotional management; some of them reported more social isolation ($n = 8$).

At admission (T0), total CNA was 30.0 ± 10.5 points indicating moderate-high needs. FSQ score was 14.6 ± 7.7, a value indicating that psychological support is "strongly recommended." At T0, caregivers with more anxiety and depression symptoms also had more burden/strain ($r = 0.6056$, $p = 0.048$ and $r = 0.7958$, $p = 0.003$, respectively). FSQ and CNA were positively correlated ($r = 0.8062$, $p = 0.003$), especially regarding the needs for social and emotional support: caregivers experiencing more strain recognized their need for support.

At follow-up (T1), there was a lower number of participants because some patients died or were admitted to other hospitals and their caregivers did not return to our Institute for the follow-up assessment. Out of 22, 13 patients were revisited in the hospital by the same psychologist. Evaluations were substantially unchanged, but the perception of support tended to increase (MQOL support: from 8.5 ± 1.3 to 7.7 ± 1.3, $p = 0.089$). At the same time, in 10 out of 18 caregivers, the family strain showed a trend to decrease (FSQ: from 14.6 ± 7.7 to 11.0 ± 6.0, $p = 0.07$) improving from "strongly recommended" support to within the "range of attention." Levels of anxiety and depression were substantially unvaried in all caregivers, except for two who asked for help, and whose anxiety levels decreased. In general, caregivers perceived more anxiety, while patients experienced more depressive symptoms.

Relation between patient and caregiver

At enrollment (T0), for patients enrolled together with their caregiver ($n = 11$), the patient's quality of life, especially the index of difficulties in daily activities (MRF-28 AQ), positively correlated with the caregiver's anxiety ($r = 0.675$, $p = 0.023$), depression ($r = 0.840$, $p = 0.001$), and strain (FSQ, $r = 0.646$, $p = 0.032$). The patient's MRF-28 total score also correlated with the caregiver's depression ($r = 0.733$, $p = 0.010$). At follow-up (T1), the caregiver's strain (FSQ) was significantly correlated with the patient's quality of life ($n = 6$, MRF-28 AQ: $r = 0.861$, $p = 0.028$) and cognitive performance ($n = 6$, MMSE: $r = -0.882$; $p = 0.048$).

At the end of the 1-year program, the psychologist reinterviewed all participants and readministered tests. She reported to the director of the MCTT service on the experience and planned, as an ongoing strategy, the stable inclusion of the psychologist in the MCTT, with the modalities of support and relative costs.

Discussion

Our study confirmed the acceptability, feasibility, and satisfaction regarding a tele-psychological support service provided "on-demand" for patients with advanced cardiorespiratory diseases (clinically followed by a nurse tutor as regards their palliative needs) and their caregivers. The assessment of quality of life, anxiety, and depression symptoms in patients with severe cardiorespiratory in relation to the strain and needs of caregivers, before and after the 1-year psychology support service, confirmed the need for a dedicated figure to provide psychological support in conjunction with the MCTT team to optimize interventions.

Based on the previous literature on palliative care in patients with severe cardiorespiratory and our previous experience in supporting respiratory patients' clinical needs (Vitacca et al., 2019) at home, through the Telehealth and Telecare service (Scalvini et al., 2018), we opened this study also to caregivers to alleviate the family/caregiver strain and improve their QoL.

The availability of psychological support was agreed to by 50% and in the event requested by 28% of participants; it proved feasible and, according to what we observed, suitable psychological support could be the goal of a future study both for patients and caregivers. This is especially true for young caregivers, who could be more at risk of developing depressive symptoms, but also for all caregivers who have anxiety symptoms and high strain, or issues to discuss regarding end-of-life management.

Nevertheless, technology, age, and cultural barriers remain a restraint for elderly participants, who were not so familiar with the use of video-call programs or other open-source technological tools (e.g., such as Teams, Meet, or Zoom). In fact, the main criticism received from some older people was that they would have preferred a *face-to-face* contact to a phone call.

In planning telepsychology support for caregivers, the psychologist encouraged active caregiver engagement (providing emotional validation and eliciting/reinforcing change talk) and sought to build connections among caregivers by proposing a help group for caregivers. However, although several participants were favorable to the idea, many unmet needs remain such as the problem of assistance and support for displacement to access such services. This was the reason why the elderly caregivers could not participate in the help group. The connection among caregivers remains an important point to implement in developing such a service. While telepsychology would be easy to implement for young people smart with technology, it remains a critical point to solve for older participants.

In this study, 11 participants asked for a psychological consultation for various reasons, such as anxiety attacks, anxiety, and depressive symptoms, worries about the patient's emotional state, need for emotional support, difficulties in patient management, fear of loss, and grief. Participants who received psychotherapy support benefitted from an increase in wellbeing. At follow-up, the family strain showed a trend to decrease, while patients' perception of support tended to increase. All participants reported high satisfaction with the service; in particular, they saw it as very useful in reducing the sense of abandonment and giving a sense of security, and they declared it was easy to utilize.

Customer satisfaction with the overall service and with the psychological support in particular confirmed a high/very high satisfaction in all cases.

Concerning the psychologist's experience with the service, it was very positive in which, during this program, she encountered a particular niche of people. Most of them lived in valleys surrounding Brescia that were isolated for very long, which contributed to creating a more reserved outlook in which the psychologist was seen as the profession that deals with severe psychiatric problems, with a subsequent fear of stigma. Of the participants eligible for the study, 50% agreed to participate and approximately one-third received support from the psychologist. This is a very good result for the cultural and age reasons mentioned earlier. Things are changing today, with more opportunities to have access to a psychologist without fear of stigma.

In light of these findings, the director of the MCTT is evaluating the stable inclusion of the psychologist in the MCTT as an ongoing strategy and its relative costs. The status of future reimbursement for telepsychology service delivery is uncertain but, given its potential to reduce barriers, it needs to be adequately evaluated.

Our study also confirms previous reports in the literature (Janssen et al., 2011) that patients with advanced COPD and CHF have an impaired health status, a clearly lower quality of life, and a high level of anxiety, but especially higher depression symptoms. Although it was suggested that female patients with COPD had higher levels of anxiety and depression symptoms (Di Marco et al., 2006), this study showed a prevalence of depressive symptoms in men. Depression is correlated with the patient's quality of life: we think that the closure of possibilities, such as the impairment in physical and daily activities, with the consequent state of more dependency and social isolation, may have led from reactive demoralization to a state of depression. In fact, patients reported worries about physical limitations, increased dependency, and fear of worsening.

However, the average palliative care quality of life (MQoL) was quite high. If compared with the general population (SF36), the quality of life is clearly lower, but the quality of life specifically related to the palliative context appears better. This seems to adequately capture the awareness of being in a state of impairment but of receiving adequate management for the end-of-life period. Caregivers had a higher level of anxiety than patients, but lower depressive symptoms; they in fact reported worries about the patient's worsening and fear of not being able to manage the patient's symptoms.

Moreover, anxiety correlated with education level, suggesting that a higher education level can lead to being more informed and aware. Anxiety may arise in caregivers who, afraid of seeing their beloved suffering, feel inadequate to manage the clinical and emotional problems and fear losing them. Our study also found that younger caregivers are at higher risk of developing depressive symptoms, which may be a reaction to social isolation and limitation in activities, and depression was related to more emotional needs. Thus, more attention should be paid to the younger caregiver in assessing emotional symptoms, needs, and early intervention. This study confirmed the presence of high strain and burden in caregivers of patients with COPD and CHF, as reported in the literature (Luttik et al., 2007; Janssen et al., 2012; Cedano et al., 2013; Malik et al., 2013; Miravitlles et al., 2015).

It also confirmed the relation between high family strain levels and depression and anxiety, as reported elsewhere (Saunders, 2008). Importantly, this study highlights that caregivers felt more anxiety, depression symptoms, and strain when patients reported a low quality of life. Thus, it seems important to early assess patients and offer appropriate support for their needs in order to preserve their QoL as much as possible and to monitor/support caregivers in order to maintain the wellbeing of both. It is important to offer adequate support early to caregivers to maintain an acceptable QoL and reduce anxiety/depressive symptoms, in order to help caregivers reduce their strain and have a good influence on patients (Janssen et al., 2012), creating a virtuous circle. Moreover, the correlation between the patient's cognitive status and caregiver strain confirmed that low cognitive performance in patients increases the difficulty for caregivers to manage the clinical and emotional situation, i.e., increases the caregiver burden.

Gardener et al. (2018) identified, in patients with COPD and their relatives, 13 domains of support needs in COPD that are valid other clinical conditions: understanding the disease, managing symptoms and medication, maintaining a healthy lifestyle, managing feelings and worries, living positively with the disease, thinking about the future (including end-of-life planning), limiting anxiety and depression, obtaining practical support, managing finance/work/housing, developing family and close relationships, social and recreational life, maintaining independence, and ease in navigating the service. This psychological service within MCTT aims to address many of these needs. Obviously, further development is necessary to try to be as inclusive as possible.

Limitations

This study has some limitations. First, the sample of participants was limited, resulting in insufficient statistical power in the pre-post analysis. Second, the phone as a medium for communication meant that many body language indicators of active listening and eye contact were difficult for the psychologist to perceive; a video call would enhance nonverbal communication. A further limitation was the nonavailability of an in-house transportation service for participants to access the hospital.

Conclusion

Our study suggests that telepsychology support associated with a telehealth and telecare service is feasible for clinicians and participants. Participants expressed high satisfaction with the service provided by the psychologist–it was particularly important in reducing the sense of abandonment and providing an easy way to solve needs. Based on these observations, a suitable supportive program should be the goal of future research, in seeking to early evaluate and respond to patients' and caregivers' needs. Improving the QoL is especially important for young caregivers who may be at more risk of developing depressive symptoms, but for all caregivers, it is important to reduce their anxiety symptoms and high level of strain.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Istituti Clinici Scientifici Maugeri CE2018, 11 July 2017. The patients/participants provided their written informed consent to participate in this study.

Author contributions

LG and MV designed this study, collected and evaluated data, and prepared and critically reviewed the manuscript. LC performed the literature search, statistical analysis, and prepared and critically reviewed the manuscript. IT and SS collected data and critically reviewed the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Study protocol of a randomized controlled trial of motivational interviewing-based intervention to improve adherence to continuous positive airway pressure in patients with obstructive sleep apnea syndrome: The MotivAir study

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Objective: This study aims to evaluate the effectiveness of the MotivAir program—a phone-based intervention based on Motivational Interviewing (MI) principles and techniques—in enhancing adherence to Continuous Positive Airway Pressure (CPAP) therapy among patients with Obstructive Sleep Apnea Syndrome (OSAS).

Methods: A multicenter randomized controlled trial (RCT) design with random allocation at the level of the individual will be conducted to compare the impact of the experimental program (usual care *plus* MI) with a control group receiving usual care only in improving selected clinical and psychological parameters in the patients. A minimum sample of 80 participants (40 patients per group) will be recruited in each center according to the inclusion criteria. After the initial screening, participants will be randomly assigned to either the experimental group or the control condition. The program will last 180 days and will be delivered by a trained nurse. The impact of the MotivAir program on selected primary (adherence to CPAP in terms of average hours of usage per night and the Apnea-Hypopnea Index, AHI) and secondary (motivation, perceived competence, quality of life, sleepiness) outcomes will be measured at baseline, and after 1-, 3-, and 6-month from CPAP initiation.

Discussion: Participants are expected to show an increased level of adherence to CPAP and to acquire the skills and self-confidence necessary to deal with the psychological consequences of their chronic condition.

KEYWORDS

sleep disorders, obstructive sleep apnea syndrome, continuous positive airway pressure, motivational interventions, adherence to CPAP, randomized controlled trial, randomized control trials (RCTs)

Introduction

Obstructive sleep apnea syndrome (OSAS) is a chronic illness characterized by a complete or partial obstruction of the upper airway. It has been demonstrated to be a risk factor for several diseases—including hypertension, impairment of cognitive functions, ischemic heart disease, and stroke (Garvey et al., 2015)—and to be correlated with other non-medical consequences—such as work-related injury, and motor vehicle crash (Garbarino et al., 2015, 2016)—that increase OSAS's clinical and economic burden. Also, persons with OSAS often exhibit a poor health-related quality of life (HRQoL) (Lo Bue et al., 2020), which has a demonstrated negative impact on physical health outcomes (e.g., negative health perceptions, increased bodily pain, and poor physical functioning) and psychosocial functioning (e.g., mood disturbance, poor academic performance, and reduced social life) of individuals with OSAS (Timkova et al., 2020). In Italy, despite the impact of OSAS is highly underestimated due to substantial diagnosis gaps—it affects 27% of the adult population, of which 65% are males (Armeni et al., 2019).

Continuous positive airway pressure (CPAP) is the first-line treatment for moderate/severe OSAS. It increases the individuals' clinical parameters and HRQoL by eliminating daytime sleepiness, and also decreases morbidity and mortality rates related to cardiovascular diseases (Luyster, 2017; Morsy et al., 2019; Lo Bue et al., 2020). Still, the effectiveness of the device is often limited by suboptimal adherence (Gay et al., 2006; Giles et al., 2006). Indeed, it has been suggested that improvements are more consistent with over 5.5 h of usage per night (Batool-Anwar et al., 2016; Bakker et al., 2019), but the literature reports that between 29 and 83% of patients enrolled in research studies use CPAP < 4 h per night (Bakker et al., 2016; Weaver, 2019) or refuse treatment (Baratta et al., 2018; Rezaie et al., 2021).

Adherence to CPAP treatment depends on several factors, including individual characteristics, features associated with the device (Crawford et al., 2014; Batool-Anwar et al., 2016) and its side effects, as well as psychological and social determinants (Crawford et al., 2014; Sanna and Lacedonia, 2018).

Understanding barriers and facilitators to CPAP adherence is vital for the development of effective interventions. Over the years, it has become evident that suboptimal adherence is largely predicted by psychological measures of behavior change—including motivation and perceived self-efficacy (Philip et al., 2018; Wong et al., 2020; D'Rozario et al., 2021). For example, in a multiethnic sample of 248 patients, self-efficacy (which describes the extent to which a patient believes that he or she is capable of attaining positive outcomes from treatment) was significantly associated with adherence to CPAP after adjusting for several other potential determinants (Wallace et al., 2013).

Motivational Interviewing (MI) is often used in healthcare settings to increase motivation to change and self-efficacy in patients with chronic illnesses (Pietrabissa et al., 2012, 2013, 2015; Pietrabissa, 2018; Nedjat-Haiem et al., 2019; Scott et al., 2019), and has a demonstrated positive impact in increasing adherence to CPAP among patients with OSAS (Miller and Rollnick, 2002, 2013; Rapelli et al., 2021). Consistent with several models of behavior change, including the transtheoretical model of change (TMC, Prochaska and DiClemente, 1983), this approach is mainly aimed at addressing the individuals' inner ambivalence to change. Expressing empathy, developing discrepancy, rolling with resistance, and supporting self-efficacy are the principles encompassed by MI on which intervention strategies with existing empirical support (Olsen et al., 2012) are based to help patients to develop specific goals and increase their readiness to change.

A few studies have considered adherence to CPAP as compliance maintained over time correlated with disease awareness and change to a healthier lifestyle (e.g., Weaver and Sawyer, 2010) but to our knowledge, even fewer are studies that address these aspects in correlation with technological advances such as telemonitoring and telephone assistance (e.g., Hu et al., 2021). However, the recent study conducted by Hwang et al. (2018) shows that telemonitoring

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Abbreviations: AHI, Apnea-Hypopnea Index; COPD, Chronic Obstructive Pulmonary Disease; CPAP, Continuous Positive Airway Pressure; ESS, Epworth Sleepiness Scale; FEV1, Forced Expiratory Volume in the 1st second; FVC, Forced Vital Capacity; MI, Motivational Interviewing; NYHA, New York Heart Association.

with automated feedback messages improved adherence to CPAP at 90 days in OSAS patients. Furthermore, beyond the single clinical and sociodemographic factors, the studies of Aloia et al. (2007) and Budhiraja et al. (2007) indicate that long-term adherence is determined by the results conquered in the first 2 weeks of treatment. In fact, telemedicine interventions and action plans provided at home are increasingly supporting patients in health communication, self-monitoring, and self-treatment. These interventions have made information easily accessible, helping patients to early detect symptoms, with more timely treatment, reduction in hospitalizations, and improved health-related quality of life (Hu et al., 2021). Furthermore, telemedicine-based interventions may be able to facilitate assisting patients with physical limitations and those who need a frequent evaluation of their health status. They also have the potential to foster greater patient engagement and less costly interventions (Hu et al., 2021). Although more research into the effectiveness of these telemedicine interventions is still needed because research in patients with OSAS is underdeveloped.

More investigations should focus on the use of the different formats of delivering motivational interventions including the use of new technologies, in fact to our knowledge results regarding the effects of remote-MI interventions for naïve patients using CPAP are still scant and inconsistent. Furthermore, only one RCT (Sparrow et al., 2010) tested the effect of a MI-based intervention using telemedicine in the long-term after 12 months from CPAP initiation, and collected interesting results. In fact, research that can effectively be provided digitally to patients with OSAS using CPAP could represent advantages and reduced costs (Appel et al., 2011; Bus et al., 2018).

Concerning the educational and formative aspects, Olsen et al. (2012) applied an educational program to naive patients that integrated the MI—which was recognized as best practice by the Agenzia di Tutela della Salute of Lombardy in Italy for the promotion of a healthy lifestyle—based on the work of Rollnick and Miller (1995) with the modifications indicated by Aloia et al. (2004) for OSAS patients.

For these reasons, we develop the MotivAir project—a phone-based motivational intervention that integrates telemedicine and telephone assistance based on MI principles and techniques to support adherence to CPAP in naïve patients with OSAS. This is the first study in Italy that will use MI-based intervention for OSAS patients by integrating telemedicine and telephone assistance and in-person sessions. Furthermore, it will be based on personalized care plans in response to the patient's profile (e.g., patient age, socio-demographic variables, and distance to hospital) and this approach could identify who needs intensive care and further increase CPAP adherence. A personalized-based intervention represents a golden standard for the cost-effective impact, but only one study has been achieved with personalization of care for patients with OSAS using CPAP.

Rudilla et al. (2021b) already showed increased compliance with the device, as well as increased self-efficacy, and quality of life in terms of daily activities, and social relationships in CPAP-naive patients with severe OSAS after receiving a personalized motivational intervention plan. The purpose of this randomized controlled trial (RCT) will be to determine whether MI-based strategies delivered by a nurse, and added to a standard pulmonary rehabilitation program, will be superior to usual care in improving adherence to CPAP. Specifically, we hypothesize that adding MI feedback to standard care will result in improved adherence to CPAP in terms of average hours of usage per night and increased Apnea-Hypopnea Index (AHI) after 90 days from CPAP initiation. We also hypothesize that results will be maintained or increase at 6 months of follow-up and that patients will also show increased levels of motivation, perceived competence, and sleepiness.

Methods/design

The effectiveness of the MotivAir program will be assessed in a multi-center randomized controlled study with two arms: an experimental arm with TAU plus personalized MI carried out by a trained nurse (MotivAir group), and a TAU control.

The study was approved by the Ethical Committee of the Istituto Auxologico Italiano, Italy (ID: 2021_03_23_02). All procedures performed in the study will be run following the ethical standards of the institutional and/or national research committee and with the Helsinki Declaration and its later amendments or comparable ethical standards.

Study population

All patients diagnosed with OSAS and CPAP referring to the IRCSS Istituto Auxologico Italiano, San Giuseppe hospital, and San Luca Hospital will be screened for admission into the study during their first week of a pulmonary rehabilitation program. Patients will be eligible if meeting the following inclusion criteria: (1) being over 18 years old; (2) have a diagnosis of OSAS confirmed by polysomnography; (3) being recommended for treatment with CPAP; (4) being naïve to this type of intervention; (5) being fluent in the Italian Language; and (6) having signed the written informed consent to participate in the study. Exclusion criteria will be: (1) use of oxygen therapy > 2 l/min; (2) history of severe cognitive disorders; (3) history of COPD: FEV1/FVC (Tiffeneau Index) $\leq 60\%$ with FEV1 $\leq 50\%$; (4) dyspnea on exertion (Borg > 6); (5) diagnosis of Long COVID or COVID-19 infection < 4

months; (6) chronic heart failure (NYHA: Grade III and IV); (7) unstable ischemic heart disease; 8) presence of visual, or hearing impairments that will prevent the patients from following the intervention and filling in the questionnaires.

Before enrolling in the study, all patients will be informed in detail about the study criteria and procedure and will be asked to sign the consent form to participate.

Randomization procedure

Randomization will be stratified within each center through permuted randomized blocks. Randomization will take place after the baseline measurements (**Figure 1**).

Sample size calculation

A sample of 80 patients (40 in each group) will allow detection as a significant effect size of 0.67 (based on the average daily difference in apnea hours between groups) measured at the 6-month follow-up, a first type error of 0.05, a power of 80% and a drop-out of 10%. Data related to the effect size were retrieved from the PIMA study (Rudilla et al., 2021b), while the mean daily difference in apnea hours and the standard deviation were provided by the researchers. The sample size was assessed using PASS 14 software (Power Analysis and Sample Size Software (2015). NCSS, LLC. Kaysville, Utah, United States, ncss.com/software/pass).

Measures

Demographic information about age, gender, education, and civil status will be self-reported at baseline.

Clinical variables will be recorded during the initial visit with the physician and retrieved by the patients' medical records by a clinical psychologist working in the clinic, independent from the study. They will include the (1) *Epworth Sleepiness Scale* (ESS; Johns, 1991; Vignatelli et al., 2003) as a measure of daytime sleepiness. Respondents will be asked to rate, on a 4-point scale (0–3), their usual chances of dozing off or falling asleep while engaged in eight different activities. The ESS score can range from 0 to 24. The higher the ESS score, the higher that person's average daytime sleepiness; and the (2) *Apnoea-Hypopnea Index (AHI)*, which determines the presence and severity of OSAS.

Primary outcome

The primary outcomes of this study will be the participants' *adherence to CPAP therapy* (mean hours/night) and the AHI score after 180 days from the treatment beginning. CPAP usage (hours/night) will be automatedly recorded by the device, while AHI will be measured by polysomnography during follow-up visits at the hospital.

Data will be also analyzed after 30 and 90 days of treatment as a secondary outcome.

Secondary outcomes

The following psychological measures will be collected at baseline (T1), and after 1 month (T2), 3 months (T3), and 6 months (T4) from treatment beginning.

Questionnaires will be administered by a clinical psychologist working in the clinic and independent from the study.

The *Questionnaire of Evaluation of Perceived Competence in Adherence to CPAP in OSAS* (CEPCA; Rudilla et al., 2021a) will be used to assess the participants' perceived self-efficacy. It comprises 13 items grouped into three categories: knowledge of OSAS and its associated risk; expectations regarding CPAP treatment; and confidence in overcoming barriers associated with the use of the device. The scores obtained in the CEPCA are positively related to the quality of life and motivation and negatively related to daytime sleepiness.

The participants' perceived quality of life will be assessed using the *Visual Analogical Well-being Scale for apnea* (Masa et al., 2011).

Moreover, the individuals' motivation will be assessed according to the Prochaska and Di Clemente transtheoretical model of change Prochaska and DiClemente (1982). Based on the answer to a single question ["What is the level of motivation that motivates you to undertake CPAP therapy? This includes a 5-point Likert response scale (none, a little, somewhat, motivated, very motivated)?"] each patient will be classified as in the: pre-contemplation (no motivation), contemplation (low motivation), determination (some motivation), action (quite motivated), or maintenance (high motivation) motivational stage.

Procedure

Socio-demographic (age, level of studies, presence of caregiver at home), psychological (motivation and perceived competence) clinical variables (somnolence and apnea-hypopnea index), and variables concerning the time the patient spends from home to the care center and the confidence in using electronic applications will be used to classify patients' adherence to treatment as low, moderate or high, and to create a tailored motivational treatment plan for the subjects assigned to the experimental group. Patients showing low adherence will receive a more intensive care plan, than those recognized as highly compliant with CPAP use. The results are patients

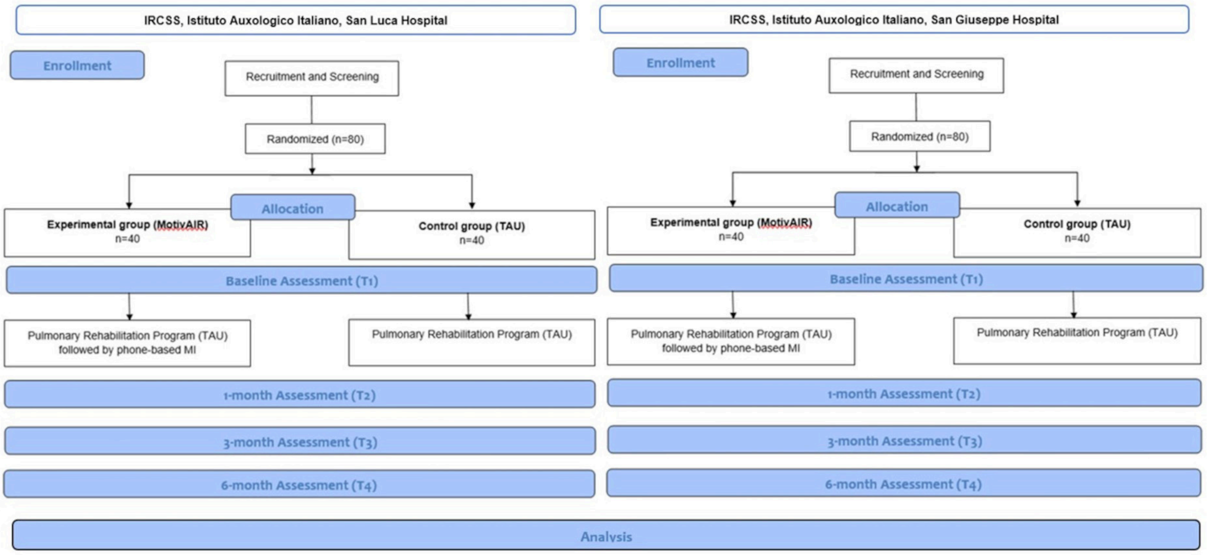

FIGURE 1
Flow chart of the MotivAIR study.

with the "a" profile (characterized by autonomy and mobility, predisposition to remote-controlled follow-up), patients with the "b" profile (need for more intensity in follow-up), or patients with the "c" profile (more difficulties to move around and require more intensive treatment). Profile "d" was applied to patients who were professional drivers, as they require specific interventions based on their occupation (see Rudilla et al., 2021b).

Participants assigned to the control group will receive a usual pulmonary rehabilitation program for patients with OSAS receiving CPAP therapy, which is a standard technical training comprising information regarding the use, maintenance and safety measures of the device, plus a home inspection delivered by a technician who has the only task of doing maintenance to the machinery.

In addition, subjects in the MotivAir group will follow a telephone-based intervention—lasting ˜45 min—based on MI principles and techniques delivered by a nurse. For the specific purpose of the study, the nurse will preliminarily receive 8 h of MI training provided by two psychologists experts in the MI approach (authors GR and GP). During the training, the nurse will learn about the collaborative, evocative, and client-centered spirit of MI, and the characteristics that define each stage of change and will be instructed to apply the basic communication and listening skills of this approach (open-ended questions, affirmations, reflective listening, summarizing). Then she will learn to reinforce and elicit change talk, while also responding in ways that reduce counter-change talk and to roll with the patients' inner resistance to change by affirming the patients' autonomy and reflecting their resistant speech with empathy. Next, the issues of how and when to introduce the development of a change plan, and enhance the individuals' commitment to change will be addressed.

The treatment plan will be implemented based on each patient's level of adherence. To low adherence (score below 16 on the ESS and CEPCA questionnaires) a more intensive telephone-based assistance (days 1, 8, 16, 30, 90, 120, 180 from the end of the rehabilitation period) will follow. In the case of high adherence (score greater than or equal to 16 on the ESS and CEPCA questionnaires), phone encounters will be set on days 1, 8, 30, 90, and 180 after treatment termination.

At 1-, 3- and 6-month follow-up, adherence to the device will be assessed by automatedly recorded CPAP usage (hours/night) and AHI. Changes in the selected psychological variable will be also examined.

Treatment fidelity

MI sessions were audio-recorded, transcript verbatim, and—some of them—randomly selected to be critically supervised by an expert in the field not involved in the study (Martino et al., 2008).

Statistical analysis

Descriptive statistics (means ± SD, or median and interquartile ranges, as appropriate) will be used to describe the study sample with regard to baseline characteristics. Before selecting the most appropriate statistical tests, assumptions for parametric analyses will be checked. Continuous variables will be reported as mean and standard deviation (or median and interquartile range when needed). Categorical variables will be reported as absolute and relative frequency. The mean daily apnea hour will be compared between groups by repeated-measures analysis of variance. To account for the correlation of within-patient measurements, a linear mixed model with a covariance variance matrix chosen based on the lowest Akaike Information Criterium (AIC) index value will be used. The model will also possibly include some characteristics of patients that are found to influence the level of expected adherence identified with preliminary multinomial logistic regressions. All tests will be two-tailed and the *p*-value will be significant if less than 0.05. Analyses will be conducted with SPSS statistical software.

Expected results

The results of this multicentric RCT will provide evidence for the effectiveness of the MotivAir program in supporting adherence to CPAP use among patients with OSAS.

Specifically, based on the results of previous research (e.g., Sparrow et al., 2010; Aloia et al., 2013; Dantas et al., 2015; see for a review: Rapelli et al., 2021), participants assigned to the experimental group are expected to show increased clinical and psychological parameters compared to the control condition. Indeed, according to MI theoretical assumptions, positive changes in the post-treatment levels of readiness to change and perceived self-efficacy will result in increased adherence to behavioral change plans.

Furthermore, it is expected that personalized MI treatment based on the individuals' initial levels of adherence to CPAP therapy will result in further improved outcomes up to 180 days after completion of the standard rehabilitation program compared to TAU.

Finding from this study will, therefore, contribute to the evidence-based knowledge of how MI may enhance the cost-effectiveness of clinical interventions to increase adherence to CPAP among patients with OSAS and will provide suggestions on how to implement traditional health care services.

Author contributions

GR, GP, and GC conceived the study, participated in its design and coordination, and helped to draft the manuscript. LA and GM participated in the study design and made substantial contribution to the manuscript drafting. EP, PF, and CL participated in the study design and revised the draft critically. IT and SG participated in the study design and helped to draft the manuscript. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Assessing the needs and perspectives of patients with obesity and obstructive sleep apnea syndrome following continuous positive airway pressure therapy to inform health care practice: A focus group study

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Objective: This study aims to investigate the lived experience in patients with obstructive sleep apnea syndrome (OSAS) and comorbid obesity following after continuous positive airway pressure (CPAP) therapy made with the disease the device, and to identify barriers and facilitators to the use of CPAP to improve rehabilitation provision and aid in disease self-management.

Methods: Qualitative research was conducted using three focus groups with a representative sample of 32 inpatients (37% female) undergoing a 1-month pulmonary rehabilitation program at the IRCSS Istituto Auxologico Italiano San Giuseppe Hospital, Verbania, Italy. The focus groups were recorded on tape, and contemporaneous notes were made. The tapes were transcribed verbatim, and Interpretative Phenomenological Analysis was used to develop themes.

Results: Six main themes were extracted: (1) Living the diagnosis as a shock; (2) You should not sleep on it: the importance of prevention; (3) The adjustment to CPAP; (4) Barriers and facilitators to the use of CPAP; (5) Three in a bed; and (6) The relationship with the healthcare system.

Conclusion: Results of this study suggest potential avenues for interventions to increase adherence to CPAP, including the provision of information and continued support. Individual counseling providing strategies aimed at helping the person to cope with the emotional problem and relational difficulties associated with the use of CPAP, and at strengthening self-efficacy and self-management skills are also encouraged for optimal care during the rehabilitation program.

KEYWORDS

obstructive sleep apnea syndrome, continuous positive airway pressure, obesity, focus group, interpretative phenomenological analysis, clinical psychology

Introduction

Obstructive sleep apnea syndrome (OSAS) is an increasingly prevalent chronic sleep disorder affecting 3–7% of adult men and 2–5% of adult women worldwide (Lyons et al., 2020). It is characterized by a partial or complete obstruction of the upper airway affecting sleep quality and ensuing daytime fatigue and sleepiness (Cancino and Rivera, 2018; Gibson et al., 2018).

Obstructive sleep apnea syndrome is frequently associated with several clinical problems, including hypertension, cardiovascular disease, abnormal glucose metabolism, and reduced quality of life (Garvey et al., 2015).

Additionally, studies show that patients with OSAS utilize health care resources almost twice as much as control patients do (Lee et al., 2008).

Weight gain is commonly known to be the most important risk factor for developing OSAS. Furthermore, there is a bidirectional relationship between obesity and OSAS, with OSAS potentially leading to faster weight gain, and the entertainment of a vicious cycle of increasing weight and worsening OSAS (Ong et al., 2013).

Continuous positive airway pressure (CPAP) is the main treatment for OSAS symptoms. It has been shown to reduce breathing disturbances, increase blood pressure, and decrease mortality rates, and was associated with improved daytime sleepiness, and daily functioning in several investigations (Ye et al., 2017; Adams et al., 2020).

However, the success of this treatment relies on treatment adherence, which is frequently suboptimal in this population of patients (Weaver and Grunstein, 2008; Rapelli et al., 2021a; Gabryelska et al., 2022).

Improving CPAP adherence is commonly a challenging process—as affected by different factors including age, gender, symptoms severity, socioeconomic and marital status, perceived social support, and technical issues associated with the device (Mehrtash et al., 2019). The acceptance of CPAP is a process that is perceived as a difficult challenge and requires a period of adjustment that is frequently associated with the personal perception and experience of patients (Gibson et al., 2018; Rezaie et al., 2021). In fact, patients often seek an alternative before accepting CPAP, and even when they decide to adhere to CPAP, they may do it with skepticism (Rezaie et al., 2021). This period is often associated with negative perceptions of CPAP and this may hinder acceptance (Gibson et al., 2018). Another key concern for patients regards their appearance and body image while wearing the mask in front of other people because they feel embarrassed and uncomfortable (Luyster et al., 2016; Shapiro and McCrone, 2017; Ward et al., 2017; Ye et al., 2017). Also, CPAP is often described as bothersome during the night because of the difficulties to adjust the mask, the noises that disturb sleep, the air directed toward the bed partner, and the consequent loss of intimacy with the partner (Luyster et al., 2016; Ye et al., 2017). CPAP may also represent a problem for traveling patients: from a logistic viewpoint, the device is difficulty difficult to carry and it needs electricity to function (Luyster et al., 2016).

Pulmonary rehabilitation is effective in reducing symptoms among patients with OSAS, providing disease education and self-management components (Ward et al., 2002; Pearson, 2004; Nici et al., 2006) to improve exercise capacity, quality of life, and the patient's understanding of the disease and treatment (McCarthy et al., 2015).

However, a few studies examine the understanding or information needs of patients with OSAS in CPAP, or whether the educational component of pulmonary rehabilitation meets these needs.

Examining the perspectives and lived experiences of this population is fundamental to gaining a better understanding of their needs, and factors that facilitate and hinder CPAP use.

To this aim, the present study employs a qualitative method using focus groups, (1) to assess knowledge, beliefs, and attitudes about OSAS syndrome and CPAP therapy, and (2) to identify specific barriers and facilitators to CPAP use among patients with OSAS and comorbid obesity.

The results presented in this article are from the preliminary phase of a larger project to develop and implement a telephone-based behavioral and motivational intervention to improve adherence to recommended OSAS treatment (Rapelli et al., 2022).

By identifying patients' needs, researchers and health professionals may be able to develop effective interventions capable of reducing the sleep health disparities observed in this population.

Materials and methods

A qualitative research design using focus groups was used to elicit an in-depth understanding of the participants' perceptions about OSAS and to identify barriers preventing the utilization of CPAP. This methodological approach builds on group interaction and is especially valuable for capturing how views are constructed and negotiated (Kitzinger and Barbour, 1999; Dahlgren et al., 2007).

The study was approved by the Ethics Committee of the IRCCS Istituto Auxologico Italiano, Milan, Italy (research project code: 2021_03_23_02; acronym: MotivAir) and was in accordance with the Helsinki Declaration of 1975, as revised in 2008. The purpose and objective of the study were explained to each subject and written informed consent was obtained before starting the study.

Participants

Participants were recruited from the Department of Pulmonary Rehabilitation of the IRCCS Istituto Auxologico Italiano, San Giuseppe Hospital, Verbania, Italy.

They were selected for inclusion in the study during their first week of the pulmonary and metabolic rehabilitation program, according to the following criteria: (1) having a diagnosis of OSAS confirmed with polysomnography;(2) being recommended for the use of CPAP for at least 6 months; (3) having a body mass index, BMI $\geq$ 30 kg/m^2; (4) being 18 years or older; and (5) being Italian speakers. Subjects with severe apnea, and cognitive or hearing impairments were excluded from the study. Before enrollment in the study, all patients were informed in detail about the study procedure and signed the consent form to participate.

A purposive sample of 32 patients (9–11 participants in each focus group) with OSAS using CPAP (37% female) in the age range of 37–77 years ($M = 59.61$; $SD = 11.18$) were enrolled in the study and participated in three focus groups.

Demographic and clinical information of the sample is reported in Table 1.

Procedure

Data were collected from August 2021 to January 2022, until data saturation was achieved. Data saturation was reached when no new themes emerged from additional participants (Morse et al., 2002; Silverman, 2010).

To minimize researcher bias, the interventions were led and moderated—using a phenomenological hermeneutic approach (Lindseth and Norberg, 2004)—by a female research psychologist (PhD) with no prior relationship with participants, who received specific training in conducting focus groups.

Individuals were made clear that their participation was voluntary, and that they could leave the focus group at any time—but none of them did. Participants were informed about the aim of the study and they knew that would participate in a face-to-face discussion with other patients with the same diagnosis and it would be the subject of scientific publication. Participants did not receive any reward/remuneration for participation in the study.

Focus groups were conducted during working hours and were held in a dedicated room of the hospital. No one other than the participants and the moderator was present in the room. All meetings were audio-recorded and lasted from 50 min to 1 h. To ensure consistency between groups, a semi-structured interview schedule guided the discussions (Table 2)—to investigate the lived experience participants made of OSAS diagnosis and CPAP treatment and to explore their general knowledge, attitudes, and beliefs about the disease and its treatment.

A storytelling approach with probing questions (such as “tell me more about that experience” and “how did that make you feel?”) was also used during the focus groups to clarify or expand the meanings presented by the participants, thus facilitating a dialogic interaction process. This is fundamental when conducting a phenomenological study to help participants express their deepest thoughts and feelings as freely as possible (Eatough and Smith, 2008). Each focus group ended when participants had nothing more to add. The interviewer did not field notes during or after the session.

Data collection also included age, sex, education, marital status, employment, and BMI—which were retrieved from patient medical records by a clinical psychologist working in the hospital and independent of the study. Data were registered and stored in a password-protected database, and only accessible by the clinician and the researchers.

TABLE 1 Demographic and clinical information about the sample (N=32).

	Focus Group 1 (N = 11)	**Focus Group 2 (N = 11)**	**Focus Group 3 (N = 10)**
Gender			
Male	6 (55%)	7 (64%)	3 (30%)
Female	5 (45%)	4 (36%)	7 (70%)
Age	M = 55.82; SD = 12.22; Range = 37–77	M = 61.91; SD = 9.52; Range = 43–76	M = 61.10; SD = 11.79; Range = 42–76
Education level			
High School	5 (45%)	6 (55%)	7 (70%)
Bachelor’s degree	4 (36%)	3 (27%)	3 (30%)
Master’s degree	2 (18%)	2 (18%)	0
Smoking			
smoker	4 (36%)	3 (27%)	3 (30%)
non-smoker	6 (55%)	5 (45%)	6 (60%)
ex-smoker	1 (9%)	3 (27%)	1 (10%)
Living with…			
Alone	7 (64%)	2 (18%)	3 (30%)
Partner	1 (9%)	7 (64%)	7 (70%)
Parent/parents	1 (9%)	0	0
Siblings	1 (9%)	0	0
Son/sons	1 (9%)	2 (18%)	0
Age at OSA Diagnosis, mean, range	45, 35–68	51, 45–70	47, 42–70
Weight Status, n (%)			
Underweight/normal weight (BMI $\leq$ 24.9 kg/m^2)	0	0	0
Overweight (BMI 25.0–29.9 kg/m^2)	0	0	0
Obesity Class I (BMI 30.0–34.9 kg/m^2)	7 (64%)	8 (73%)	7 (70%)
Obesity Class II (BMI 35.0–39.9 kg/m^2)	4 (36%)	3 (27%)	3 (30%)
Obesity Class III (BMI $\geq$40 kg/m^2)			

Data analysis and rigor

All recordings were transcribed verbatim and thematically coded by two researchers independently without using any software. Field notes were also taken for the examination of contextual information and general impressions during the sessions.

TABLE 2 Focus group questions.

1. What are the side effects of the treatment?
2. What are the benefits you have experienced?
3. Is it a problem to use CPAP? For whom?
4. What was it that motivated you to start CPAP treatment?
5. What motivates you to continue treatment?
6. Were there any tiring moments when you thought about giving up using CPAP?
7. What is the most tiring aspect of using CPAP?
8. What problems have you experienced using CPAP?
9. Did your partner help you in the decision to use CPAP?
10. Has CPAP changed your quality of life? How?
11. What expectations do you have about the treatment?
12. Has having or not having a bed partner influenced your decision to use CPAP?
13. How capable do you feel you are of managing CPAP?
14. What or who might help you feel more capable?
15. What things have helped you in using CPAP?
17. Are there any aspects of treatment that you consider uncomfortable?
19. How much would it help you to have a professional following you during use monitor and encourage you?
20. What more can the CPAP provider do?
21. What are the things you would tell a person who is about to start using CPAP? What are the recommendations?
22. How satisfied are you with CPAP?

Transcriptions were analyzed qualitatively using the interpretative phenomenological analysis (IPA; Smith et al., 2009) to develop and label themes and sub-themes originating from the data.

In particular, IPA is most frequently applied to one-on-one interviews, and only a few studies have employed this approach to provide detailed examinations of personal lived experiences through focus group discussions (Palmer et al., 2010). Still, focus groups are an important source of experiential data (Palmer et al., 2010) as they (1) allow multiple voices to be heard in one sitting, thus drawing a larger sample into a smaller number of data collection events; (2) elicit more experiential reflection than one-to-one interviews; and (3) are cost-effective for hospital settings.

The data-driven approach (vs. theory-driven) was then used for text analysis, as considered the most effective way to investigate subjective experiences (Davidson et al., 2008). Comparison of findings with the research literature was carried out only at the end of the whole process as a sort of "return to the theory"—since emerging themes were derived inductively from the words of participants, rather than preconceived theoretical concepts and research evidence.

The analytical process initially involved line-by-line reading of each focus group transcript to provide a preliminary description of relevant topics, with notes recorded directly in the text. In this primary recursive phase, transcriptions were read and re-read, first for each session of the focus group, and then across sessions to let new insights and conceptual aspects dense with meaning come through. During the process, some themes were also dropped, for example, those that did not fit well with the emerging framework or those that were less represented.

Also, aspects within the themes that related specifically to the ongoing pulmonary rehabilitation program, and were therefore not transferable to a wider context, were not presented but fed back to the hospital as part of their evaluation process.

After the decoding procedure, disagreements between three coders were solved through extensive in-person discussion. Furthermore, the findings were shared and discussed with the multidisciplinary team, which improved the researchers' reflexivity simultaneously reducing the influence of potential preconceptions and biases that could arise throughout the analytic process, with increased rigor.

The goal was to make sure that the analysis matched the participants' accounts and that each account presented was justified by the data. Patients did not participate in the analytical process and did not provide their feedback on the findings.

Results

Living the diagnosis of OSAS as a shock

Some respondents experienced the diagnosis of OSAS as a traumatic event. This is particularly true in obese patients who attended the rehabilitation program with the aim of losing weight.

> *"I found out about my apneas here* (during the weight loss rehabilitation program). *I have always slept, I did not realize I had this problem."*
>
> *"Doctors detected a high risk of apneas and I was shocked because I did not expect to have severe apneas with significant desaturations."*

> *"For me it was traumatic. I was 35 when they first told me I suffer from OSAS."*

Often the diagnosis of OSAS comes as a surprise. Still, receiving a diagnosis of OSAS also surprised patients who are hospitalized for weight loss; it is an ominous diagnosis for patients, but also an explanation of the symptoms they have had for years whose symptoms were previously recognized and informed by significant others.

> *"After the diagnosis, I told my mom that she was right, that I sometimes stopped breathing while sleeping. I have never believed but got mad at her because she used to wake me up."*

The presence of significant others is very important in recognizing the prodromal signs of the disease, but often the person carrying the diagnosis is unaware that he or she has an airway problem while sleeping.

You should not sleep on it: The importance of prevention

In addition to being poorly recognized and diagnosed, OSAS symptoms are often confused with other diseases, including mood disorders, and then treated with suboptimal solutions. This tendency significantly increases the likelihood of developing additional medical problems and compromising the quality of life of the person, thus driving the need for prompt informative and preventive actions. This was reflected in the narrations of the respondents.

> *"All the mental confusion, the lack of memory that I could not explain, I thought I was depressed. There is not enough communication or explanation about this pathology, and you almost feel wrong."*
>
> *"Polysomnography could also be used as a routine screening test for the driving license. I was unaware of it* (OSAS) *until I started having overweight problems. People may be at risk when driving even if they do not know it because apnoea is a problem on which there is no communication and knowledge."*

Patients agree that the diagnosis came late and that they had several other diagnoses. This lack of diagnosis pushed them toward doctor-shopping behaviors, to search for the cause of their symptoms. For this reason, sometimes patients did not feel heard and listened to by the health service. They agree that it is important to do more prevention and screenings at the doctor's, especially to avoid risks when driving, as OSAS is responsible for many road accidents.

The adjustment to CPAP

The patients adjusted to the device differently. Some of them fully accepted CPAP and experienced a process of real embodying process: the machine was considered an extension of themselves and part of their everyday life. These showed a positive attitude toward their use due to the perceived beneficial effects on their quality of life and health status.

> *"I have been using it* (CPAP) *since 2018. It took a while to get used to it but now it is something I cannot do without because I use it even for a nap in the afternoon and I feel well"*
>
> *"The CPAP makes me feel relaxed and breathe better. If I don't have the CPAP with me - which rarely happens when I took short trips or when I cannot bring it with me - I have a lot of trouble falling asleep. It gives me such a sense of relaxation, and well-being that I have to use it."*

As reported above, for some respondents, it was even difficult to think about living without the CPAP anymore. They were so used to it that they were not willing to give up. In addition, a portion of the patients also stated that the device acquired such a great value in their lives that they referred to it as if it was a person.

> *"I welcomed it with open arms."*
>
> *"I use it since 2020, I had 95 apneas per hour and I no longer had the REM phase, I love my CPAP, nobody can take it away."*

On the contrary, other respondents found it intolerable to be in the need of using the CPAP, and some of them even considered it a detrimental factor in their quality of life.

> *"I don't want to become addicted to it* (CPAP)*."*
>
> *"I'm now using it* (CPAP) *for 4-6 hours per night, but at first it was traumatic … After 3-4 hours of sleep, I just wanted to stop.'"*

They used the device, but for fewer hours than prescribed—although they recognized a slight improvement in their health status. These patients did not intimately consider CPAP as life-saving but as a weird, uncomfortable tool that they were forced to use.

> *"We feel a little disadvantaged because, with this mask, we look like extraterrestrials …Pipes here, pipes there."*
>
> *"I have started to use it for one/two hours per night and now I use it a little longer, like four or five hours per night, but honestly, I'd rather be without it, I don't like to use it. My aim in life is to stop using it, maybe by losing weight…I would be very happy. I will keep using it if I have to but it is not normal anyway. It's a foreign body that I am forced to use and presses on my face."*

Among the respondents, resistance to CPAP was not driven by health and medical concerns, but the feeling of annoyance, discomfort, and even hate. Their likelihood of adhering to the therapy was based on the hope of being able to do without. Therapy seemed to them a never-ending "battle"—as they did not want to surrender completely to the device.

> *"Honestly, I would not use it anymore - and I will certainly do it sooner or later because, by losing weight, it can be possible. This is what I am here (at the hospital) for."*
>
> *"With CPAP, is a nonstop battle but I used it.'*

Moreover, not only is the CPAP a voluminous device but it also requires ongoing adjustments to perform adequately. Furthermore, patients struggle to accept the idea to be seen by other people wearing the mask, and for all these reasons they often chose not to take the device with them during work trips or holidays—meaning they do not see it as part of their routine and are not worried about not using it for days.

> *"If I have to go to the mountains or the seaside for a weekend, I will not take it with me"*
>
> *"I'll go on holiday for ten days and share the room with other people and it is a little… it might bother them because obviously … and I feel a little embarrassed, that's it.*

A third category of patients comprises those who have a more neutral approach to CPAP use: they rationally accepted the treatment due to its health benefit—without any particular emotional rebounds.

> *"It's like wearing glasses: if I can't see anything, I get glasses; if I can't breathe, I use CPAP. The benefits are more than the discomfort caused by the CPAP, trust me."*

Balancing the pros and cons of the use of the CPAP, the health improvement appears to be more important than the discomfort caused by the device. The therapy is simply accepted and followed by the patient as the only solution to reduce the impact of their chronic condition.

Barriers and facilitators to the use of CPAP

Adherence to therapy is fundamental to pursuing a healthy status—but for several reasons commonly difficult to achieve. In this regard, the respondents acknowledged both facilitator and barrier to adherence were acknowledged by the respondents.

In the first phase of the treatment—when patients receive the diagnosis and the process of acceptance and understanding of the disease begins—obtaining information on OSAS and CPAP, as well as being followed up by the medical team seemed to represent important facilitators for the use of the device.

> *"I got used to CPAP while hospitalized - as they taught me how to manage it. A doctor came to check if everything was fine, to change the mask if needed… until I was ready to go home"*
>
> *"Here (during hospitalization) I understood the importance of using CPAP. A month's stay here was very useful, as the doctors came to check on me during the night."*

The presence of healthcare professionals helped the patients to worry less anxious and feel better, as they had the opportunity to ask questions, receive personalized treatment, and receive emotional support.

This was particularly relevant for "naïve" CPAP users since the device represents something very difficult to deal with from both a medical and a psychological point of view.

Hospitalization also offered the respondents the opportunity to meet other people suffering from the same conditions. This represented both a facilitator and a barrier to CPAP adherence. Indeed, when roommates had a positive attitude toward the CPAP and more experience with it, they could provide important practical support and technical advice to respondents, as well as emotional help.

> *"My roommate was important to me because she helped me and she fixed my mask in the right position. She supported me a lot."*

In contrast, roommates who showed a negative attitude toward CPAP fueled fears and doubts about therapy in the respondents.

> *"In my room, there was a woman who used CPAP but she didn't want it, she wanted to take it off because she felt more tired than rested. I don't want to think I should use it, I wouldn't use it (the CPAP)"*

The support from others was mentioned as a facilitator for the use of the CPAP even after the person returns home. In fact, the role of family members in helping patients to stay in therapy was fully recognized.

> *"When I came home, my husband helped me, he used to tell me< wear the mask because you will feel better>, and he was happy because I was doing fine."*
>
> *"If there is no one who tells me to wear CPAP, I don't wear it. Therefore, my granddaughter advised me <Grandpa every night I will come to check if you use it>."*

The support received from their spouse or other family members was significant not only from a practical point of view (i.e., in wearing the mask or checking the machine) but also as emotional aid.

Accordingly, patients living alone felt less motivated to use the CPAP because of the absence of somebody encouraging and supporting them—including the medical team.

> *"Since I live alone I stopped using it (the CPAP), and I started using it again here in the hospital two weeks ago."*
>
> *"…You can gain or lose weight and wonder if the machine is still well-calibrated. The happy/sad face* (on the device) *only shows if the mask is well placed but it does not tell you if the pressure is correct, so you don't know if you need to contact the pulmonologist, the doctor, or the technician. Here* (in the hospital) *a pulmonologist comes to check if the machine is well-calibrated every morning and eventually fix it - but when you are at home it doesn't happen."*
>
> *"I don't know if something is wrong… doctors must tell me."*

Relying on a support figure, especially during initial adjustment to the device, also represented an important emotional aid for the patients.

> *"A support figure is useful because you suddenly find yourself with this mask without being mentally prepared…"*
>
> *"Being followed up by somebody is important, it's like walking together with someone who gives you a hand, which makes you feel you are not alone. It's essential in my opinion."*

Among the motivational factors, the interviewees also mentioned the digital solution (i.e., mobile apps) that informs patients about their signs of progress in the treatment of the disease and the correct use of CPAP.

> *"I'm also fine with an app, telling me if everything is fine or if I need to call the technician for a check."*

In addition to monitoring and providing feedback on CPAP usage, mobile applications help patients to develop self-management skills, which increase their self-efficacy and ability to deal with negative emotions associated with device use.

Three in a bed

Sleep is often a shared experience with a partner for many adults. Since the hallmark symptoms of OSAS (i.e., snoring and apneas) occur during the night, partners are likely to experience sleep disturbance that may contribute to daytime exhaustion, problems at work, and in their intimate relationships—that might be overcome with the use of CPAP.

> *"No one could stay with me because I snored so much, but with the mask, I have no problems anymore."*
>
> *"My wife is happy since I have been using CPAP because I don't snore anymore and we are sleeping together again."*

In these quotes, patients reported that the quality of their partners' sleep improved since they started to use the CPAP - and consequently, their couple relationship, as severe OSAS made in some cases necessary for them to sleep in separate rooms.

However, the presence of a "third" in a bed might also negatively impact couple intimacy—especially at CPAP initiation, with important implications for the patients' likelihood to adhere to therapy.

> *"It's not the most sensual thing…"*
>
> *"It's like a Kamasutra between the pillow, the air hose, and the CPAP hose."*
>
> *"You might throw air on your partner's face, and it's embarrassing to wear the mask when you sleep with someone."*

Patients noted that CPAP is a cumbersome device that negatively impacts libido as aesthetically unpleasing and not particularly appealing. They also reported feeling embarrassed about having to deal with the side effects of the mask while in bed: in some cases, partners may wear earplugs not to hear the noise of the machine, while others shelter themselves with pillows at night to avoid air blowing.

The relationship with the healthcare system

The use of the CPAP implies for patients with OSAS to be in contact with the health care system, which provides them with the device and follow-ups at home or remotely for adaptation of some parameters. Still, patients often express concerns about the maintenance of the machine due to the not always responsive feedbacks from the healthcare system, and the long detailed procedure they need to follow.

> *"One con is the supply of the CPAP spare parts, sometimes the healthcare system suffers delays."*
>
> *"A hot topic is communication with CPAP providers, the healthcare system and the motorization* (DMV), *as drivers' license holders we are treated like drug addicts or alcohol abusers. I use the CPAP every night and the technician could download my data from the CPAP and report it directly to the DMV. Instead, I need to undergo a DMV test for no reason. Streamlining this procedure could be a benefit in my opinion."*

TABLE 3 Emerging themes and related illustrative quotes.

Themes	Quotations
1. Living the diagnosis as a shock	*"For me it was traumatic. I was 35 when they first told me I suffer from OSAS"*
2. You should not sleep on it: the importance of prevention	*"Polysomnography could also be used as a routine screening test for the driving license. I was unaware of it* (OSAS) *until I started experiencing overweight problems. People may be at risk when driving even if they do not know it because apnoea is a problem on which there is no communication and knowledge."*
3. The adjustment to CPAP	Positive adjustment: "I welcomed it (the CPAP) with open arms." Negative adjustment: "I do not want to become addicted to it (the CPAP)." Neutral adjustment: "It's like wearing glasses: if I cannot see anything, I get glasses; if I cannot breathe, I use CPAP. The benefits are more than the discomfort caused by the CPAP, trust me."
4. Barriers and facilitators to CPAP use	*"I got used to the CPAP while hospitalized - as they taught me how to manage it. A doctor came to check if everything was fine, to change the mask if needed… until I was ready to go home"*
5. Being three in a bed	*"You might shoot air on your partner's face, and it's embarrassing to wear the mask when you sleep with someone."*
6. The relationship with the healthcare system	*"A hot topic is the communication with CPAP providers, the healthcare system, and the motorization* (DMV), *as those with driving licenses are treated like drug addicts or alcohol abusers. I use the CPAP every night, and the technician could download my data from the CPAP and report it to the DMV directly. Instead, I need to undergo a test at DMV for no reason, because the data can be reported directly. Streamlining this procedure could be a benefit in my opinion."*

Maintenance of CPAP has been shown to be a potential barrier for patients because it may require a great deal of time and resources and a constant relationship with the healthcare system and its bureaucracy. Sometimes, there are delays and problems in obtaining the CPAP and its spare parts. This could cause frustration in patients, and further put those less motivated at risk of not adhering to CPAP use.

Furthermore, patients recognized that having this disease involves dealing with DMV paperwork and doing periodic check-ups to get a driving license. This may represent a barrier, because the patient may neglect his disease, which may worsen, and prefer not to have these problems with the license.

The emerging themes and related illustrative quotes are reported in Table 3.

Discussion

To our knowledge, this paper for the first time describes the lived experience that Italian inpatients with OSAS and comorbid obesity using the CPAP made of their pulmonary disease and its treatment.

During the focus group, most patients reported that the diagnosis of OSAS was experienced as a traumatic event because they were unaware of their symptoms, as also found in previous studies (Bakker et al., 2019; Weaver, 2019; Waldman et al., 2020).

Indeed, OSAS often goes undiagnosed because its symptoms are commonly mistaken for "normal" snoring, tiredness, or mood disorders—among others. Specifically, the multidirectional relationships between depression, disturbed sleep, and OSAS are a source of potential diagnostic confusion and may explain why OSAS and depression are both generally under-diagnosed among the general population (Schröder and O'Hara, 2005). Failure to recognize these conditions may lead to inappropriate treatment—with consequent worsening of the health status of the person. Recent studies demonstrate that CPAP therapy also contributes to reducing depressive symptoms in patients with OSAS (Garbarino et al., 2020). Accordingly, this content emerged from our focus groups, with one of the interviewees stating that he thought to suffer from depression instead of OSAS, and stressing the importance of informing preventive actions in sleep disorders.

Furthermore, several large epidemiological studies have shown a strong reciprocal association between weight gain and an increase in the odds of developing OSAS, to the point that the number of people with known sleep apnea continues to grow as the obesity epidemic worsens (Ong et al., 2013). While the treatment of chronic diseases is undeniably complicated by the presence of comorbidities, the results of this study show that the presence of obesity can represent an opportunity for the detection of OSAS symptoms in patients undergoing weight loss rehabilitation, thus preventing the worsening of snoring and OSAS, and the associated obesity-related comorbidities (i.e., hypertension, insulin resistance, and cardiovascular problems).

However, the use of the CPAP—the gold standard treatment for this chronic condition—may be frustrating and necessarily place persons with OSAS in the need to redefine their daily routine.

However, the process of adjustment to the device varied consistently among respondents depending on its perceived beneficial effects and the personal experience patients had with the device. Notably, resistance to CPAP was not influenced by the individuals' medical condition or health concerns, but by the social and practical aspects surrounding its use: most respondents did not feel comfortable wearing the mask in the presence of other people or bringing it with them while traveling and, therefore, preferred to stop using the device for a few days regardless of the severity of their apneas.

Those who were more inclined to adhere to therapy were not naïve patients—probably because they already had the opportunity to experience the positive effects of the treatment. Among those most resistant to change, instead, the use of the device was frequently motivated by the hope of being able to do without—and since losing weight also reduces the symptoms of sleep apnea, the goal of living without CPAP seems to represent an important factor in facilitating weight loss among the respondents. These results confirm the importance of the constructs of motivation and self-efficacy in determining adherence to treatment referring to the Self-Determination Theory (Ryan and Deci, 2000). In fact, previous studies showed that patient education on the consequences of poor adherence is not sufficient, and in some cases, it is detrimental because it forced the decision to not adhere to the treatment. Conversely, as suggested by studies conducted with a motivational interviewing approach (e.g., Aloia et al., 2004; Sparrow et al., 2010; Dantas et al., 2015; see for a review: Rapelli et al., 2021a), working in line with the values and orientating them toward the health goal could be more effective.

Among acknowledged facilitators to CPAP use were being informed and followed up by the medical team, but also receiving support from both the professionals and other patients.

This is particularly true for patients at their first use of the device and this underlines the delicate phase of the first adjustment to the device and the importance played by social influence.

Moreover, as also demonstrated in previous studies (Hagedoorn et al., 2000; Rapelli et al., 2020, 2021b), receiving support (both emotional and in dealing with technical issues of the machine) from the partner leads to improved adherence and clinical outcomes in patients with OSAS using CPAP. On the contrary, adherence appears scant among patients living alone (Luyster et al., 2016; Rapelli et al., 2022). Indeed—as shown in other research (Sawyer et al., 2010)—unmarried patients in this study reported lower perceived ability to manage the device and fewer positive experiences with the CPAP compared to their married counterparts. Also, living alone may be a risk factor for late diagnosis of OSAS. This is particularly obvious when one of the most common presentations of OSAS is loud snoring bothersome to the bed partner.

Therefore, conceptualizing OSAS from a dyadic perspective—when possible—is likely to be more effective in identifying sleep problems and developing strategies to improve adherence to CPAP therapy than focusing solely on the individual (Ye et al., 2017). Indeed, studies show that CPAP might have an impact on co-sleeping (Lewis et al., 2004; Cartwright, 2008), and the quality of intimate relationships (Baron et al., 2009). Many stated their apprehension about sleeping all night with "wires" and a mask, while others were concerned about the effect that wearing the CPAP might have on their sleep partners and the couple functioning. The negative psychological effects of the equipment and harmful attitudes toward CPAP treatment identified as putative barriers to adherence to treatment mirror those found in previous studies (Broström et al., 2010; Shaw et al., 2012).

Another facilitator mentioned by inpatients is the support of an app/device that could be a source of motivation for the patient that could know signs of progress. The telemedicine is already considered a best practice in order to have positive health-outcomes related, and the literature demonstrated the increase in CPAP adherence levels among patients with OSAS who used mobile health devices (e.g., Isetta et al., 2017; Hu et al., 2021), but our study is the first that recognized the need of patients and the importance to actively engage the patient in the treatment.

Still, concerning barriers to CPAP adjustment, another emerging theme was the relationship with the healthcare system—whose long-term support was largely perceived as ineffective and not promptly available due to long bureaucratic procedures. This generates concerns in people, in particular among subjects suffering from OSAS and comorbid obesity, who wonder how the CPAP re-calibration will work in relation to their loss of weight.

One key limitation of this study relates to the inclusion of a convenient sample of patients with OSAS and comorbid obesity—with a consequent lack of generalizability of the results to the OSAS population. However, to yield insightful results, an important factor when selecting the sample is its homogeneity. Other possible limitations of this study, including not having distinguished between patients at their first use of the CPAP and those who already experienced CPAP treatment relapse(s); and not having specifically investigated the role of the presence of one or more comorbid conditions in influencing adherence to CPAP use among patients with OSAS. Giving voice to informal caregivers—and especially spouses—of this patient population would also have enriched the results of this study with additional reflections and suggestions for the implementation of care actions. The involvement of the patients' sleeping partners and the exploration of their needs and psychological status are fundamental, as participants described the impact on the relationship as a potential barrier.

Furthermore, our findings further stress the importance of increasing patient awareness and knowledge to help their understanding of the health implications of OSAS, which can be done at the community level through public health awareness campaigns or during individual physician-patient encounters. Moreover, the implementation of customized motivational interventions would increase the inner reason to change and promote their self-efficacy, variables that are considered fundamental to improve adherence to treatment among patients with chronic diseases.

Conclusion

The findings of this study reveal that, despite the fact that the decisions to use CPAP are individualized; the barriers to the adoption and possible adherence to sleep apnea treatment are a combination of functional and interpersonal concerns that depend largely on the patient's support environment and early experiences and beliefs about the CPAP.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Istituto Auxologico Italiano. The patients/participants provided their written informed consent to participate in this study.

Author contributions

GR, LA, and GP contributed to the development of the study, analysis of the results, and writing of the manuscript. IB, IT, PF, and GC contributed to the development of the study and writing of the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Multi-layer relationships between psychological symptoms and life adaptation among humidifier disinfectant survivors

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In April 2011, the Korea Centers for Disease Control and Prevention (CDC) announced the results of an epidemiological investigation that an unknown cause of lung disease that occurred throughout Korea was caused by humidifier disinfectants. The unprecedented social catastrophe caused by humidifier disinfectants, a household chemical, has so far reported 1,784 deaths and 5,984 survivors in South Korea. This study was designed to investigate the multi-layer relationships between psychological symptoms and adaptive functioning in survivors of the Humidifier disinfectants in South Korea caused by chemical toxic substances. Specifically, this study aimed to explore how psychological symptoms affect actual interpersonal relationships and job adjustment with two variable sets, six internalizing and externalizing subscales, and three adaptation subscales. A total of 224 survivors recruited from a program to support humidifier disinfectant survivors by the government participated in this study. This research was approved by the Institutional Review Board of one of the Universities in South Korea. The age range of the participants was 18–73years (M =42.23, SD =10.90), 37.1% (n =83) were male, and 62.9% (n =141) were female. The participants responded to the Adult Self-Report (ASR) of the Achenbach System of Empirically Based Assessment (ASEBA). A Canonical Correlation Analysis (CCA) generated three unique patterns in the relationships between psychological symptoms and adaptive functions. Humidifier disinfectant survivors in the first pattern were more vulnerable to psychological symptoms and showed maladaptive functioning in life. Survivors in the second pattern showed intrusive behaviors and appeared to be adaptive in relationships with friends. Finally, survivors in the third pattern showed aggressive behaviors and reported poor partner relationships while showing good relationships with friends. The practical implications of the interventions are also discussed.

KEYWORDS

humidifier disinfectant survivors, psychological symptoms, adaptive function, canonical correlation analysis, Achenbach system of empirically based assessment

Introduction

Chemicals have become necessities of modern society and are sold in many places in our daily lives. These products are not only useful to humans but also harm the human body at the same time. The humidifier disinfectant sold between 1994 and 2011 in Korea was developed to prevent bacterial diseases caused by microorganisms; however, it caused fatal lung damage to random consumers who purchased it (Choi et al., 2018; Ryu et al., 2019). Humidifier disinfectants include polyhexamethylene guanidine phosphate (PHMG-P), polyhexamethylene guanidine hydrochloride (PHMG-H), oligo (2-(2-ethoxy)ethoxyethyl) guanidinium (PGH), chloromethylisothiazolinone (CMIT), methylisothiazolinone (MIT), etc., and products including CMIT and MIT had been sold since 1994 (Yoon et al., 2017; Ryu et al., 2019).

In 2011, the Korea Center for Disease Control and Prevention (KCDC) and the Korean Ministry of Environment reported that inhalation of a humidifier disinfectant was associated with lung damage such as lung fibrosis symptoms in animal experiments (Park et al., 2017). The number of victims of humidifier disinfectant use increased from 2008 to 2011 and showed a marked increase between 2010 and 2011. This was the first reported unprecedented biocide death from household chemicals in South Korea, and the impact and extent of the damage are not yet clear (Choi et al., 2018). As of November 2021, the number of people who apply for damage was 7,642 including 1,740 deaths (Comprehensive Humidifier Disinfectant Damage Support Portal, 2021).

Humidifier disinfectant damage adversely affects not only individuals' physical health but also their psychological health. Among the victims, 57.5% experienced depression, 55.1% experienced guilt and self-blame, 54.3% were anxious, 27.6% had suicidal thoughts, and 11% attempted suicide (Leem et al., 2020). Ko et al. (2021) compared the mental health status of 228 victim-survivors with 228 members of the general population from 2018 to 2021. They reported that victim survivors had much higher scores on anxiety, depression, atrophy, physical discomfort, thinking problems, attention problems, and aggressive behavior than the general population. In addition, it was found that victim survivors with high economic status showed much higher psychological distress than their counterparts (e.g., low and middle classes), and it was revealed that economic stability and psychological pain can be independent in the sample of victims of humidifier disinfectants. Thus, it is important to carefully examine the mental health status of humidifier disinfectant survivors by utilizing a more comprehensive psychological assessment.

Most psychological symptom assessments are categorized as the ASEBA (Achenbach System of Empirically Based Assessment), which is used to evaluate the adaptive states and problem behaviors of adults (Kim et al., 2014). The ASEBA include two psychological syndrome constructs: internalizing and externalizing problem behaviors. While internalizing problem behaviors hide problems inward and internalize and overcontrol problems, externalizing problem behaviors consist of apparent behavioral problems and externalized and under-controlled problems (Achenbach and Rescorla, 2003). There are three subscales for both internalizing and externalizing. The internalizing subscales are anxious/depressed, withdrawn, and somatic. On the other hand, the externalizing subscales include aggressive behavior, rule-breaking behavior, and intrusiveness. Internalizing and externalizing subscales can differentially contribute to the overall problem behavior of adults.

In addition to psychological symptoms, the ASEBA also includes the Life Adaptation Scale, which consists of relationships with friends, spouses/partners, as well as job adjustment. Therefore, it is possible to closely analyze how psychological symptoms may affect actual functioning in daily life. In Italy, the ASR was conducted to monitor changes in the first 4 weeks of isolation in order to assess the mental health status of young people during the COVID-19 pandemic (Parola et al., 2020). The results showed a significant increase in both internalizing and externalizing behavior and a decrease in social relationships due to isolation and containment. Jang et al. (2020) also utilized the ASR to examine the psychological symptoms of earthquake victims in Nepal and reported that more than half of the adult victims of the Nepal earthquake showed symptoms of post-traumatic stress disorder (PTSD). In addition, more than half of them had internalization problems requiring clinical intervention, and a significant number had externalization problems. The research also reported that parents' internalizing and externalizing symptoms are significantly correlated with children's PTSD symptoms; in other words, the occurrence of a disaster is not only related to one's psychological pain but also to the psychological pain of close relationships such as family. For example, victims of the Fukushima incident experienced psychological pain as well as the dissolution of their families or complained of extreme stress in parenting in structurally difficult conditions (Tsujiuchi, 2021). Therefore, social disasters have a psychologically and physically impact upon relationships, such as those within families or within interactions with others.

This study aimed to explore the multi-layer relationships between psychological symptoms (both internalizing and externalizing) and maladaptation factors in daily life (e.g., friends, family, and work adjustment). Specifically, this study aimed to explore how psychological symptoms affect actual interpersonal relationships and job adjustment by utilizing a canonical correlation analysis between two variable sets, six internalizing and externalizing subscales, and three adaptation subscales. A canonical correlation analysis (CCA) predicts the simultaneous correlation between two or more independent variables and two or more dependent variables. As the multivariate statistical analysis, a CCA was used for the observation and quantification of associations between two sets of measurements (Härdle and Simar, 2015). Thus, the results of this study can systematically reveal how individuals' six externalization and internalization psychological symptoms function with actual life adjustments in humidifier disinfectant survivors. By examining the patterns of how survivors' mental health problems manifest in real life, we can identify important variables when designing individualized intervention strategies for survivors of humidifier disinfectants. The research question is as follows. How does psychological symptom variable sets associate to life adaptation sets among humidifier disinfectant survivors?

Materials and methods

Participants

In March 2021, this research was approved by the Institutional Review Board of one of the Universities in South Korea. The participants were recruited from a program to support humidifier disinfectant survivors by the government in South Korea. Humidifier disinfectant survivors voluntarily completed the mental health questionnaire through the portal website for supporting survivors. The study used data from 224 survey respondents who finished their responses, out of the total participants. The age range of the participants was 18–73 years ($M = 42.23$, $SD = 10.90$), 37.1% ($n = 83$) were male, and 62.9% ($n = 141$) were female. Using the G*Power 3.1 program, the number of samples in this study was found to be 111 when the significance level required for CCA analysis, the medium effect size was 0.3 and the variable was set to a total of 9, indicating that the minimum number of samples in this study was satisfied.

Measures

The Adult Self-Report (ASR) of the Achenbach System of Empirically Based Assessment (ASEBA) was adopted to comprehensively assess the adaptive and maladaptive functioning of survivors. The ASR consists of 120 items with three rating levels: *0 = not true, 1 = somewhat or sometimes true, and 2 = very true or often true* about experiences of the preceding 6 months. The ASR can be divided into two categories: internalizing and externalizing problem behaviors. While internalizing problem behaviors include anxiety/depression (18 items), withdrawal (nine items), and somatic complaints (12 items), externalizing problem behaviors include aggressive behavior (15 items), rule-breaking behavior (14 items), and intrusive behavior (six items). A sample item from the anxious/depressed subscale is "I feel lonely," and another is "I cry a lot." These questions are related to feeling emotionally depressed and overly worried or anxious. "I would rather be alone than with people" and "I am not liked by others" are two sample items from the withdrawn sub-scale, which includes questions about withdrawal and inactive attitudes as well as not exhibiting interest in the environment. The somatic complaints subscale measures complaining of various physical symptoms even though there is no clear medical cause, "I feel dizzy or lightheaded" and "I feel tired without good reason" are the sample items. This aggressive behavior measures verbal and physical destructive and aggressive behavior or hostile attitudes, "I damage or destroy my things" and "I break rules at work or elsewhere" are the sample items. The rule-breaking behavior subscale evaluates behavior that impulsively acts on problematic behaviors that do not comply well with rules or go against social norms in the workplace or society, and "I damage or destroy my things" and "I break rules at work or elsewhere" are the sample items. The intrusive subscale accesses behavior that annoys or interferes with others; examples include "I brag" and "I attempt to attract a lot of attention."

The adaptive functioning subscales of the ASR consist of the relationships with friends (four items), spouse/partner (eight items), and job adjustment (eight items). The adaptive functioning scale consists of questions to determine the subject's level of adaptation in each living environment. The adaptive functioning scale assesses the degree of overall adaptability in terms of the subject's capacity to build connections and carry out duties at home, school, and work.

Statistical analysis

A Canonical Correlation Analysis (CCA) was conducted to explore the relationships between six problem behaviors and three adaptive functioning variables. As suggested by Baggaley (1981) and Thompson (1991), the CCA is a multivariate statistical method that can analyze two variable sets, with each set consisting of two or more variables. In this study, six problem behaviors were used as multivariate independent variable profiles and three adaptive functions (Friend, Spouse/Partner, and Job Adjustment) were used as multivariate dependent variable profiles.

Results

When analyzing the data, researchers strived to maintain neutral and objective perspective by excluding their own bias. In order to maintain objectivity, various previous studies were reviewed to explore and broaden the understanding of the participants' context. Descriptive statistics for the psychological syndrome and adaptive functioning subscales are listed in Table 1. The CCA tested the differential predictive validity of the psychological symptoms for adaptive functioning. The analysis of the dependent variables of the three adaptive functions and the independent variables of the six psychological syndromes demonstrated three canonical functions (see Table 2). All three canonical correlations between the two sets of variables were statistically significant, with canonical coefficients (*Coeff*) and squared canonical correlation (R_c^2) effect sizes of 68.6, 21.8, and 10.8%, respectively. Because Wilks' λ represents the amount of variance not explained by variable sets, by taking $1 - \lambda$, the full model effect size was yielded in an R_c^2 metric. In addition, three functions had interpretable squared canonical correlation effect sizes of 59.8, 12.3, and 10.8%, respectively. Thus, all three functions

TABLE 1 Inter-correlation matrix with descriptive statistics for research variables.

Variables	1	2	3	4	5	6	7	8	9
1. Anxious/Depressed	1								
2. Withdrawn	0.645**	1							
3. Somatic complaints	0.712**	0.591**	1						
4. Aggressive behavior	0.648**	0.587**	0.558**	1					
5. Rule-breaking behavior	0.527**	0.548**	0.479**	0.616**	1				
6. Intrusive	0.329**	0.198**	0.250**	0.518**	0.449**	1			
7. Friend	−0.206**	−0.402**	−0.223**	−0.200**	−0.149*	−0.014	1		
8. Spouse/Partner	−0.364**	−0.359**	−0.316**	−0.396**	−0.307**	−0.106	−0.306**	0.1	
9. Job adjustment	−0.416**	−0.411**	−0.409**	−0.359**	−0.363**	−0.209**	−0.214**	0.413**	1
M	0.856	0.747	0.676	0.628	0.219	0.307	2.459	1.141	1.376
SD	0.431	0.422	0.489	0.373	0.243	0.325	0.664	0.346	0.255

$^{*}p < 0.05$ and $^{**}p < 0.001$.

TABLE 2 Canonical solution for adaptive functioning predicting psychological symptoms.

	Function 1			Function 2			Function 3			
Variables	**Coef**	r_s	r_s^2 (%)	**Coef**	r_s	r_s^2 (%)	**Coef**	r_s	r_s^2 (%)	h^2 (%)
Independent variables										
1. Anxious/Depressed	0.361	0.878	77.2	0.745	0.238	5.7	0.103	0.016	0.0	82.9
2. Withdrawn	0.315	0.854	73.0	−0.869	−0.375	14.1	−0.963	−0.325	10.5	97.6
3. Somatic complaints	0.141	0.778	60.6	0.295	0.173	3.0	−0.421	−0.177	3.1	66.7
4. Aggressive behavior	0.119	0.766	58.7	−0.853	−0.186	3.9	1.199	0.478	22.9	85.5
5. Rule-breaking behavior	0.308	0.777	60.4	0.441	0.197	3.9	0.356	0.241	5.8	70.1
6. Intrusive	−0.076	0.340	11.5	0.499	0.402	16.1	−0.397	0.121	1.5	29.1
R_c			75.4			33.2			29.0	
R_c^2			56.9			11.0			8.4	
Dependent variables										
7. Friend	−0.142	−0.402	16.2	0.762	0.729	53.2	0.670	0.554	30.7	99.9
8. Spouse/Partner	−0.445	−0.759	57.6	0.453	0.359	12.9	−0.919	−0.544	29.6	100.0
9. Job adjustment	−0.680	−0.890	79.3	−0.730	−0.387	14.9	0.467	0.241	5.8	100.0

Coef, standardized canonical function coefficient; r_s, structure coefficient or canonical loading; r_s^2, structure coefficient squared or variance explained; h^2, communality coefficient; R_c, canonical correlation coefficient; and R_c^2, squared canonical correlation coefficient. Underline for highlight numbers greater than absolute value of 0.4.

in the canonical model should be interpreted to explain a reasonable number of variable sets.

The full model across all functions was statistically significant, with Wilks' $\lambda = 0.314$, $F(21, 626.53) = 14.815$, $p < 0.001$. Wilks' λ represents the inverse effect size or the amount of variance unexplained by the model. Therefore, taking $1 - \lambda$, $1–0.314 = 0.686 = R_c^2$, the overall effect for the full model was obtained. These results indicate that the full model was statistically significant and had a large effect size that explained 68.6% of the variance shared between the variable sets. The hierarchical arrangement of functions for statistical significance was deduced using dimension reduction analysis in the CCA. As previously mentioned, the full model was statistically significant with Wilks' $\lambda = 0.314$, $F(21, 626.53) = 14.815$, $p < 0.001$. Functions 2–3 showed statistical significance, with Wilks's $\lambda = 0.782$, $F(12, 438.00) = 4.770$, $p < 0.001$. The only test for Function 3 was also statistically significant, Wilks's $\lambda = 0.892$, $F(5, 222.00) = 5.321$, $p < 0.001$.

Table 2 shows the standardized canonical function, structure, squared structure, and communality coefficients for all variables across all functions. The communality coefficients in the last column are the sum of the variables' squared structural coefficients (r_s). The communality coefficients can be interpreted as a contributing indicator of the variables across functions. Often times, communality (h^2) above 45% is regarded as the highest level of usefulness in the model. All communalities of independent and dependent variables in the present study proved to be highly useful in explaining the models, with values well over 45%.

Absolute values of the structure coefficient (r_s) greater than 0.40 were underlined for emphasis (Sherry and Henson, 2005). The structure coefficient of Function 1 indicated that the five psychological symptoms were important contributors to the synthetic dependent variables. The results for the independent variables of Function 1 showed that five variables, that is Anxious/Depressed (+), Withdrawn (+), Somatic Complaints (+), Aggressive behavior (+), and Rule-Breaking Behavior (+) subscales were useful contributors to the synthetic dependent variables: Friend (−), Spouse/Partner (−), and Job Adjustment (−) subscales. Furthermore, all structure coefficients of the synthetic independent variable set had a positive value and were negatively related to all adaptive functioning variables. This result was consistent with the theoretical hypothesis, in which psychological syndromes are negatively related to adaptive functioning in social relationships (Walton and Wilson, 2018) and in work place (Ford et al., 2011).

In Function 2, the only significant independent variable was the Intrusive subscale (+) and the only significant dependent variable was the Friend (+) subscale. The Intrusive subscale was positively related to the Friend subscale, which meant that higher intrusive behavior scores indicated better functioning in the Friend relationship. A large body of research has reported an association of Intrusive behavior with friendship (Rubin et al., 2006; Cook and Fletcher, 2012). These findings mainly focused on intrusive behaviors as a factor in externalizing problems and malfunctions of adaptive variables. On the other hand, the results from Function 2 in the present study showed that intrusive behavior corresponding to withdrawal could have a positive effect on friendship. This result could be supported by research on the adverse effects of shyness/withdrawal on friendships in various aspects (Rubin et al., 2006). The result of Function 3 suggested that aggressive behavior (+) was negatively related to the relationship with the spouse or partner (−) but positively related to relationships with friends (+). Thus, this finding revealed that aggressive behavior worsens relationships with spouses/partners. On the other hand, aggressive behavior was positively related to relationships with friends (see Figure 1).

Discussion

The research question of the present study is as follows: how does psychological symptom variable sets associate to life adaptation sets among humidifier disinfectant survivors? To answer the research question, the present study examined the relationship between psychological symptom subscales and life adaptation subscales using a CCA. The psychological symptom subscales were considered as independent variables, and life adaptation subscales were considered as dependent variables in the CCA, in which the relationship between two variable sets was modeled. According to the results of the canonical correlation, three unique patterns of relationships between psychological symptoms and life adaptation were found. The main statistic of the CCA is aimed at maximizing the correlation between the two synthetic variables (Sherry and Henson, 2005). The CCA derives as many canonical functions as there are sets of variables in the smaller set. The Function 1 was created to maximize the canonical correlation between the five independent variables (Anxious/Depressed, Withdrawn, Somatic Complaints, Aggressive Behavior, and Rule-Breaking Behavior) and the dependent variables (Friend, Spouse/Partner, and Job Adjustment). After excluding the variance of Function 1, Function 2 was created to maximize the other canonical correlations between the two other variable sets. In other words, the second function was created under the condition that these new synthetic variables were perfectly uncorrelated with all the other preceding functions. Function 2 concerned Intrusive Behavior and Friends. Finally, Function 3 was created to correlate two more variable sets as strongly as possible with the remaining variance in the observed variables. Function 3 deduced the correlation between Aggressive Behavior in the independent variable set, and Spouse/Partner and Friend in the dependent variable set.

Function 1 shows individuals who have both internalizing (i.e., high scores on Anxious/Depressed, Withdrawn, and Somatic Complaints) and externalizing symptoms (i.e., Aggressive Behavior and Rule-Breaking Behavior). These individuals presented maladaptive functioning in life adjustment (i.e., low scores on relationships with Friends and Partners and Job Adjustment). These results show how painfully humidifier disinfectant survivors suffer from a myriad psychological problems (Ko et al., 2021). These results are consistent with those of previous studies (e.g., Dell'Osso et al., 2012; Lee et al., 2017; Tian et al., 2020) that reported a significant relationship between psychological symptoms (e.g., posttraumatic stress symptoms, depression, and anxiety) and maladaptive behaviors (e.g., problematic Internet use, alcohol or drug abuse, no self-scare, risk-taking behavior, and negative coping) among the sample of disaster survivors. Since disasters are mostly unpredictable, survivors are in a state of shock, have a tendency to deny the loss, and try to escape from reality. In a denial state, survivors are vulnerable to stress, anxiety, and maladaptive reactions (Makwana, 2019). As humidifier disinfectant disasters occur in the family dimension (Park and Kwon, 2020), humidifier disinfectant survivors could be more vulnerable to psychological symptoms and show maladaptive functioning. As each family member witnesses and experiences the loss caused by humidifier disinfectants, the atmosphere in the family becomes depressed, anxious, and lethargic, leading to the disruption of family bonds and feelings of insecurity at home (Peek, 2008; Figley and Kiser, 2013). In addition, a lack of social resources aggravates survivors' mental status and life adaptation (Norris et al., 2002a). Therefore, there needs to be active intervention at the societal and community levels to target the recovery of mental health as well as the life adaptation of humidifier disinfectant survivors (Norris et al., 2002b).

As previously mentioned, Function 2 was created using the remaining variance after excluding Function 1. Function 2 presents individuals who exhibit intrusive behaviors (high scores on the Intrusive scale). These individuals appear to be adaptive in their relationships with friends. Considering the sample items of intrusive behaviors (e.g., bragging, demanding attention, showing off, talking too much, and being loud), individuals with high scores in intrusive behaviors can be seen as showing an overreaction to making friends. Yet, these individuals could be seen as sociable to others. Nonetheless, when individuals brag and boast consistently, their relationship with friends eventually

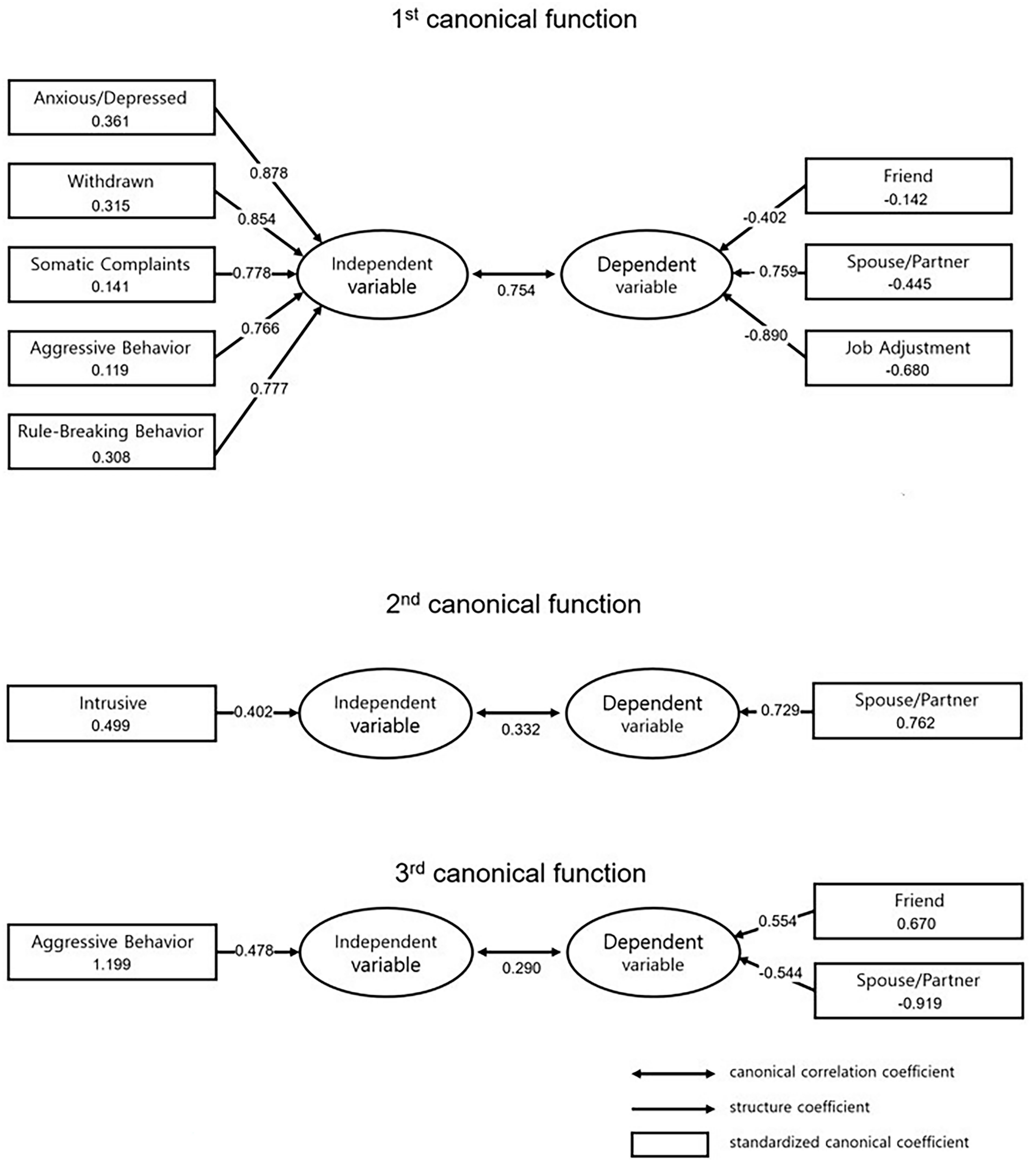

FIGURE 1
Illustration of the first, second, and third function in a Canonical Correlation Analysis (CCA).

deteriorates (Yager, 2010). Therefore, there is a need for education or counseling on how to appropriately establish and maintain good connections with friends.

Function 3 is created with the remaining variance after excluding Functions 1 and 2. Function 3 describes individuals who exhibit aggressive behaviors (high scores on the Aggressive Behavior scale). These individuals reported poor partner relationships while showing good relationships with friends. These results could be explained by resource control theory (RCT; Hawley, 1999). According to RCT, individuals who present high levels of aggressiveness can achieve better social outcomes than non-aggressive individuals when they balance high levels of coercive strategies (e.g., aggression) with high levels of prosocial strategies (e.g., cooperation; Hawley et al., 2007, 2009). People who employ both coercive and prosocial strategies are likely to use relationships instrumentally to attain their goals (Hawley et al., 2009). Therefore, it seems that some humidifier disinfectant survivors use both coercive and prosocial strategies to attain their goals. To illustrate, they utilize aggressive behaviors while endeavoring to interact with friends to accomplish a sense of belongingness that cannot be satisfied in partner relationships.

Even though they showed good relationships with friends, cautious attention must be paid to the fact that they showed poor partner relationships. Poor partner relationship could be a significant risk factor for chronic depression and suicidal thought and behavior (Patel et al., 2002; Kazan et al., 2016). Moreover, when humidifier disinfectant survivors lose the power to use prosocial strategies, only aggression remains, which might ultimately harm the relationship with friends. Couple or marriage counseling, which aims to lessen aggressive behavior toward each other, is often needed for this group.

There are several limitations of the present study that need to be acknowledged. First, since the participants were all adults, it was difficult to generalize the results to different ages of humidifier disinfectant disaster survivors. It is possible that children and adolescents may show different patterns. Therefore, future studies should expand the age range of the samples to generalize the results. Second, CCA, which is based on Pearson's *r* correlation statistics (Thompson, 1991), limits the understanding of the causal relationship between psychological symptoms and life adaptation. Further studies should adopt a longitudinal method to establish a true cause-and-effect relationship between psychological symptoms and life adaptation. Knowing the causal relationship will allow for more effective interventions for humidifier disinfectant disaster survivors because it gives hints about what should be intervened first. Third, a self-reported assessment restricts the understanding of each function in a more comprehensive way. For a more comprehensive understanding, future studies need to analyze more objective data, such as the amount of damage compensation, degree of damage to the family member, and counseling records of people in each function.

Despite these limitations, the results of the present study have both clinical and research implications. First of all, the present study provide a clear picture of what to target when intervening in humidifier disinfectant disaster survivors, based on each psychological symptom. For groups that display both internalizing and externalizing problems, the government and society should actively target the recovery of mental health as well as life adaptation. In addition, when designing the supporting system which aims at mental health and life adaptation, delicate and integrative approach is needed to protect humidifier disinfectant disaster survivors from individual and social risk (Jin, 2019). Education or counseling aimed at acquiring skills to form intimate relationships with friends is needed for those showing intrusiveness. Moreover, there should also be a monitoring process to check whether they are maintaining the intimate relationship or not. Couple or marriage counseling, which aims to lessen aggressive behavior toward partners, is needed for those who show such behaviors. Along with lessening the aggressive behavior, their intention, purpose, and emotion behind the aggressive behavior should also be explored. The present study also has research implication. It establishes the foundation of humidifier disinfectant disaster research by providing an empirical evidence for the practical direction of medium-and long term systematic support for the survivors.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by this research was approved by the Institutional Review Board of Yonsei University (No. 7001988-202104-HR-1178-02l). The patients/participants provided their written informed consent to participate in this study.

Author contributions

SL: conceptualization, supervision, and project administration. ML: methodology and data curation. HL: formal analysis. HK: investigation. S-HR: raw data management and funding acquisition. ML, H-JL, and HK: writing—original draft preparation. SL, ML, H-JL, and HK: writing—review and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Patient activation is a treatable trait in patients with chronic airway diseases: An observational study

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Background: Self-management is key for reducing the burden of disease in chronical illness. However, applying self-management presupposes behavioral change. Sufficient knowledge, skills, confidence and motivation to make the needed behavior changes are important prerequisites. During the past years the Integral Diagnostic Trajectory was developed for patients with asthma or COPD which aims to identify treatable traits and activating patients for self-management.

Objective: In the present study the effects of the Integral Diagnostic Trajectory on the Patient Activation Measure (PAM®) were examined. In addition, predictive variables for PAM baseline scores and change scores were sought.

Materials and methods: A total of 241 patients with asthma or COPD referred to the pulmonologist at the Radboud university medical center, location Dekkerswald, Nijmegen were included. Patient activation was measured before the first visit and after the intervention with the 13-item PAM®. Additional, patient characteristics and health status were measured with the Nijmegen Clinical Screening Instrument (NCSI), modified Medical Research Council (mMRC), Asthma Control Questionnaire (ACQ), and COPD Clinical Questionnaire (CCQ).

Results: Fifty percent of the patients with asthma and seventy percent of the patients with COPD had low levels of activation at baseline (PAM level 1–2). Baseline PAM scores could be explained in patients with asthma for 7% by number of severe problems in health status. And for 18% in patients with COPD by number of severe problems, age and employment status. After the intervention both groups significantly improved on the PAM (T_0: 56.0 ± 13.1

vs. T_1:63.3 ± 14.0 in asthma, and T_0: 50.0 ± 8.8 vs. 58.4 ± 11.1 in COPD). Multivariate stepwise regression analysis showed that only 24% of the change in score could be explained by baseline PAM score and being employed in patients with asthma, and 18% of the variance in change score could be predicted by baseline PAM score in COPD.

Conclusion: The present study showed that low level of activation is a common feature in patients with asthma and COPD. With a relatively short and seemingly simple intervention patients can reach higher levels of patient activation, which is a prerequisite for adopting self-management techniques in daily life.

KEYWORDS

self-management, pulmonary disease, decision making, consultation, motivation, COPD, asthma

Introduction

Adequate self-management of one's health is deemed a crucial issue in patients' chronic conditions to reduce its burden for both the individual and for society (Allegrante et al., 2019). For instance, patients with chronic conditions and poor self-management are more often subjected to emergency room visits, to be hospitalized and/or to be readmitted (Barker et al., 2018). Also for patients with asthma and chronic obstructive pulmonary disease (COPD), improving self-management has been acknowledged as key component of individual disease management (Pinnock et al., 2015; Effing et al., 2016). An international group consensus defined a self-management intervention as structured but personalized and often multi-component, with goals of motivating, engaging, and supporting the patient to positively adapt their health behaviors and develop skills to better manage their disease (Effing et al., 2016). The ultimate goals of self-management are: (a) optimizing and preserving physical health; (b) reducing symptoms and functional impairments in daily life and increasing emotional wellbeing, social wellbeing, and quality of life (QoL); and (c) establishing effective alliances with healthcare professionals, family, friends, and community (Effing et al., 2016).

To successfully take on the challenges that lie within applying self-management in daily life, that is, making the required behavioral adaptations, people need knowledge, skills, and confidence. This is defined as the level of activation for self-management, which can be measured with the Patient Activation Measure (PAM®) (Hibbard et al., 2004; Rademakers et al., 2012). Indeed, studies have shown that patients with COPD with higher levels of activation have a better ability to perform self-management activities (Greene and Hibbard, 2012), have a lower likelihood of having a severely impaired health status (van 't Hul et al., 2020), better health outcomes (Hibbard and Greene, 2013), better health care experiences (Hibbard and Greene, 2013), better knowledge and self-efficacy (Chang and Dai, 2019), more motivation to persist in exercise (Nguyen et al., 2009), better mood (Titova et al., 2017), and show lower healthcare utilization (Titova et al., 2017).

Unfortunately, several cross-sectional studies in primary and secondary care settings have shown that PAM scores are generally low in patients with chronic respiratory conditions, showing percentages of 50–75% of patients with a PAM level 1 or 2, meaning they are not aware of their problems and their own role or miss knowledge and self-esteem to embrace the need for treatment (Bos-Touwen et al., 2015; Korpershoek et al., 2016; Collinsworth et al., 2018; Janssen et al., 2020; Bloem et al., 2022). Clearly there is a need to improve patient activation in usual care. Moreover, there is emerging evidence that personalized interventions support building better skills and confidence and are effective in increasing patient activation (Hibbard and Greene, 2013). Ideally, both the patient as well as the healthcare provider have to take a role and share the responsibility for improving activation levels and adopting self-management techniques. However, studies applying and evaluating patient activation are scarce (Yadav et al., 2018). During the past years, the COPDnet integrated care model was developed for patients with chronic airway diseases and a series of studies was conducted to objectify the added value on change in health status (Koolen et al., 2018b, 2020). The COPDnet integrated care model consist of an Integral Diagnostic Trajectory in a secondary care setting, which is followed by non-pharmacological interventions in primary or secondary care based on the individual care plan that was composed during the integral diagnostic trajectory (Koolen et al., 2018a). In the present study, we will focus on the first part, the Integral Diagnostic Trajectory. The Integral Diagnostic Trajectory aims at making a comprehensive analysis of patients' overall health status, and simultaneously increase the patients' level of activation for self-management. We will examine the effect of the Integral Diagnostic Trajectory on PAM scores. In addition, predictive variables were sought for baseline PAM scores as well as changes that occurred at completion of the Integral Diagnostic Trajectory.

Materials and methods

Research design and participants

This observational study was conducted with data from 241 patients with asthma or COPD who were referred to the pulmonologist at the Radboud university medical center, location Dekkerswald, Nijmegen, the Netherlands. In this study all patients were included for whom this was the first-time referral to the pulmonologist, with a confirmed diagnosis of asthma or COPD and who completed the Integral Diagnostic Trajectory between July 2016 and January 2020. Patients were excluded from this study for the following reasons: those who had an acute exacerbation in the past 3 months prior to referral, who were unable to complete the questionnaires due to cognitive impairment or who were unable to speak or understand the Dutch language.

Ethical considerations

The study was conducted in accordance with European Union directive 2001/20/EC and the Declaration of Helsinki. The Research Ethics Committee of the Radboud University Medical Centre reviewed and approved the study and considered that the study protocol did not fall within the remit of the Medical Research Involving Human Subjects Act (WMO) (ref: 2017/3597). As this study had an observational nature all measurements were obtained as part of usual care. No additional measurements were needed for this study. Data was anonymized before analysis. Baseline results have been presented before at the European Respiratory Society annual congress (Koolen et al., 2017).

Measures

To measure patient activation level the Patient Activation Measure-13 (PAM®) (Hibbard et al., 2005; Rademakers et al., 2012) was assessed before the first visit (T_0) and directly after visit two or three (T_1). The PAM® consists of 13 items with response categories on a 4-point Likert scales ranging from "totally disagree" to "totally agree," and "non-applicable." The PAM® appears to be a valid and reliable instrument to measure activation (Hibbard et al., 2005). The study by Hibbard et al. (2005) shows that the Cronbach's coefficient α was 0.91 in a group of 486 respondents, of which 120 cardiac rehabilitation patients and 366 employees in a large health system in second community, of whom in total 76% reported having a chronic condition. In the current study the Cronbach's coefficient α is 0.67 at T_0 and 0.82 at T_1. With a calculation tool, provided by Insignia Health, raw data was transformed to a standardized patient activation score ranging from 0 to 100. Higher scores indicate greater activation. Based on the score patients were assigned into one of four activation levels: level one (PAM score ≤ 47) "people tend to be overwhelmed and unprepared to play an active role, and are considered passive recipients of care," level 2 (PAM score 47.1-55.1) "individuals lack knowledge and confidence for self-management," level 3 (PAM score 55.2-67.0) "people are beginning to take action, but still may lack confidence and skills to support new behavior," level 4 (PAM score ≥ 67.1) "people have confidence and perform adequate behavior, but may not be able to maintain them in the face of stress." An improvement in 4 points on the PAM scale is considered a minimal clinically important difference (MCID). Permission for using the PAM® was obtained from Insignia Health.

Health status was measured with the Nijmegen Clinical Screening Instrument (NCSI) before the first visit (T_0). (NCSI) (Peters et al., 2009). The NCSI is a valid and evidence-based battery of different instruments to measure many aspects of health status with as little items as possible. The NCSI covers three domains of integral health status: Symptoms, Functional impairment and QoL, which each are subdivided into several sub-domains. The main domain symptoms is subdivided into the three subdomains dyspnea, dyspnea- related emotions and fatigue and measures the overall burden of pulmonary symptoms (Vercoulen et al., 2008), the level of frustration and anxiety a person experiences when dyspnoeic (Vercoulen et al., 2008), and the level of experienced fatigue (Vercoulen et al., 1994). The Cronbach's α in this study are, respectively 0.86, 0.87, and 0.90. The domain functional impairments consist of the two sub-domains behavioral impairment and subjective impairment that measure the extent to which a person cannot perform specific and concrete activities as a result of having the disease (Bergner et al., 1981) and the experienced degree of impairment in general (Maille et al., 1997). The Cronbach's α for these two subdomains are, respectively 0.78 and 0.88 in this study. The main domain QoL consists of three sub-domains general QoL, health related QoL, and satisfaction with relations and measures mood and satisfaction of a person with his/her life (Diener et al., 1985; Beck et al., 1997), the satisfaction related to physical function and the future (Vercoulen et al., 2008) the satisfaction with the (absent) relationships with spouse and others (Vercoulen et al., 2008). The Cronbach's α in this study are, respectively 0.60, 0.63, and 0.69. For all sub-domains the higher the score the more problematic. Cut-offs are available indicating normal functioning (comparable with healthy persons), mild problems or severe problems for each of the sub-scales. The NCSI was completed by the web-based software RadQuest. Results are automatically transformed into the graphical *PatientProfileChart* (PPC) (see **Figure 1**). Lung function, number of exacerbations and body mass index are also displayed on the PatientProfileChart (PPC). In addition, the stages of the grieving process (denial, resistance, sorrow, acceptance) regarding the chronic illness were measured and displayed on the PPC (Boer et al., 2014).

Demographics were collected at first visit (T_0). These include age, gender, BMI, pulmonary function, the modified Medical Research Council (mMRC) (Mahler and Wells, 1988), employment status, and education level according to Verhage's classification (Verhage, 1965). In patients with COPD also the COPD Clinical Questionnaire (CCQ) was measured to measure the degree of disease burden (van der Molen et al., 2003). The Cronbach α in this study is 0.86. A cut-off of 1.9 points was used to discriminate between low or high disease burden. In patients with asthma the level of asthma control was measured with the Asthma Control Questionnaire (ACQ) (Juniper et al., 1999). The Cronbach α in this study is 0.84. Scores below 0.75 points indicate the asthma is under control, scores between 0.75 and 1.5 partially controlled and score above 1.5 indicate uncontrolled asthma.

Integral diagnostic trajectory—Intervention

Briefly, the intervention consisted of two to three visits, with exactly 1 week between the first and second visit. On indication a third visit was scheduled 3–6 weeks after the second visit. Before the first visit patients were asked to fill in the PAM at home.

During the first visit assessments were performed to get a comprehensive picture of the patients' overall health status (van 't Hul et al., 2020). Symptoms, Functional Impairment and QoL were assessed using the NCSI (Peters et al., 2009). At the same visit, the pulmonologist and specialized respiratory nurse consulted with the patients. During these consultations they focused on the biomedical aspects, including optimizing and adherence to pharmacotherapy, smoking, activity behavior, nutritional status, mood, coping with the disease, and self-management behaviors. During the consultations, besides gathering and providing information, most important was establishing a working relation between the patient and clinician. Main goals of visit one: to confirm the medical diagnosis, identify the level of activation and identify the number and complexity of the problems in health status (van 't Hul et al., 2020).

During the second visit the results of all assessments from visit 1, gathered from the performed tests, activity monitor, questionnaires and consultations, were discussed with the patient. Main goal of the consultations (and if necessary, a third consultation) is to construct an individual care plan together with the patient for optimizing the patients' health status that fits their own needs, capabilities and desires. To come to this, several steps had to be taken. During the appointment with the pulmonologist among other things the diagnosis and other medical issues were discussed with the patient. During this discussion the pulmonologist checked for gaps in the patients' knowledge, his/her attitude toward treatment options, provided information to fill the knowledge gap or correct irrational/unhelpful ideas, and discussed possible treatment options in order to optimize the biomedical aspects. The respiratory nurse discussed the PPC in a semi-structured way with patient and partner/spouse. In fact, this specific intervention entails Motivational Interviewing, but is greatly aided by the semi-structured discussion of the PPC. A detailed description of the NCSI-intervention and motivational processes involved can be found elsewhere (Vercoulen, 2012). This intervention has several effects which increase patient activation: (1) The patient becomes aware of the severity of his health status problems; (2) Resistance is easily dealt with as the patient has completed the questionnaire himself and the visual presentation has far more impact than mere words; (3) The patient becomes aware of the role of his own behavior in the health status problems seen on the PPC; (4) Not only the patient and caregiver get these insights, but also the partner.

The objective of the second visit is to let the patient formulate treatment goals and to establish an individual care plan for optimizing the patients' health status. The individual care plan is made together with the specialized respiratory nurse. In some patients the individual care plan was finalized in the second consultation. For other patients a third visit was required, to give the patient time to think about all what had been discussed, more time to form their own opinion or to discuss it with their spouse or other important persons.

Statistical analysis

Due to the retrospective nature, no formal *a priori* sample size calculation was performed.

Patients who completed the PAM before the first visit (T_0) were included in this study. Baseline descriptions are presented as mean ± standard deviation for continuous variables and number and percentages for categorical data. Differences between baseline characteristics of patients with asthma or COPD were tested with an independent samples t-test for continuous variables and using the Chi-square test to compare proportions. A multiple linear regression analysis with a stepwise method was performed to identify variables from the baseline characteristics associated with the PAM score at T_0. PAM score at T_0 was used as dependent variable and sex, age, FEV_1% of predicted, education level, employment status,

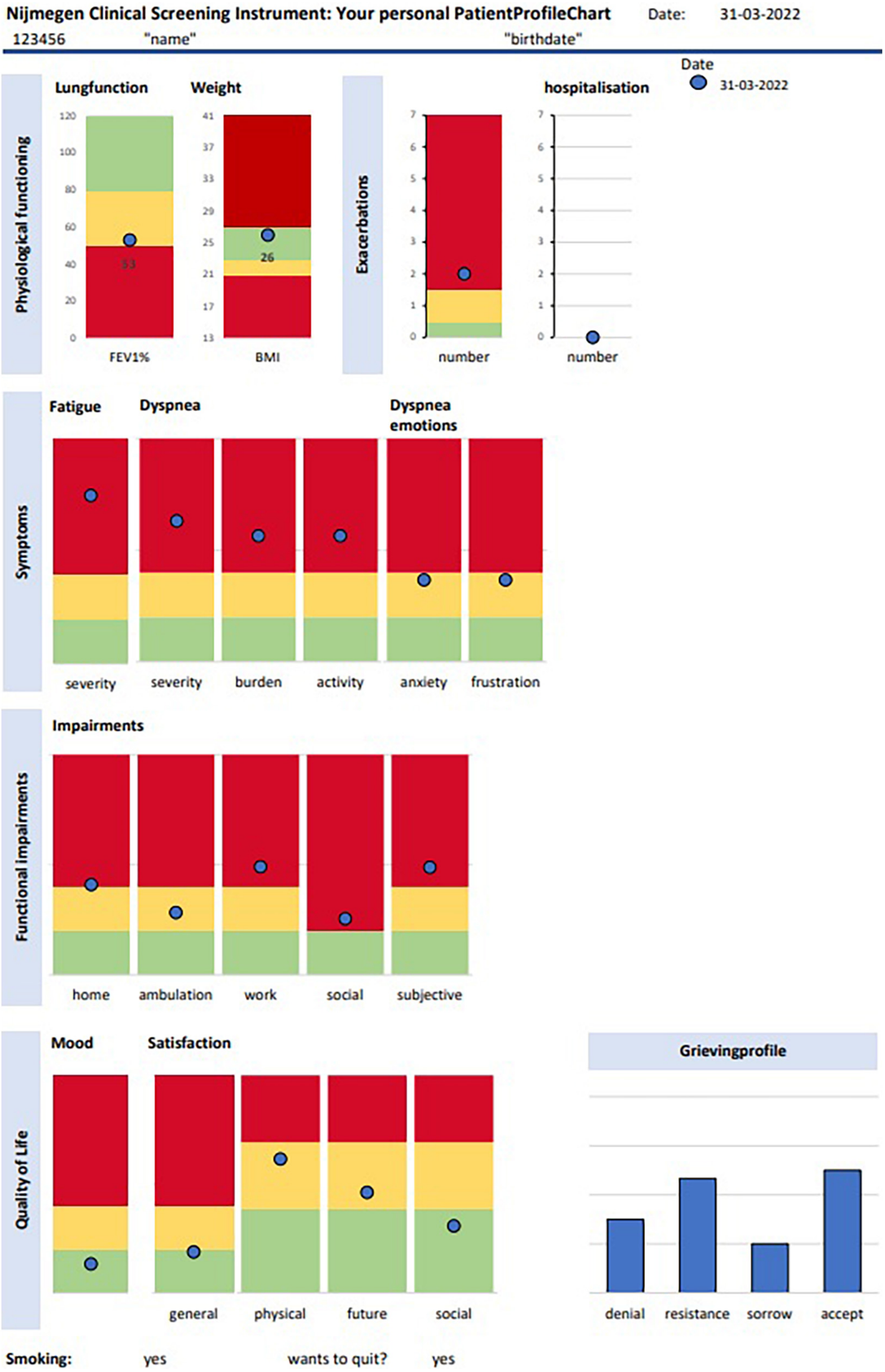

FIGURE 1
Patient profile chart. The green score range indicates "normal functioning," the yellow score range indicates "mild problems," and the red score range indicates "severe problems." Accep, acceptance.

mMRC and number of severe problems on NCSI as independent variables. The analyses are performed for both patient groups separately if PAM scores at T_0 would differ significantly between the two patient groups.

To test changes in PAM scores after the intervention a *t*-test was performed on the PAM scores at T_0 and T_1. Individual responses on the PAM score were calculated at T_1 subtracting the baseline score (T_0) from the score after the intervention (T_1). Responses were dichotomized applying the clinically meaningful change definition of 4 points and the fraction of positive responders was determined (Hibbard et al., 2007). A multiple linear regression analysis with a stepwise method was performed to identify variables from the baseline characteristics associated with change in PAM scores (Delta PAM). For this, the PAM change score from T_0 to T_1 was used as dependent variable. The following independent variables were considered: age, gender, FEV_1% of predicted, mMRC, smoking, education, employment status, number of severe problems on NCSI, PAM score at T_0, number of visits (two or more than two). SPSS version 25 (IBM, Chicago, IL, USA) was used to run the statistical analysis and a *P*-value of < 0.01 was considered statistically significant.

Results

Patient characteristics

Baseline characteristics of 241 patients with asthma or COPD of who met de inclusion criteria are presented in **Table 1**. All patient characteristics, except sex, differed significantly between patients with asthma or COPD. In one third of the patients the individual care plan was completed in two visits, no significant differences were found on PAM T_0 between patients with two consultation days and patients with three consultation days (T_0: 54.7 ± 13.0 vs. 53.0 ± 10.8; $p > 0.05$). Fifty percent of patients with asthma and sixty percent of patients with COPD had low levels of activation at baseline. Patients with COPD had significantly lower scores on the PAM at T_0, and reported significantly more subdomains with severe problems as compared to patients with asthma. On all subdomains of the NCSI proportions of patients with severe problems ranging from 17 to 71% were found in both patient groups, with highest percentages in fatigue, dypnea emotions, and QoL. Of all NCSI-domains, only behavioral impairment and subjective dyspnea were significantly different between both groups. High symptom burden was found in forty percent of patients with COPD as measured with the CCQ and uncontrolled asthma was found in half of the patients with asthma, measured with the ACQ.

A multiple linear regression analysis with PAM score at T_0 as dependent variable in patients with asthma showed that 7% of the variance in PAM T_0 score could be explained by number of severe problems, whereas gender, age, FEV_1% of predicted, education level, employment status, and mMRC did not contribute to the variance ($p < 0.001$). In patients with COPD 18% of the variance in PAM T_0 score could be explained by number of severe problems, age and employment status. Whereas gender, FEV_1% of predicted, education level, and mMRC did not contribute to the variance ($p < 0.001$).

Patient activation measure scores over time

Seventy-nine (59%) patients with asthma and 63 (59%) of the patients with COPD completed both the PAM before and after the intervention (**Figure 2**). In both patient groups no significant differences on PAM T_0 were found between patients who completed and who did not complete the PAM at T_1 (asthma mean PAM score at T_0: 56.7 ± 12.6 vs. 56.0 ± 13.1, $p = 0.77$, and COPD mean PAM score at T_0: 50.6 ± 9.2 vs. 50.0 ± 8.8, $p = 0.73$, respectively).

At first visit (T_0) half of the patients with asthma, who completed both PAM questionnaires, reported low levels of activation (PAM level 1–2, **Figure 3**). There was a significant improvement between the scores on T_0 (T_0: 56.0 ± 13.1) and T_1 (63.3 ± 14.0) in patients with asthma, $p < 0.01$ (**Table 2**). Consequently, the proportion of patients with asthma with PAM level 1 or 2 reduced to one third.

Seventy-three percent of the patients with COPD reported low levels of activation, their belief in own role and confidence levels are low before the first visit (T_0, **Figure 2**). There was a significant improvement between the scores on T_0 (T_0: 50.0 ± 8.8) and T_1 (58.4 ± 11.1) in patients with COPD, $p < 0.01$ (**Table 2**). Resulting in a decrease in patients with COPD to one third with scores belonging to PAM levels 1 or 2.

Predictors of change in patient activation measure score

Multiple linear regression analysis showed that baseline PAM score and employment explained 24% of the variance in change in PAM score between T_0 and T_1 (PAM delta = 18.032–0.285*PAM score T_0 + 8.039 in case of employment $p = 0.003$) in patients with asthma.

In patients with COPD only the PAM score at T_0 explained 18% of the variance in change score (PAM delta = 35.174–0.545 *PAM score T_0, $p = 0.001$).

Discussion

In the present study we found high percentages of patients with asthma or COPD with low activation levels at baseline who were referred to the Integral Diagnostic Trajectory. Baseline activation scores could only be predicted for 7%, by the number of severe problems, in patients with asthma, and for 18% in patients with COPD, by number of severe problems, age and employment status. In two third of the patients, we found a clinically relevant improvement in the PAM-score after two or three visits. The baseline PAM score and being employed could explain 24% of the variance in change scores in patients with asthma, and baseline score alone could explain variance in change scores for 18% in patients with COPD, leaving much room for other contributing factors. The results show that the COPDnet Integral Diagnostic Trajectory can have a positive effect on the activation level of patients with asthma and COPD.

We found high percentages of patients with low activation levels at baseline in patients with asthma or COPD referred to the pulmonologist. Moreover, the patients with COPD in the present study had significantly lower activation scores compared to patients with asthma and compared to mean scores of other studies in patients with COPD (Turner et al., 2014; Bos-Touwen et al., 2015; Korpershoek et al., 2016; Titova et al., 2017). Furthermore, the activation levels of both

TABLE 1 Patient characteristics and percentages of severe problems on NCSI, CCQ and ACQ at baseline for whole study group and for confirmed diagnosis of asthma and COPD.

	Total ($N = 241$)	**Asthma ($n = 134$)**	**COPD ($n = 107$)**	***P*-value**
Age, years	55.6 ± 15.1	48.8 ± 15.5	64.0 ± 9.1	<0.01
Sex, male	39% (94)	37% (49)	42% (45)	n.s.
Employed	50% (117)	65% (86)	30% (31)	<0.01
Educational level				<0.01
Low	14% (29)	6% (7)	22% (21)	
Medium	46% (98)	41% (48)	53% (50)	
High	40% (86)	54% (63)	24% (23)	
Smoking, yes	20% (47)	11% (15)	30% (32)	<0.01
VCmax% of predicted	95.7 ± 15.9	98.4 ± 13.6	92.4 ± 17.9	<0.01
FEV_1% of predicted	73.8 ± 23.9	83.5 ± 18.9	61.6 ± 23.9	<0.01
FEV_1/VC ratio	76.2 ± 20.4	84.8 ± 17.0	65.5 ± 19.2	<0.01
BMI, kg/m^2	27.0 ± 5.9	27.2 ± 5.4	26.7 ± 6.5	n.s.
PAM mean score, points	53.6 ± 11.6	56.3 ± 12.9	50.3 ± 8.9	<0.01
Level 1	37% (89)	28% (38)	48% (51)	<0.01
Level 2	21% (51)	22% (29)	21% (22)	
Level 3	35% (84)	40% (53)	29% (31)	
Level 4	7% (17)	10% (14)	3% (3)	
Number of visits > 2	65% (157)	64% (86)	66% (71)	n.s.
NCSI QoL, severe	56% (118)	51% (61)	61% (57)	n.s.
NCSI HrQoL, severe	33% (70)	31% (37)	36% (33)	n.s.
NCSI Sat. relations, severe	16% (33)	14% (17)	17% (16)	n.s.
NCSI Subj. impairment, severe	53% (113)	51% (61)	56% (52)	n.s.
NCSI Beh. impairments, severe	38% (81)	31% (26)	54% (50)	<0.01
NCSI Subj dyspnea, severe	53% (112)	45% (53)	63% (59)	<0.01
NCSI dyspnea emotions, severe	57% (121)	56% (66)	59% (55)	n.s.
NCSI fatigue, severe	63% (134)	57% (68)	71% (66)	n.s.
NCSI, no subdomains with severe problems	3.24 ± 2.51	2.94 ± 2.46	3.62 ± 2.53	<0.01
mMRC score	1.19 ± 1.19	0.86 ± 1.03	1.60 ± 1.26	<0.01
CCQ score*			2.04 ± 1.09	
CCQ high symptom burden*			40% (43)	
ACQ score*		1.62 ± 1.05		
ACQ controlled asthma*		19% (19)		
ACQ partially controlled*		31% (32)		
ACQ uncontrolled *		50% (51)		

*29 patients did not complete all questionnaires, and due to incorrect diagnosis at referral data was missing from 14 patients with COPD on the CCQ and from 32 patients with asthma on the ACQ. PAM, Patient Activation Measure; FEV_1, forced expiratory volume; VC, vital capacity; BMI, Body Mass Index; NCSI, Nijmegen Clinical Screening instrument; QoL, Quality of Life; HrQoL, Health related quality of life; Sat, satisfaction; Subj, subjective; Beh, behavioral; mMRC, modified Medical Research Council; CCQ, Clinical COPD Questionnaire; ACQ, Asthma Control Questionnaire; *p*-value of either *t*-test or chi-square depending on variable.

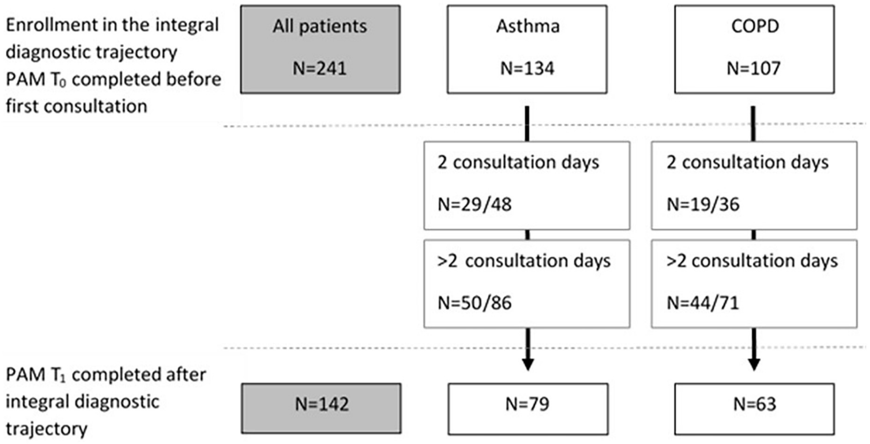

FIGURE 2
Flowchart of patients who completed the PAM at baseline (T_0) and number of patients who completed the PAM after the intervention (T_1), for the whole group and for asthma and COPD separately. For both groups the numbers of patients who completed T_1 of those with two consultations and number of patients who completed T_1 of those with more than two consultations are included.

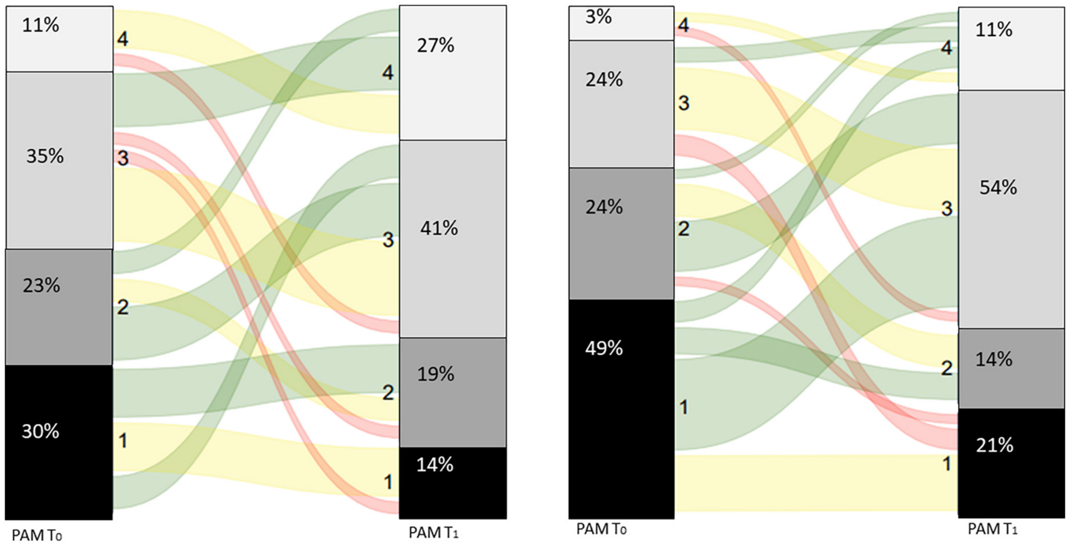

FIGURE 3
Sankey diagram for patients with asthma **(left panel)** and patients with COPD **(right panel)**.

groups were considerably lower than found in other chronic diseases at baseline (Rademakers et al., 2012; Rygg et al., 2012; Titova et al., 2017; Humphries et al., 2021). Hence, despite all care that has been provided by the general practitioner, or other professionals in primary care, these patients still seem to miss the required self-management skills and knowledge for reducing their disease burden. Having a chronic (progressive) disease affects daily life and requires adaptation of behavior by including self-management techniques such as inhalation techniques, medication adherence, energy saving techniques, breathing regulation, continuing to exercise, or apply stress-management (Effing et al., 2016). However, self-management techniques are obviously not automatically adopted. One has to be motivated, engaged, and feel supported to adapt the new desired behavior and to develop skills to better manage their disease (Effing et al., 2012). Moreover, the patient should have sufficient knowledge, skills and be confident that they can perform these behaviors adequately. The high percentages of patients with low activation levels at baseline, indicate that more than half of the patients in this study generally lack knowledge and skills about their disease and the importance of one's own role in disease management.

Increasing the patients' level of activation for self-management is central in the present care model of the hospital-based outpatient Integral Diagnostic Trajectory to improve the

TABLE 2 PAM scores at baseline (T_0) and after the intervention (T_1) for patients whom completed both measurements.

	Asthma (N = 79)		COPD (N = 63)	
	T0	**T1**	**T0**	**T1**
PAM score	56.0 ± 13.1	63.3 ± 14.0*	50.0 ± 8.8	58.4 ± 11.1*
Delta PAM T_0-T_1	7.2 ± 10.6		8.3 ± 11.7	
Delta PAM T_0-T_1 > MCID	66% (52)		65% (41)	

PAM, patient activation measure; MCID, Minimal clinical important difference. *paired t-test, $p < 0.01$.

patients' overall health status (Koolen et al., 2018a). Patients are enticed to play an active role in the consultations with the pulmonologist and specialized respiratory nurse. Together they discuss the results of the various tests, their medical diagnosis, and other aspects of the patients' health status. In addition, by increasing the patients' awareness of the role of their own behavior regarding their health problems the patient understand that they have to change behavior and adopt adequate self-management behaviors to improve their health status. Treatment goals and interventions then logically follow from these insights. During the consultations the pulmonologist and the specialized respiratory nurse apply the key components of motivational interviewing (Miller and Rollnick, 2002) and shared decision making (Elwyn et al., 2017). By forming a team, active listening, checking whether the patient understands all, has questions or concerns, and asking which goals are most important for the patient. All to increase the patients' motivation to take an active role in making an individualized care plan that involves improvement and adaptation of self-management in daily life.

Several intervention studies in patients with COPD aiming at improving self- management and patient activation found significant improvements on patient activation directly after the intervention (Deen et al., 2011) and after 3–6 months (Nguyen et al., 2009; Titova et al., 2017; Collinsworth et al., 2018; Chang and Dai, 2019) whereas other studies showed lack of improvement on patient activation after the intervention (Eikelenboom et al., 2016; North et al., 2020). The differences between the studies with a positive effect on patient activation and those without seem to be due to whether the intervention was performed as intended. Eikelenboom et al. (2016) for example argued that possible explanations could be that firstly, the general practitioners (GP) were not familiar enough with the techniques they had to use, training was not sufficient, secondly, the GPs sometimes forgot to discuss the results, results were not available at the consultation, or an extra consultation was needed. In contrast to, as far as we know, the health care professionals in the other studies all followed the study protocol, felt comfortable in their role, and every patient was offered sessions to enhance knowledge and making a self-management plan. Lack of self-efficacy, knowledge, and experience are known barriers for using shared decision making by clinicians (Driever et al., 2020; Koyama et al., 2022). Although, most clinicians would prefer using shared decision making these reasons make that they fall back to using one-sided directive advice (paternalistic decision making) in daily clinical practice (Driever et al., 2020). The pulmonologists and specialized respiratory nurses using the COPDnet Integral Diagnostic Trajectory intervention were already familiar with motivational interviewing and shared decision making in their daily practice. In fact, the discussion of the PPC is motivational interviewing with the aid of the graphical chart (Vercoulen, 2012). Yet in two third of the patients more than two consultation days were needed to complete the individual care plan based on the patients' goals. Although, time-management wise two consults would be preferable, the pulmonologist and specialized respiratory nurse were flexible in making an extra appointment when needed. The process of the patient was leading in this.

In the current study we found significant improvements in both patient groups, and in two third of the patients we observed a clinically relevant increase in activation after two or three visits. However, one-third of the patients reported low activation levels after two or three visits, patients are in other words still passive and report to lack knowledge or confidence. In these patients the motivational interviewing techniques and shared decision-making processes did not have the desired effect on improving their activation level. Additionally, when focusing on the group with low activation levels at baseline, half did move to the activated levels (level 3–4) after the Integral Diagnostic Trajectory. These patients had initially significantly but not clinically relevant higher scores, but were comparable on age, sex, lung function, number of severe problems, education level, and employment status (data not shown). This is in line with the overall results that showed that baseline activation scores and change scores could only be predicted to a maximum of 24%. On item level significantly more patients in the group who progressed from the low activated to the activated levels reported at baseline to agree with the item "I am confident I can maintain lifestyle changes, like eating right and exercising, even during times of stress" as compared the group of patients who maintained low activated. And a discriminant analysis revealed that 72% of the patients could be correctly classified in "staying low activated" or "become activated" in the group with level 1 or level 2 at baseline, based on the items "I am confident I can maintain lifestyle changes, like eating right and exercising, even during times of stress" and "I have been able to maintain (keep up with) lifestyle changes, like eating right or exercising" (data not shown). Underlining the influence of previous experiences and belief in oneself in the possibility of changing patient activation. Positive experiences can be used as examples, whereas negative experiences need a different approach.

Other studies did not find any prognostic and socio-economic factors (Turner et al., 2014) or could predict activation scores for 16% (Bos-Touwen et al., 2015) to 45%, (Wetzstein et al., 2020) leaving much room for other still unidentified factors. Possible explanation could be the variations in preference between patients and even within patients, depending on the kind of decision that has to be made, for paternalistic or shared decision making (Zizzo et al., 2017). Deen et al. (2011) found that patients who preferred an active role also had significantly higher PAM scores compared to those who preferred a collaborative or passive role. Underlining the importance of getting the patient informed, develop skills and improve their self-esteem.

Moreover, most of the patients want to gain knowledge about the disease and possible treatment options. It is important to acknowledge these personal differences and to check during the consultation what the preferences of the patient are. More research is needed to get insight in why patients do not show improvement on the PAM after an intervention aiming at patient activation, and how to identify these patients at front. A result might be that shared decision making and coming to an individual care plan is not (yet) feasible for this group and further investments in their activation needs to be made.

Strengths and limitations

Our study sample comprised of an unbiased, real-world population referred to the pulmonologist.

There are several limitations in the present study. First, the PAM score after the intervention was not collected from all patients. However, when comparing the proportions of patients of all patients who returned the baseline PAM with the proportions of patients who also returned the second PAM, the percentages of patients per activation level at baseline are comparable divided. Secondly, patients were followed only until directly after the intervention, it would be of interest to study whether these improvements in activation level are fostered and lead to changes in self-management and health status in the long run. Third, we did not include a control group so we could not confirm that the changes in patient activation are the result of the Integral Diagnostic Trajectory-intervention or whether these improvements also would have been accomplished by separate consultations with the pulmonologist and specialized pulmonary nurse.

The present study showed that a low level of activation for self-management is a common feature in patients with asthma and COPD referred for a first-ever outpatient hospital-based consultation. In addition, patients with asthma or COPD who participated in a diagnostic care pathway aiming to get a comprehensive understanding of the patients' health status and to enhance the activation for self-management, higher levels of patient activation were achieved with a relatively short and seemingly simple intervention.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by The Research Ethics Committee of the Radboud University Medical Centre. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

JP conceived the study, performed the statistical analyses, and participated in the drafting of the manuscript. JA and EK conceived the study, extracted the data from the medical records, aided in interpreting the results, and participated in the drafting of the manuscript. JV aided in interpreting the results and participated in the drafting of the manuscript. HAH, HWH, MS, and BB reviewed and edited the manuscript. A'tH was in charge of overall direction and reviewed and edited the manuscript. All authors provided critical feedback and helped to shape the research, analysis and manuscript, and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Patient engagement in the development of CF-CBT: A cystic fibrosis-specific cognitive-behavioral intervention for adults

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Individuals with cystic fibrosis (CF) are at high risk for depression and anxiety, with negative consequences for health and quality of life. Cystic Fibrosis Foundation/European Cystic Fibrosis Society guidelines recommend routine screening, treatment, and preventative efforts. Cognitive-behavioral therapy (CBT) has a large evidence-base for depression/anxiety prevention and treatment. However, traditional CBT protocols require adaptation to address the emotional challenges of coping with CF, stressors related to disease management, and barriers to access to care. The goal of this study was to partner with the CF community to develop an innovative CBT-based intervention for the prevention and treatment of depression and anxiety tailored to CF-specific needs. In-depth feedback was collected *via* audio-recorded telephone interviews with 16 adults with CF from 3 U.S. CF centers, with purposive sampling across gender, age, ethnicity, and disease severity. A semi-structured interview guide elicited discussion of patient experiences of coping with CF, and perspectives on the acceptability of the content, structure, and delivery model of the proposed intervention. Qualitative analysis utilized a content analytic approach. Participants ranged from 21 to 53 years (M=35); eight were female; three were Hispanic. Patient-reported most recent FEV1, a measure of lung function based on forced expiratory volume in in one second, ranged from 25 to 113% predicted (M=72). One participant was post-double lung transplant. Qualitative interviews were analyzed thematically revealing core themes related to the experience of coping with CF. The most frequently cited CF-related stressors were Treatment Burden, Illness Uncertainty, and Financial/Insurance Stress. Participants talked about the interaction of physical symptoms and emotional distress in their daily lives, a topic not typically discussed in routine CF care. Resilience was also a major theme with participants describing strategies they use to cope with CF and hospitalizations. Description of patients' experiences was incorporated into the program's intervention manual and patient workbook. Participants also provided direct feedback on the proposed program. Feedback was largely positive regarding program content and structure, suggesting the acceptability of a CF-specific CBT-based intervention for adults with CF. Features to increase accessibility of care including telehealth, inpatient delivery, and team-based care were perceived as advantageous, and participants emphasized the value of a *CF*-specific mental health intervention. Qualitative findings directly informed the development of CF-CBT, a cognitive-behavioral skills-based program to promote emotional well-being for adults with CF.

KEYWORDS

cystic fibrosis, program development, qualitative, depression, anxiety, resilience

Introduction

The prevalence of depression and anxiety in people with cystic fibrosis (pwCF) is 2 to 3 times the general population (Quittner et al., 2014). Untreated depression and anxiety can have a devastating impact on health outcomes for people with this chronic, genetic illness, with negative consequences for the ability to sustain daily care, health-related quality of life (HRQoL), lung functioning, and survival (Riekert et al., 2007; Havermans et al., 2008; Smith et al., 2010; Yohannes et al., 2012; Snell et al., 2014; Schechter et al., 2021). International CF Foundation (CFF) and European CF Society (ECFS) guidelines have recommended routine screening, treatment, and preventative efforts for depression and anxiety for all pwCF ages 12 and above (Quittner, et al., 2016). Screening provides a tremendous opportunity for early intervention to prevent negative outcomes. However, access to evidence-based mental health care that addresses the needs of pwCF is limited; barriers to access include insurance or financial obstacles, the lack of understanding about CF by community-based providers, limited availability of mental health care providers with training in evidence-based interventions, and long waitlists for care (Mueller et al., 2020). A survey of 1,454 CF healthcare professionals conducted by the CFF and ECFS concluded that CF centers need additional training and educational resources to implement the mental health guidelines. Notably, 47% of providers indicated a desire for training in cognitive-behavioral therapy (CBT; Abbott et al., 2015). This speaks to the need for innovative models of mental health intervention, training, and service delivery to address the unique emotional challenges of living with CF and barriers to access to mental health care.

Cognitive-behavioral therapy has demonstrated efficacy in improving HRQoL and preventing and treating depression and anxiety in general and chronic illness populations (Butler et al., 2006; Fordham et al., 2021). There is little data on evidence-based interventions like CBT for pwCF, though emerging research in this area shows promise (Graziano et al., 2021; O'Hayer et al., 2021; Bathgate et al., 2022). Existing treatment protocols, however, require tailoring to address the specialized needs of pwCF. Trials of general CBT have typically excluded people with comorbid chronic illness conditions, and standard CBT protocols are not often easily applied to chronic illness. CBT for anxiety, for example, typically targets unrealistic fears and worries (Greer et al., 2010). However, pwCF often have rational anxiety and fears related to their long-term health and medical experiences, including worries about disease progression, disability, painful medical procedures, difficulty balancing a burdensome CF daily treatment regimen with other life goals, and a shortened life span (Ratjen et al., 2015). CBT interventions for depression include core treatment components, such as increasing behavioral activation and problem-solving. However, pwCF face unique barriers to behavioral activation and problem-solving that would not be addressed in a typical CBT protocol, such as managing CF symptoms, treatment burden, and infection control. In addition, existing CBT protocols for depression and anxiety do not include content that focuses on the impact of emotional distress on the ability to sustain daily CF care, with the potential for both immediate and downstream consequences for overall health (Cameron et al., 2022).

Our team of psychologists and psychiatrists specializing in CF mental health care and research partnered with the CF community to develop an innovative CBT-based intervention for the prevention and treatment of depression and anxiety directly addressing the needs of adults with CF. In-depth individual interviews were conducted with adults with CF across three CF centers to gather critical input to inform intervention development. A structured interview guided discussion of patient experiences of coping with CF and their perspectives on the acceptability of the content, structure, and delivery model of the proposed CBT-based intervention. Two focus groups that paralleled the structured interviews with patients were conducted with CF care teams to elicit stakeholder input from multidisciplinary providers. All of this feedback informed the design of *CF-CBT: A Cognitive-Behavioral Skills-Based Program to Promote Emotional Well-Being for Adults with Cystic Fibrosis*, a modular 8-session CBT-based intervention to prevent and treat depression and anxiety.

CF-CBT is the first mental health intervention for CF that utilized qualitative input from key stakeholders throughout the development process. It was conceptualized and designed to be incorporated within an integrated model of care, delivered by trained multidisciplinary CF health care providers, offering accessible preventive mental health care as a component of routine CF care. Integrated care models are generally preferred by patients, with strong evidence that they improve access as well as outcomes (Asarnow et al., 2015). Flexibility in mode of delivery was also incorporated into the model to improve accessibility through optional telehealth visits and the ability to conduct sessions during an inpatient admission, as needed. After the CF-CBT intervention manual, patient workbook and training program for multidisciplinary providers were developed based on CF community input, the feasibility, acceptability, and efficacy of the program were examined in a multi-center pilot (Friedman et al., 2022) and an ongoing randomized waitlist-controlled trial. Clinical trials targeted adults with mild symptoms of depression and anxiety with the goals of promoting resilience, preventing the escalation of depression and anxiety, and reducing associated morbidity.

This study presents the results of a qualitative analysis of the interviews of pwCF completed in the development of CF-CBT, using an inductive process to identify frequent themes about the experiences of coping with CF and patient perspectives on the proposed CF-specific mental health intervention. These qualitative interviews guided the CF-CBT program development with the goal of creating a mental health intervention with program resources for CF care providers and patients that is highly relevant to the needs of this population. A description of qualitative findings and how these findings guided the CF-CBT program development follows.

Materials and methods

A semi-structured interview guide including 44 questions with follow-up probes, was developed by the study PIs (DF, AMG) with input from experts in CF mental health from each study site (ALQ, BAS). The interview guide was organized around two main themes: *Experiences of Coping with CF* and *Program Development Feedback*. Questions eliciting content about experiences of coping with CF included questions about CF-related stressors (e.g., "What do you think are the some of the top stressors that individuals with CF face?"), utilization of coping strategies (e.g., "Are there any specific strategies you use to cope with an inpatient admission?)," and experience with mental health treatment (e.g., "If you have had counseling, what do you think has been the most helpful aspect when it comes to managing the challenges of living with CF?"). Questions eliciting Program Development Feedback included the following: (1) General impressions of the program, (2) Program structure and delivery model (e.g., "Do you see any advantages or disadvantages to the program being delivered by a member of the CF team?"), and (3) session by session feedback on proposed CF-specific content (e.g., "What do you think of these examples? Do they seem relevant? Can you think of any other examples of situations that may cause anxiety in CF?"), perceived barriers (e.g., "Do you see any specific barriers to practicing relaxation for individuals with CF?"), and suggested modifications (e.g., "Do you see any ways to tailor this topic so that it can be made especially useful for individuals with CF?").

Individual one hour audio-recorded interviews following the interview guide were conducted by phone with 16 adults with CF recruited from three U.S. CF centers between March 2017 and January 2018. Interviewers were MD and PhD investigators (DF, ALQ, and BAS). Purposive sampling was used to obtain diverse perspectives across gender, age, ethnicity, and CF disease severity. Institutional review board review determined this protocol to be exempt. Focus groups of CF care teams (pulmonologists, nurses, nutritionists, physical and respiratory therapists, and social workers) at two CF centers were also conducted. Interviews and focus group feedback informed the design of the intervention manual and patient workbook. Two of the 16 patient interviews were not recorded due to technical difficulties. In these cases, detailed hand-written notes from the interviewers were utilized. Thus, while feedback from all interviews and focus groups informed intervention development, 14 transcribed adult patient interviews were included in formal qualitative analysis in which interview text passages were categorized by theme.

Transcribed interviews were pseudonymized to preserve confidentiality and analyzed qualitatively using NVivo content-analysis software, version 12. Content-analytic methods were used to identify primary, secondary and tertiary themes based on line-by-line coding, creating a coding frame or codebook (Hsieh and Shannon, 2005). A hybrid analytic process utilized inductive reasoning to identify themes regarding the experience of coping with CF, and a mixed inductive and deductive approach to analyzing program feedback. For example, several questions elicited content regarding the deductively derived theme of "*Modifications to CBT Skill Application in CF*," (e.g., "What do you think are barriers to staying active and social for people with CF?"), but the barriers that emerged based on that question and throughout the interviews were further coded into the subthemes of *Mental Health*, *Physical*, and *Social Considerations* in an inductive process (Bingham and Witkowsky, 2022). Consensus coding was utilized by a team of three PhD-level investigators (DF, MMK, and ALQ) to establish the major themes and codebook. Subsequently, two of the investigators (DF, MMK) met together to discuss and code the remaining 11 interviews utilizing this codebook, reaching consensus on the categorization of each text passage. The coders created codes and subcodes for each text passage until thematic saturation was reached after eight transcripts were coded, and then subsequent text passages were categorized within these themes. Participant-reported demographic information was collected during interviews and descriptively summarized.

Results

Participant characteristics

Patients ranged from 21 to 53 years ($M=35$); eight were female; three identified as Hispanic/Latinx; and one was post-transplant. Of the 10 providing these data, most recent patient-reported forced expiratory volume in one second (FEV_1), a marker of lung function in pwCF, ranged from 25 to 113% of predicted ($M=72$). As noted above, of the 16 interviews conducted, 14 were able to be transcribed and included in the formal qualitative analysis presented here. See Table 1 depicting patient characteristics.

Qualitative themes

There were two overarching topic areas elicited by the interview questions: (1) Experiences of Coping with CF and (2) Program Development Feedback. Figure 1 displays the coding frame that was developed in these two topic areas. Themes that were identified from the interviews within these two topic areas are presented in Tables 2–6, indicating the number of interviews in which each theme was identified, with accompanying representative quotes.

Topic 1: Experiences of coping with CF

Coding of the themes related to Experiences of Coping with CF identified three major themes: *CF-related Stressors*, *Connections between Emotional and Physical Health*, and *Resilience*.

Participants were asked directly about their "top CF-related stressors," and themes related to CF stressors emerged throughout the interview when discussing how best to address these concerns in the proposed CBT-based intervention. The most frequently cited CF-related stressors were: (1) *Treatment Burden* (i.e., the amount of time and energy required for daily CF self-care), (2) *Illness Uncertainty* (i.e., difficulty planning or setting life goals due to unpredictability of exacerbations, need for hospitalization, or disease progression), and (3) *Financial/Insurance Stress* (i.e., concerns about paying for treatments and hospitalizations). See Table 2 for exemplar quotes. One participant described *Treatment Burden* as follows:

> Participant 04: *"The overall burden of managing the illness with medications and the time that takes, and I think the inability to really fully engage in life like you would like to."*

Illness uncertainty, a common component of chronic illness conditions, refers to the experience of unpredictability in relation to symptom presentation and long-term course. As noted, in CF, there is a lack of predictability in relation to illness exacerbations, need for hospitalization and disease progression. The following are several additional illustrative quotes describing the theme of *Illness Uncertainty*:

> Participant 03: "*It's hard to plan for the future. It's hard to make long-term plans*"
>
> Participant 04: "*I think with …not being able to plan ahead, like with school, with work, are you able to meet the demands of that situation, like am I going to be have to be out of work, am I going to be sick and not be able to be there.*"
>
> Participant 04: "*And I think, … am I able to – am I going to be able to have a so-called normal life, you know, get married, have kids, contribute to society, have a job.*"

Additional CF-related stressors that were mentioned in at least six interviews were: *Hospitalizations*, *Self-Perception/Social Comparison*, *Disease Progression*, and *Fear of Death/Dying*. However, many other CF-related stressors were identified in five or fewer interviews, such as *Clinic Appointments and Medical Procedures*, *Communication and Disclosure about CF*, *Survivor Guilt*, *Dating and Relationships*, and *Family Planning*. In total, a list of 18 CF-related stressors were ultimately included in the initial CF-CBT session focused on increasing awareness of one's response to stress, linking attitudes and actions in response to stress and well-being, and identifying coping strengths. The rationale for including a long list of CF-related stressors that were identified by study participants was to normalize these experiences and decrease the stigma related to discussing these concerns.

Connection between emotional and physical health

Participants were asked whether they saw a connection between emotional and physical health in their own lives, and this mind–body link was a major theme mentioned throughout the interviews. Three subthemes were identified. The first was *the Impact of Emotional Health on the Ability to Sustain Daily CF Care*. Exemplar quotes illustrating this theme are included in Table 3. Participants described how low mood significantly affected their motivation to complete their daily treatments. Not surprisingly, negative thinking patterns that affect motivation were described as more prevalent during periods of low mood. Negative thought patterns often involved "all-or-nothing" thinking, for example, believing

TABLE 1 Participant characteristics.

Age in years, mean (*SD*; range)	35.4 (12.3;21–53)
Male	8 (50.0%)
Hispanic/Latino	3 (18.8%)
FEV1, % predicted (patient reported)	71.5 (26.0;25–113)*
Post-transplant status	1 (6.3%)
Ever diagnosed with depression/anxiety	8 (50.0%)
Had participated in mental health treatment (therapy/medication)	13 (81.3%)

*Based on *N* of 10 due to missing data.

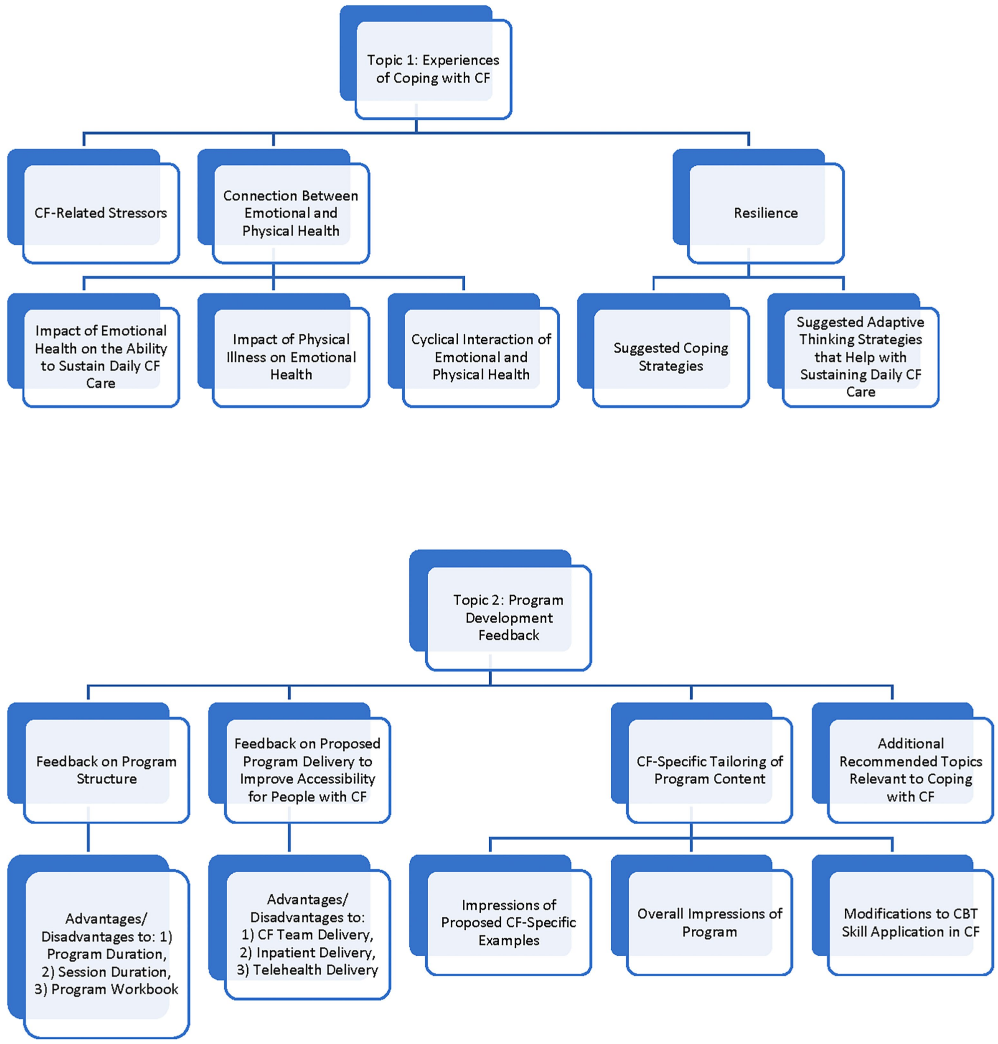

FIGURE 1
Coding frame.

that if it was not possible to do 100% of treatments, it was not worth doing any treatments. Other participants noted that negative thoughts about how they would be viewed by others interfered with doing treatments. For example, one participant stated:

> Participant 01: *"…it's embarrassing…I mean I can't imagine having been in college and having to break out my neb or a vest."*

Another subtheme was the *Impact of Physical Illness on Emotional Health* (Table 3). Participants described the impact of physical illness on their mood, noting increased symptoms of anxiety and depression during times of CF symptom exacerbation. Many participants talked about feeling a *Loss of Control* when they were experiencing an exacerbation of symptoms or a need for hospitalization, despite their best efforts to maintain their health. Negative thinking patterns emerged as a prevalent subtheme, with participants describing overgeneralized patterns of thinking that nothing they do affects their health status; self-critical thoughts that they should be doing better or be able to contribute more to their families or to society; and negative thoughts comparing themselves to peers or worrying about being judged negatively by others for CF-related symptoms, disability, or treatment requirements. Exemplar quotes are included in Table 3. An additional example follows:

> Participant 12: *"it was something I always could sort of control and maintain and stay on top of…Like, I could do my therapy and then I could feel pretty good after that… It was probably when things got out of hand with me that I couldn't control anymore – that I just knew, I was on the losing end of it and I just didn't know what the next day or next week would bring upon me."*

TABLE 2 *CF*-related stressors.

Theme/Subtheme	Frequency	Exemplar quote
Treatment burden	10	Participant 08: "Making sure you do all your treatments, you take all your medicines, you make all the appointments you have to, and you go to them, and then making sure you refill everything in time so you do not run out. It is just a constantly moving thing. It's like you are never done with it."
Illness uncertainty	9	Participant 08: "When you are healthy, thinking about the next time that you are going to get sick… the anticipation of being sick again is definitely getting to me, and made it hard to enjoy being healthy."
Financial/insurance stress	8	Participant 12: "The highest payment issue in our lives is to not lose our house over my health. That was always a huge 'keep me awake at night' issue."
Hospitalization	6	Participant 11: "There's probably nothing more stressful than being hospitalized and being treated like a pin cushion."
Self-perception/social comparison	6	Participant 06: "Comparing yourself to your peers … me and my friends, we are on the same page all the way through college … and then … you start to see, your friends have moved on. They moved out and they have got careers, some are getting married, and me, you know, I have gotten sicker."
Disease progression	6	Participant 07: "Acquiring other illnesses kind of related from CF whether it's severe diabetes or liver issues or bone issues.… Knowing that these things may come out as you get older, even though you are taking good care of yourself is scary."
Fear of death/dying	6	Participant 10: "When I was growing up, they always had a number, a life expectancy number, and it was 8, when I was born, you know, you are not going to live past grade school and then you get past grade school and the number is like 15 and then it's 18 and then it's, 24, then 30. Growing up, you are always trying to get above the age."

TABLE 3 Connection between emotional and physical health.

Theme/Subtheme	Frequency	Exemplar quote
Impact of emotional health on the ability to sustain daily CF care		
Low motivation	4	Participant 02:"I also notice … when my mood is not as good, it's harder to – I cannot say I'm ever enthusiastic about treatment, breathing treatments for my airway clearance, but I feel less motivated … I'm feeling lousy anyway so what does it really matter if I miss a treatment … those thoughts creep in more easily."
Negative thoughts that impact adherence	9	Participant 08: "Sometimes when I'm not feeling well, that's really overwhelming … so sometimes I think, if I cannot do all of them at once, then I just will not do them."
Impact of physical illness on emotional health		
Loss of control	5	Participant 14: "If I wake up, let us say, coughing a lot, shortness of breath, I already know it has to do with CF – it does get me mad because I do not understand how I'm feeling [awful] that day – if I'm doing everything I'm supposed to do."
Mood, anxiety, and depression	7	Participant 02: "Sometimes the first thing I notice [when I'm having an exacerbation] is that my mood is not as good, you know, that I'm maybe a little bit more irritable, that I become impatient or things annoy me that might not typically even bother me… So I think it's very tied together, for me anyway."
Negative thoughts	7	Participant 04: [I think] "I do not have any impact on my health anyway."
Self-critical thoughts	5	Participant 04: [I think] "I'm not good enough. I'm not able to do the things I want to do. I'm not contributing to my family like I should. I'm not worthy."
Social comparison	7	Participant 13: "I also am wondering, at work when I'm coughing – what do people think? And even like if I'm in a breakroom, I kinda step aside and take my medicine in the bathroom because I do not want people to see me. My mind wonders what people are thinking – and if they think I'm weird … a big thing is doing treatments around other people. Unless it's a close family or friend, I'm having a hard time learning how to do that around others."
Cyclical interaction of emotional and physical health		
Description of cycle	7	Participant 09: "They are 100% in every single way possible to the highest degree tied…You immediately start to see the integration of your mental health when your body starts to feel awful…because you just become so weak and unable to do all the things you want to do, and that has a serious effect on your mental health. Likewise … I know myself and I know a bunch of other CF'ers too, when they start to develop or go through life stressors or anxiety flares up or depression is bad, that may just be a mental thing, but next thing you know, it affects their physical ability to take care of themselves or to keep eating correctly, or frankly to really [care] that they need to do what they need to do on a daily basis. And it severely impacts your physical health because …. you just start to get sick…. So, [physical and emotional health] go hand in hand in every way possible."

TABLE 4 Resilience.

Theme/Subtheme	Frequency	Exemplar quote
Selected suggested adaptive thinking strategies that help with sustaining daily CF care*		
Self-Compassion/Do not be too hard on yourself	6	Participant 08: "I would have to tell myself, I'm not feeling well and I need to take care of myself and I'm not in a rush. There's no reason really that I have to do all these things at once because I'm not going to go anywhere today. I'm going to stay home and not feel well, so I can just sit on the floor with my vest all set and do a nebulizer first, and then do the vest and I can shut it off as many times as I need, to take a break, and then I can do the other nebulizer afterwards or later if I'm feeling really bad. I think it's good that I conditioned myself to do these treatments consistently in a certain way, but then it was also good to realize it's okay if I restructure the way that I normally do things to adapt to how I'm feeling."
Identifying your personal goals and values	3	Participant 11: "Finding yourself good goals, knowing what you want to do, what you want to feel like, what you want to look like."
Selected suggested coping strategies: coping with hospitalization*		
Distracting, fun activities	10	Participant 01: "What do you do at home to make yourself feel better? Do you have a cup of tea and listen to music? Do you read a book? Do you read a magazine?"
Stay active	8	Participant 06: "Physical activity. I try to do it right away; getting out of the room helps."
Social support	7	Participant 04: "I normally reach out to people and make sure I'm in contact with friends and family."
Acceptance	3	Participant 08: "The main thing I had to do was just accept that I was there and no amount of not wanting to be there was going to change that, and then keep myself busy with little things… I have my computer, I have games on it. I bring crossword puzzles to focus my brain on something… I would look forward to the food tray coming… anticipating that… I would not say making the most, but - making a better time out of little things."

*Categories were included in the table when mentioned by 3 or more participants.

Finally, participants described a *Cyclical Interaction of Emotional and Physical Health*. In different ways, they described how physical illness and emotional health are intimately tied together. It can be difficult to tease apart whether the cycle begins with increased stress and low mood or with decreased physical well-being, and there is an interactive effect in which each symptom complex (emotional or physical) intensifies and maintains the other. See Table 3 for one participant description of this cycle. Additional quotes exemplifying the cyclical interaction between physical and emotional health follow:

> Participant 03: *"The worse you feel, you want to do less, but then the less you do, the [worse] you feel. It's a cycle."*
>
> Participant 06: *"(Emotional and physical health are) very related … Depression can come at any time and can make you feel physically sick. I feel really fatigued and I don't want to do anything, and then the next day I feel fine, so what was going on? Even when you are feeling physically well, it can weigh you down."*
>
> Participant 07: *"If you don't feel well physically, you may… think more negatively and that can have a dire effect long term… In a way, your mental health may be even more important than your physical health."*

Resilience

Resilience was a third major theme in the topic area of Experience of Coping with CF, in which participants described strategies they use to cope with CF on a daily basis and more specifically, to help with sustaining daily CF care and inpatient admissions for CF exacerbations (Table 4). At least three participants endorsed the following strategies for coping with CF-related stress: *Relaxation, Meditation, or Mindfulness; Physical Activity or Exercise; Distraction; Identifying Sources of Anxiety and Breaking these Down into Manageable Parts; Practice Disclosing about CF to Others; Reframing Negative Thoughts and Positive Self-talk; and Use of Social Support*. Fewer than three participants shared that they managed CF-related stress by *Preparing in Advance for Admissions; Focusing on Structure or Routine; or Focusing on Rest*.

When asked about what helps pwCF to stay motivated to sustain daily CF care, participants identified several types of adaptive thinking patterns which align well with a CBT-based approach to stress management and were included in the intervention manual. The most often cited thinking patterns were coded as *Self-Compassion* ("Do not be too hard on yourself") and *Identify Your Personal Goals/Values*. For example, regarding *Self-Compassion*, one participant (01) stated *"[I think:] I did not do my best work today, but I have another shot at it tomorrow,"* and another (Participant 13) stated "*Do not punish yourself if you fall back*." At least two participants also identified the strategies *Do not Overthink* and *Make CF Treatments a Routine* as helpful in staying motivated to complete daily CF treatments.

Participants were also asked about strategies they used to cope with being in the hospital for treatment of a CF exacerbation. Frequently cited strategies were coded into the following categories: *Distraction/Fun Activities*, *Stay Active/Engage in Physical Therapy*, and *Social Support* (e.g., reaching out to friends and family, engaging with hospital staff whom they know), and *Acceptance*. The category of Acceptance can be described as letting go of the fight to stay out of the hospital, which may have been adaptive up to that point, and instead focusing on the benefits of being treated and making the best of the current admission.

Topic 2: Program development feedback

In addition to seeking input on coping experiences, participants were asked in-depth questions about the acceptability of the proposed CBT-based program structure, mode of delivery, and content. The four major themes that emerged were: (1) *Feedback on Program Structure*, (2) *Feedback on Proposed Program Delivery to Improve Accessibility*, (3) *CF-specific Tailoring of Program Content, and* (4) *Additional Recommended Topics*.

Feedback on program structure

Participants were given information on the proposed program, beginning with a description of the rationale for a CF-specific intervention and the benefits of CBT. Participants were informed that the proposed program consisted of eight individual, weekly sessions of CBT, each session lasting approximately 30 minutes and facilitated by an existing member of the patient's CF-care team who would receive specific training in the program. Participants were also told that each session would be guided by a workbook that included more information and opportunities for skill practice. Responses to the proposed length of the program (eight sessions) were mixed, with nine of fourteen participants describing it as reasonable, two describing it as too short, one describing it as too long, and the remaining two participants believing that program length should be dependent on individual need. For example, one participant mentioned that some people might require more sessions for skill practice:

> Participant 09: *"I'd [recommend] a little more flexibility, maybe [for] somebody who is having a hard time developing CBT skills."*

Flexibility was also recommended by 11 of 14 participants regarding program length, with several recommending a range of 45–60 minutes rather than the 30 minutes initially proposed. However, nine of fourteen participants described 30 minutes as reasonable, with Participant 06 noting that some pwCF *"can get tired from talking for longer."* Participants were also asked about their impressions of a patient workbook that covers the core topics. Thirteen of fourteen participants described advantages to the workbook, including the ability to take notes, use the workbook for reference and to guide practice between sessions. For example, one participant stated:

> Participant 05: *"Retention is always based on repetition…being able to reinforce [what you learn] is good if it ties into the workbook."*

One participant shared a potential disadvantage of the workbook, noting that some pwCF might have challenges with reading comprehension and miss important content.

Feedback on proposed program delivery to improve accessibility for people with CF

The intervention was developed to facilitate greater access to evidence-based care for pwCF. These included (1) integration into routine CF care through delivery of the intervention by trained multidisciplinary CF care team members, (2) use of telehealth, and (3) inpatient delivery for those who were medically hospitalized to maintain to maintain continuity of care. For each of these domains, the following question was posed, "What do you think are the advantages and disadvantages?" to this specific aspect of the model (Table 5). CF team-based care integration was largely viewed as a beneficial component to the proposed intervention model. Advantages of CF care team delivery were discussed in thirteen of fourteen interviews and included statements about the benefits of familiarity and comfort with CF care team members, the provider's knowledge of CF, and easier access to care. For example, one participant stated:

> Participant 02: *"Advantages, I think, are that it's very easy to access and you don't have to bring another care provider in, get to know somebody and build a level of comfort with them"*

Eight participants also noted possible disadvantages to an integrated delivery model, with six citing privacy/confidentiality and role conflict possibly limiting a patient's ability to be as open as they might otherwise be with a provider who is not also a member of their CF care team. For example, the same participant who cited the advantage above also stated:

> Participant 02: "*The only disadvantage I can really think of was if, you know, I know that in our clinic staff pretty much know everything about our lives anyway, but if there was something that you weren't comfortable discussing or that you wanted to have somebody sort of out of that loop, that would be the only drawback that I could think of, if you wanted to kind of compartmentalize it and to keep that separate.*"

One participant noted that CF care team delivery may increase the burden on the CF care team and another noted concern about the level of training or expertise of non-mental health CF providers delivering this intervention.

Numerous advantages to telehealth delivery were cited, such as decreasing the burden of travel to the hospital, and not having to travel or cancel appointments when sick or due to weather. One participant stated:

> Participant 13:*"I think it's a great advantage because I have a hard time now getting in therapy sessions with my work schedule, so even to be able to set a time on a lunch break, to be able to talk, I think that's a great idea."*

Participants also noted that they may feel more open to talk about their concerns in their home environment. The few disadvantages to telehealth delivery included wanting to meet

TABLE 5 Increasing accessibility/delivery considerations.

Theme/Subtheme	Frequency	Exemplar quotes
CF Team Delivery		
Advantages	13	Participant 01: "If … CBT is part of the overall cystic fibrosis care… it's letting the patients know that CBT is real and it works, and that there's a lot of valuable lessons [in CBT]." Participant 06: "The CF team knows us very well … and it's their specialty." Participant 11: "They're already familiar with the disease so you do not have to explain to them what [CF] is."
Disadvantages	8	Participant 02: "If there was something that you were not comfortable discussing or … if you wanted to kind of compartmentalize it and to keep that separate." Participant 04: "It may be hard to be honest with a member of the team if you are trying to say you are compliant but you are really not."
Inpatient Delivery		
Advantages	13	Participant 01: "Continuity is important." Participant 03: "When I'm inpatient…it's lonely and you have a lot of time with yourself … sometimes that's a little rough because I'm hardest on myself and sometimes I'm not my own best friend." Participant 07: "You might get more even heightened fear and anxiety when you are in the hospital … so it could be really beneficial."
Disadvantages	1	Participant 14: "From experience, I'd rather just concentrate on getting better. And once I feel better, I can…have an appointment."
Telephone Delivery		
Advantages	10	Participant 04: "Having it accessible via phone would make the follow-through better because you'd get more [people] sticking with the program." Participant 09: "Definitely an advantage…for some people including myself who live a little bit further from the hospital. They [may] have…long work hours, [so phone delivery is] more flexible."
Disadvantages	4	Participant 02: "Personally, I like eye contact and…feel a little bit more comfortable in person." Participant 11: "There's a lot of body language you'd be missing out on."

with the provider in person, at least initially, or feeling more comfortable in-person, and two participants noted that there may be difficulty finding a quiet, private space for a session at home. The CF-CBT intervention model was originally proposed to include an initial in-person visit followed by optional in-person or telephone visits. However, during the COVID-19 pandemic, the study team pivoted to telehealth visits for all eight sessions.

The option of inpatient delivery was also seen as positive by participants, with thirteen of fourteen interviews mentioning the benefit to continuity of care, access to a stress-management intervention during a particularly stressful time, and the ability to target the specific types of stressful experiences that arise during an inpatient admission. One participant stated:

> Participant 02: "*Oh, I think that's huge because that's such a stressful time and there are always things that arise that don't come up in everyday life. I think it would be incredibly helpful to be able to continue that while you're inpatient. Sure. That's a huge plus.*"

CF-specific tailoring of program content

The theme of *CF-Specific Tailoring of Program Content* encompassed three subthemes: (1) *Modifications to CBT Skill Application in CF*, (2) *Overall Impression of the Program,* and (3) *Impressions of Proposed CF-Specific Examples.*

Feedback regarding overall impressions of the program was positive and emphasized the value of a CF-specific mental health intervention and greater access to evidence-based mental health care (Table 6). Participant 06 stated:

> "*It's an aspect of CF that has been neglected over the years,*" and another (Participant 01) said, "*Where have you been all my life?… It's so fundamentally important.… Mental health is a real big issue.*" A 3rd participant (07) stated, "*I think it's very beneficial for a large majority of CF patients.*"

Examples of how CF-specific content could be integrated into the intervention were provided to participants for feedback. This included common negative thought patterns (e.g., worry and self-critical) for a session identifying maladaptive thoughts and building adaptive thinking skills (e.g., comparing self unfairly to others who have CF or peers who do not have CF), common anxiety-provoking situations for a session on developing an anxiety-management coping plan (e.g., worrying that others will have a negative reaction to coughing in public), and potential health-related goal areas for a session on individualized goal-setting and problem-solving (e.g., completing a specific CF treatment more often or more consistently, or communicating better with their CF team about their needs). Participants were uniformly positive about these, found them relatable, and provided additional CF-specific examples that were subsequently incorporated into the CF-CBT program materials.

Participants were asked directly how each component of CBT skill development included in the proposed intervention should be modified to make it more relevant or accessible for pwCF. After describing the CBT skill, each participant was asked about CF-specific barriers to skill practice and suggested modifications (e.g., "Do you see any ways to tailor this topic so that it can be made especially useful for individuals with CF?"). Participants noted CF-specific barriers and suggested modifications for teaching relaxation skills or creating behavioral activation plans to prevent or relieve depressive

TABLE 6 CF-specific tailoring of program content.

		Overall Impressions of Program
Exemplar quotes		Participant 01: “It’s an important component that’s missing from overall care.” Participant 02: “I have used CBT in the past, but my experience was that it was difficult to access…. To say that it changed my life would be an understatement…. It was so helpful, so valuable…. In the end, I really felt different.” Participant 08: “One of the most helpful things was receiving the validation that this was a significant problem I was having, because I had never gone for mental health treatment before. I was always so focused on physical health.… This is a valid issue that lots of people struggle with, and I’m not just being a crazy person because I feel like I am having these problems. They are legitimate, and there are ways to treat them and take care of them, just like there are ways to treat cystic fibrosis.”
		Suggested Modifications to CBT Skill Application in CF
Relaxation		
Theme/Subtheme	**Frequency**	**Exemplar quote**
Physical considerations	8	Participant 08: “If I’m having an exacerbation and not feeling well, trying to breathe deeply makes it worse and makes me cough a lot.”
Suggested Modification	7	Participant 09: “Some of us can take huge breaths … but [for] others … guided imagery that does not require a lot of physical effort might be infinitely better and a little bit more tailored.”
Behavioral activation		
Theme/Subtheme	**Frequency**	**Exemplar quote**
Mental health considerations	4	Participant 03: “It’s so much easier to say oh, let us just cancel it…. It’s so much easier to just say that than to push yourself and try.”
Suggested Modification	3	Participant 08: “There does not have to be a specific concrete goal that you need to reach and you are not failing if you do not reach a certain level … you are just accomplishing what you are able to at that time, which is better than doing nothing.”
Physical considerations	14	Participant 05: “Well, it goes back to … the physical limitations. I have a hard time when I’m not using oxygen, being able to maintain a conversation for extended periods of time. So like, you know, I have to do – even just doin’ stuff like, you know, making sure I have planned out what I’m gonna say, so that I’m not saying too much. So I do not run out of breath.”
Suggested Modification	3	Participant 04: “Think about what’s realistic … a half hour activity is good as opposed to a 3-h activity.”
Social considerations	7	Participant 01: “I have a fear of being around too many people and in public areas and being exposed to germs.”
Suggested Modification	4	Participant 02: “I know when I’m not feeling as well … I do not tend to reach out to friends so … if I’m in regular contact with people, say, ‘if you guys do not hear from me for a week, could you just send me a text and say hey, how you doing’ or have friends check in.”

symptoms (See Table 6 for exemplar quotes). For example, while diaphragmatic breathing is a common relaxation technique that is taught in CBT-based programs, several participants commented that relaxed breathing may be particularly challenging for pwCF, noting experiences in which attempts to practice deep breathing induced coughing fits or a focus on breathing increased anxiety. Participants provided strategies that circumvented barriers to practicing relaxed breathing (e.g., sitting up instead of laying down, focusing on the rhythm of breathing rather than aiming for a specific length of exhalation) and also suggested other types of relaxation strategies, such as guided imagery, may be less aversive and more helpful for some pwCF. When asked about potential barriers to behavioral activation planning, participants identified barriers related to symptom burden that were further coded/categorized as *Mental Health*, *Physical*, and *Social Considerations*. *Mental Health Considerations* included low motivation to be active or social when feeling stressed, anxious or in a depressed mood. These are typical concerns that need to be addressed when helping patients develop a behavioral activation plan. *Physical* and *Social Considerations* that were noted, however, were unique to the specific context of living with a chronic illness. *Physical Considerations* included not feeling well, fatigue, pain, and mobility limitations, shortness of breath, and treatment burden. Barriers categorized as *Social Considerations* involved concerns about infection control in social/public spaces and social anxiety about coughing in public. Participants also provided suggestions for CF-specific modifications to address these barriers; including setting reasonable goals, pacing activity, and reaching out to friends virtually or through text when in-person contact was limited. See Table 6 for quotes illustrating these identified barriers and suggested modifications to address barriers.

Additional recommended topics

Finally, a fourth theme within the major topic areas of Program Development Feedback was *Additional Recommended Topics*. Topics in this theme were categorized as *Content/Context-Oriented* and *Process-Oriented*. Under the heading of *Content/Context*, participants noted that the developers should consider including biological factors that might affect anxiety and mood (e.g., menopause, medication side effects, impact of poor sleep, or physical fatigue related to coughing). Developmental and disease-severity contexts were also discussed as important considerations. Participants noted that there would be different challenges for individuals with CF depending on age, spoke to the importance of addressing anxiety about disease progression and experience of advanced disease, and suggested the need for a developmental adaptation for adolescents with CF. Participants also suggested content on mindfulness, addressing financial stress, survivor’s guilt, and relationships/communication, as well as comorbidities, such as substance use disorder. Process-oriented suggestions included ensuring that the written material was at an appropriate reading level, and the need to emphasize a supportive and flexible approach that normalizes and destigmatizes mental health concerns in CF and that was customizable to the situations and needs of individuals.

Discussion

Interviews were conducted with key stakeholders to inform decisions about how to tailor the design and implementation of a novel CBT-based intervention to prevent and treat depression and anxiety for adults with CF. Themes highlighted salient stressors for pwCF, especially *Treatment Burden*, *Illness Uncertainty*, and *Financial/Insurance Stress*. *Hospitalizations*, *Self-Perception/Social Comparison*, *Disease Progression*, and *Fear of Death/Dying* were also frequently identified stressors. The identification of *Treatment Burden* as a significant stressor is consistent with prior research (Sawicki, et al., 2013). The daily treatment regimen in CF is estimated to take 2–3 h per day, with treatment complexity and time commitment highest for adults with CF (Sawicki, et al., 2013; Cameron et al., 2022). Illness uncertainty, which has been defined as a complex experience in which it is difficult to find meaning in illness-related events and outcomes are perceived as unpredictable (Mishel, 1983), has been linked with psychological distress and coping in children and adults with chronic illness (Wright et al., 2009; Tackett et al., 2016; Szulczewski et al., 2017). The identification of illness uncertainty as a key stressor in the experience of living with CF further validates the need to modify existing CBT interventions to help patients cope with circumstances in which there is unpredictability in the course of their disease and it is difficult to make plans for the future. As such, the CF-CBT sessions devoted to teaching cognitive coping strategies have been modified from existing CBT protocols that focus on challenging unrealistic or exaggerated thought patterns to emphasizing balanced and flexible thinking and self-compassion. In addition, a session devoted to anxiety management highlights coping skills to manage anxiety about current and future health. As noted above, a comprehensive list of CF-related stressors identified by patients with CF is included in the initial CF-CBT session to decrease stigma about discussing the many concerns that arise. Personally salient stressors that are identified by patients in the initial session can then be targeted in subsequent sessions during which CBT-based coping skills are learned and practiced.

A second major theme identified as part of coping with CF was the interaction of physical symptoms and emotional distress, a topic not often discussed in routine CF care but one that emerged throughout the patient interviews. The negative emotional impact of experiencing a CF exacerbation was highlighted, as was the way in which emotional distress can have both a direct negative impact on physical functioning and an indirect negative impact through disruptions in the ability to sustain daily CF care. Disruptions to sustaining daily care and worsening physical symptoms then become more distressing. This is a foundational theme of the CF-CBT program: helping patients increase their self-awareness of these connections in their own lives, self-advocate for holistic care, and educating CF interventionists in how to better understand and assess these connections with pwCF.

Resilience, which is often defined as the capacity for positive adaptation in the face of adversity (Connor and Davidson, 2003), was identified as a third major theme. While pwCF are at higher risk for depression and anxiety than the general population (Quittner et al., 2014), they have also been shown to report higher rates of resilience (Mitmansgruber et al., 2016). Participants in this study discussed the coping strategies they used in the context of illness and hospitalization and identified adaptive thinking patterns that helped them maintain motivation to sustain daily CF care. As such, the CF-CBT program was developed to teach coping strategies to build on strategies already being used by pwCF. Patient-identified coping strategies and examples of adaptive thinking patterns were incorporated throughout the CF-CBT workbook with direct quotes from these interviews, included with participant consent. While CF-CBT is conducted with patients individually, the quotes that appear throughout the workbook may enhance the impact of the intervention by both normalizing the experience of coping with CF and offering a form of peer support.

The second major topic area of the semi-structured interview was patient perceptions of the proposed intervention. This feedback was critical to ensuring the acceptability of program structure, delivery, and CF-specific content. This feedback indicated a high degree of acceptability, and both positive and constructive feedback informed the final design of the intervention. CF-specific modifications, suggested by patients, were incorporated throughout to address potential barriers and facilitate CBT skills practice. Components of the CF-CBT treatment approach, highlighting modifications that were made to tailor the intervention for adults with CF, are summarized in Table 7.

Patient community engagement was invaluable to adapting CBT-based protocols in the development of CF-CBT to better address the following goals: (1) normalize and destigmatize distress related to managing a progressive chronic illness, (2) emphasize the intersection of physical and emotional health in ways that are specific to the experience of CF, particularly the impact of depression and anxiety on sustaining daily CF self-care, (3) address health-related anxiety, (4) problem-solve CF-specific barriers to skill implementation, and (5) address CF-specific barriers to mental health care (e.g., existing burden of medical/daily self-care).

There were limitations to this qualitative study. While a wide range of age and disease severity was represented among participants, gathering additional feedback from a more broadly diverse sample, especially with regard to race and ethnicity, would improve the intervention's relevance for a diverse population of pwCF. CF-CBT was developed prior to the advent of highly effective modulator therapy in CF and the COVID-19 pandemic. Each of these events individually and interactively had an impact on coping. Additional qualitative work will follow to better understand the impact of these events on pwCF and to update the program materials accordingly.

TABLE 7 CF-CBT sessions: summary of goals and CF-specific modifications.

CF-CBT session	Summary of session goals	CF-specific modifications
Session 1: Introduction to CBT	• Identify stressors and increase awareness of one's response to stress • Learn about the CBT model and its application to coping with CF • Learn a mindfulness strategy to increase awareness of daily moments of joy	• Comprehensive list of CF-related stressors included • Awareness of the connection between emotional and physical health in CF is emphasized
Session 2: Relaxation Skills	• Practice relaxation skills, including guided imagery and progressive muscle relaxation	• Two options offered and neither are breathing techniques • Discuss how relaxation skills can be applied to manage medical and procedural anxiety
Session 3: Depression in CF: What Helps?	• Learn about depression and its impact in CF • Develop a personalized behavioral activation plan	• Psychoeducation about the increased risk for depression and health consequences of untreated depression in CF • Planning includes problem-solving back-up options and adaptive pacing of activities to manage interference of CF symptom and treatment burden • Create a specific plan for behavioral activation that could be especially helpful in times of illness or hospitalization
Session 4: Adaptive Thinking Skills	• Increase awareness of thinking patterns that contribute to depression and anxiety	• Learn about maladaptive thinking patterns that relate to coping with CF • Address thinking patterns that decrease motivation to sustain daily CF care
Session 5: Adaptive Thinking Skills, Part 2	• Practice strategies for developing new thought patterns that are more adaptive	• Balanced and flexible thinking and self-compassion is emphasized • Incorporate mindful "letting go" of maladaptive thoughts to manage CF-related stress
Session 6: Taking Charge of My Health	• Learn goal setting and problem-solving skills and apply toward a patient-identified health-related goal	• CF-specific examples include goals of improving consistency of daily CF care, communication with the CF team, and increasing comfort with disclosure about CF when needed
Session 7: Anxiety in CF: What Helps?	• Learn about anxiety and strategies for coping • Develop a personalized anxiety management plan	• Psychoeducation about the increased risk for anxiety and health consequences of untreated anxiety in CF • The ways that anxiety can interfere with self-care are addressed • Anxiety about current and future health and coping with uncertainty is discussed
Session 8: Maintaining Positive Changes	• Create an individualized follow-up plan that includes continued practice of preferred coping skills to face future challenges	• Plan is coordinated within CF-team based care, allowing for coproduction and flexible, longitudinal follow up

Although the program will be further refined, results of these qualitative analyses indicate the acceptability of a CF-specific CBT-based mental health intervention for adults with CF that was designed to be integrated into routine CF care. CF-CBT was subsequently piloted, with positive preliminary findings regarding feasibility, acceptability, and effectiveness (Friedman et al., 2022), with additional changes made prior to an ongoing multi-center randomized waitlist-controlled trial. Qualitative results directly informed the content of CF-CBT, increasing its validity and potential to accurately reflect CF-specific experiences and accommodate CF-specific coping needs. Positive participant feedback on acceptability was received for the pilot study confirming the value of including the patient community in intervention development. Given the elevated prevalence of depression and anxiety across chronic illness populations, the approach described here may be replicable for co-developing mental health interventions for chronic illness populations tailored to patient needs. Interventions that target the contextually relevant challenges faced by individuals with a specific chronic condition are more compelling to patients and more effective (Quittner et al., 2019). Customized interventions can decrease stigma and increase patient engagement in evidence-based mental health care.

Data availability statement

The datasets presented in this article are not readily available because the datasets for this study cannot be made publicly available per the hospital review board policies. Requests to access the datasets should be directed to dfriedman@mgh.harvard.edu.

Ethics statement

The studies involving human participants were reviewed and approved by Massachusetts General Hospital Institutional Review Board. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

DF: conceptualization, methodology, data collection/interviewing, data management, formal analyses, writing—original draft preparation, reviewing, editing, visualization, and formatting. MK: conceptualization, methodology, formal analyses, writing—original draft preparation, reviewing, and editing. AQ: conceptualization, methodology, data collection/interviewing, formal analyses, reviewing, and editing. BS: conceptualization, methodology, data collection/interviewing, reviewing, and editing. AG: conceptualization, methodology, reviewing, and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

DF reports grant support from the Cystic Fibrosis Foundation (CFF), Dutch Cystic Fibrosis Foundation, and Vertex Pharmaceuticals, and travel reimbursement from the CFF. BS reports grant support, personal fees and travel reimbursement from CFF. AQ reports consulting fees from Vertex Pharmaceuticals and Insmed, and grant support from the CFF, American Cochlear Implant Alliance, PCORI, and the NIH. AG reports personal fees and travel reimbursement from Cystic Fibrosis Australia; grant support, personal fees, and travel reimbursement from CFF; grant support from the Dutch Cystic Fibrosis Foundation; travel reimbursement from the European Cystic Fibrosis Society; personal fees from Johns Hopkins University/DKBmed; personal fees from Saudi Pediatric Pulmonology Association; and grant support and personal fees from Vertex Pharmaceuticals. MK reports no commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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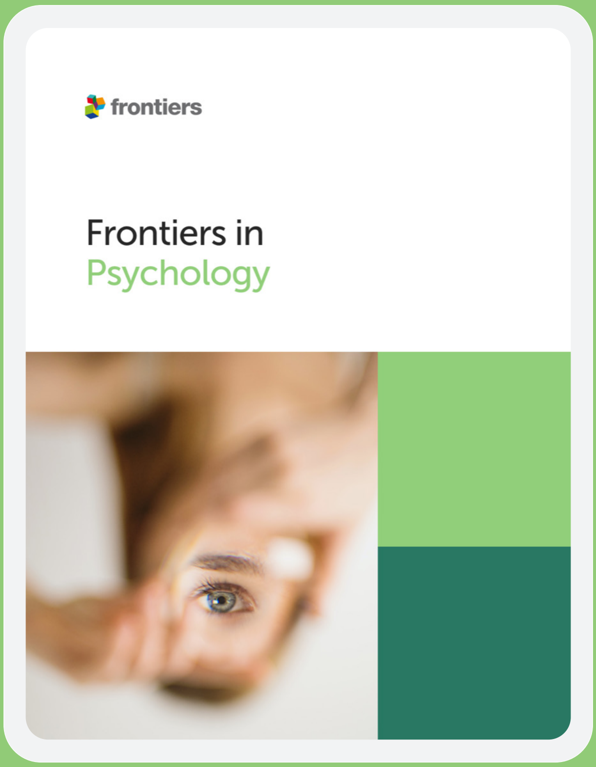

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