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The Experience of Social Isolation in Adults with Cystic Fibrosis: Results of a Mixed-Methods Feasibility Study

Amy Gulledge
Medical University of South Carolina

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Amy Gulledge

A dissertation submitted to the faculty of the Medical University of South Carolina in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the College of Nursing.

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Approved by:

Sarah Miller, PhD, RN
Sarah Miller, PhD, RN, Chair, Advisory Committee

Susan Newman, PhD, RN, CRRN
Susan Newman, PhD, RN, CRRN

Lillian Christon, PhD
Lillian Christon, PhD

Patrick Flume, MD
Patrick Flume, MD

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ABSTRACT

There is a lack of exploration into if, and how, adults with cystic fibrosis experience social isolation, a social condition associated with detrimental physical and psychological effects. Adults with cystic fibrosis experience barriers that may enhance the risk of social isolation, such as time-consuming treatment modalities, hospitalizations, fatigue, activity intolerance, and recommendations encouraging segregation from others with cystic fibrosis to prevent respiratory pathogen transmission. Additionally, these barriers may be augmented by social distancing guidelines related to the SARS-CoV-2 pandemic. While adults with cystic fibrosis have needed to long adhere to infection control guidelines with others with cystic fibrosis, this social distancing now extends to their whole social network.

The purpose of this dissertation was to address this gap in knowledge. The concepts of social isolation and social support and their relationship to this population were investigated through an integrative review, which further supports this gap. A subsequent integrative review explored coping in adolescents and adults with cystic fibrosis; the findings of this review will be relevant when designing future studies. The final step in this dissertation was gaining a preliminary understanding of objective and subjective social isolation in adults with cystic fibrosis through the following aims, using Cornwell and Waite's Model of Social Isolation: Aim 1: To evaluate the process and resources of the proposed study methodology using Tickle-Degnen's feasibility model in preparation for future studies of social isolation in adults with cystic fibrosis; Aim 2: To develop a preliminary characterization of social isolation in adults with cystic fibrosis using a parallel convergent mixed methods approach; Sub Aim 2a: To measure objective

and subjective social isolation using the Patient-Reported Outcomes Measurement Information System - Social Isolation Short Form 8a Scale and the Lubben Social Network Scale – Revised version; Sub Aim 2b: To identify preliminary signals of relationships between objective and subjective social isolation, demographic data, health information, and health-related quality of life; Sub Aim 2c: To elucidate experiences and perceptions of objective and subjective social isolation using semi-structured interviews; Sub Aim 2d: To compare and contrast the relationship of objective and subjective isolation through the triangulation of quantitative and qualitative data.

The results of this mixed-methods feasibility study indicate that while there are opportunities to improve recruitment strategies, survey methods, and interview questions, this study design is a feasible approach for future work. Results reveal that participants were relatively healthy and, overall, experienced less social isolation than others with chronic illness. While exploring preliminary signals, relationships between objective and subjective social isolation, as well as relationships between many of the Cystic Fibrosis Questionnaire - Revised domains and subjective social isolation were discovered. Qualitative exploration revealed five main themes: importance of socialization and social support, effect of cystic fibrosis on socialization, feelings of isolation, importance of cystic fibrosis-specific support, and COVID-19-related socialization and support. Quantitative data was supported by qualitative data during triangulation. This study provides an initial glimpse of how adults with cystic fibrosis experience social isolation.

Key words: adults with cystic fibrosis, social isolation, social support, coping, mixed-methods

INTRODUCTION

Overview of Dissertation

Many chronic diseases, such as cystic fibrosis (CF) are progressive in nature and come with complex treatment regimens. CF is a genetic disease associated with a multitude of physiological and psychological symptoms; CF-related symptoms and treatments may potentially lead to social isolation (SoI).[1-3] While social isolation (SoI) has been correlated with many detrimental physical and mental health effects,[4-6] it has not been studied in the adult CF population. An integrative review exploring these concepts confirmed the lack of exploration into SoI among adults with CF. Therefore, the specific aims of this dissertation were:

Aim 1: To evaluate the process and resources of the proposed study methodology using Tickle-Degnen's feasibility model[7] in preparation for future, larger studies of SoI in adults with CF.

Aim 2: To develop a preliminary characterization of SoI in adults with CF using a parallel convergent mixed methods approach.

Sub Aim 2a: To measure objective and subjective SoI using the Patient-Reported Outcomes Measurement Information System - Social Isolation Scale Short Form 8a (PROMIS-SoI) and the Lubben Social Network Scale – Revised version (LSNS-R).

Sub Aim 2b: To identify preliminary signals of relationships between objective SoI, subjective SoI, demographic data, health information, and the Cystic Fibrosis Questionnaire – Revised (CFQ-R) domains.

Sub Aim 2c: To elucidate experiences and perceptions of objective and subjective SoI using semi-structured interviews.

Sub Aim 2d: To compare and contrast the relationship of objective and subjective isolation through the triangulation of quantitative and qualitative data.

The overarching research question driving this study was: To what extent do adults with CF experience objective and subjective SoI as a result of the symptoms and treatments associated with their chronic disease process? The overall objective was to test the feasibility of the proposed methodology and gain a preliminary understanding of objective and subjective SoI in adults with CF. The long-term goal long-term goal is to use this data to inform future studies aimed at characterizing physiologic and psychologic implications of SoI, as well as future development of interventions aimed at decreasing SoI's negative effects.

Background and Problem Statement

CF is a genetic, progressive disease that causes impaired respiratory function, gastrointestinal disturbances, and increased rates of psychological symptoms (i.e. anxiety and depression).[1-3]. As recently as the 1980s, people born with CF typically did not live past their teenage years; however, scientific discoveries have improved the median predicted age of survival for those born between 2015 and 2019 to 46 years, with 56% of the CF population now being over the age of 18.[8,9] With this increased life expectancy comes a longer lifetime of managing complex therapeutic regimens, pulmonary exacerbations, frequent visits to the provider, and treatments for CF-related complications (i.e. CF-related diabetes [CFRD]). The symptoms and treatments associated with CF may decrease the ability to socialize, potentially leading to SoI. Furthermore, guidelines

prohibiting face-to-face contact between people with CF to avoid respiratory pathogen cross-contamination prevents this population from forming close bonds with others who intimately understand their experiences.[10] To add to this potential decrease in socialization, the SARS-CoV-2 (COVID-19) pandemic has further limited the ability to closely interact with others, which may substantially decrease how those with chronic illness socialize and receive support. SoI comes with its own risks, which are comparable to risks noted in deleterious health behaviors such as cigarette smoking; SoI can lead to increased morbidity and mortality, cardiovascular events, neuroendocrine dysfunction, inflammation, adult clustered risk factors (i.e. hypertension, hyperlipidemia, increased body mass index), depression, and suicidal thoughts.[4-6] Despite the risk factors for SoI that adults with CF face, this construct has not been investigated in this population. Therefore, this study focuses on testing the feasibility of a study methodology exploring SoI in adults with CF and describing SoI in this population.

Gaps in Knowledge

There are multiple studies investigating SoI in other chronic medical populations, such as older adults, after spinal cord injury (SCI), alpha-1 antitrypsin deficiency, sarcoidosis, multiple sclerosis (MS), Parkinson's disease (PD), and young adult cardiac patients; [11-15] however, it has not been explored in the CF population to our knowledge.

When SoI was explored among older adults, it was discovered that feelings of belongingness were related to positive health outcomes, such as improved disease control. Feelings of loneliness were more prevalent among those with lung disease and arthritis, and that loneliness was associated with decreased instrumental support.[5,6] In the study investigating SoI and social support among those with alpha-1 antitrypsin

deficiency or sarcoidosis, SoI was present and the importance of social support was evident.[12] Among those with MS and PD, feelings of SoI increased as symptoms progressed, which coincides with people after SCI who reported greater social disconnectedness with higher levels of injury.[11,13,14] Conversely, older participants with SCI reported less perceived SoI, especially among those with a greater time lapse since the injury occured.[11] SoI was very prevalent among young people after experiencing an acute cardiac event, with themes of feeling misunderstood, psychosocial difficulties, and difficulty transitioning away from toxic relationships; however, these feelings tended to resolve within a year or so after the cardiac event.[15]

These studies demonstrate that various chronic medial populations experience SoI and its precipitating factors differently. Given the knowledge gained from these studies, it is reasonable to anticipate similarities among the CF population, however, this cannot be assumed. With the lack of knowledge on how SoI affects adults with CF, studies are warranted to gain an in-depth understanding of this potential problem to develop interventions that increase socialization and social support.

Design and Method

This study was a feasibility mixed-methods study based on Tickle-Dengnen's feasibility model;[7] the parallel convergent mixed-method design was developed using Creswell & Plano Clark's model.[16] A quantitative descriptive approach was utilized to describe subjective SoI through the PROMIS SoI, a validated 8-item Likert scale measuring perceived SoI .[17] For objective SoI, the LSNS-R was used. This is a 12-item validated Likert scale measuring one's social network.[18] A qualitative description of SoI was elicited through semi-structured interviews during which participants described

experiences with social support, SoI, and how CF has affected socialization. The parallel convergent methodology allowed for the quantitative and qualitative data streams to be collected concurrently; data was analyzed separately and then merged to assess for patterns of convergence and divergence. This triangulation of data allowed for a richer description of the experience of subjective and objective SoI among adults with CF.

Key Concepts

Social Isolation

The concept of SoI has been defined and operationalized in various ways. The construct of SoI must consider human nature, the need for socialization, and effects of reducing or removing socialization on physical and psychological health. SoI is by no means a new concept; it has been described as far back as the 1890s.[19] However, it is a relatively new concept emerging in the literature. During exploration of SoI among various populations, definitions use diverse terminologies, such as loneliness, disconnectedness, aloneness, and seclusion. Regardless of the operationalization of SoI, the detrimental effects on health are clear; these include increased morbidity and mortality, cardiovascular events, neuroendocrine dysfunction, inflammation, adult clustered risk factors (increased body mass index, hypertension, hyperlipidemia, etc.), and psychological distress.[4-6]

SoI can be a rather difficult to operationalize and measure because of its abstract nature. Some see SoI as a more objective concept, citing a lack of interaction with others and smaller social networks; whereas others see SoI as a subjective concept that results in feelings of loneliness or being disconnected from others.[20,21] Additionally, many studies

exploring SoI may only focus on objective or subjective SoI, which may limit a robust picture of SoI within that population.

Framework

With a relatively broad description of SoI in the literature, the investigator chose to use Cornwell and Waite's model of SoI, which focuses on the two facets of this social construct: social disconnectedness and perceived isolation.[21] Social disconnectedness refers to objective SoI, such as limited social networks, restricted contact with others, and a decreased ability to participate in social events.[21] Perceived isolation refers to subjective isolation and is portrayed by feelings of loneliness, not belonging, or a lack of companionship.[21] For purposes of this study, social disconnectedness is referred to as objective SoI and perceived isolation as subjective SoI.

Brief Overview of Manuscripts

The first manuscript of this compendium presents an integrative review of SoI and social support in adults with CF.[22] The Social Ecological Model (SEM) was used to organize, analyze, and synthesize findings into 5 systemic domains that influence health: intrapersonal, interpersonal, organizational, community, and public policy.[23] There was a clear lack of empirical evidence describing SoI in this population. However, the investigator learned about this population's social spheres through the social functioning and interpersonal relationship domains of validated CF-specific health-related quality of life (HRQOL) instruments.[22] Results indicate that adults with CF who experience more physical and mental health symptoms are more likely to experience social dysfunction.[22] It was evident that social support from friends, family, significant others, and the CF

community is an important aspect of living with CF. This manuscript informed the design of the dissertation study, as one of the aims is to describe SoI in this population.

The second manuscript of this compendium presents an integrative review on coping in adolescents and adults with CF.[24] An in-depth understanding of coping styles in this population will aide in future work; coping is likely an important aspect of managing SoI and will be explored during future similar studies. The Moos and Holahan Coping Skills were used as a guide to organize, analyze, and synthesize findings.[24] Results of this integrative review found that the use of coping styles was dependent on the individual and situation, but positive reappraisal, seeking guidance and support, and acceptance and resignation seem to offer the most potential as effective coping management strategies.

The third manuscript of this compendium presents the results of the feasibility mixed-methods study exploring SoI in adults with CF. This dissertation study presents results related to both feasibility aspects of the study and initial exploration into how adults with CF experience SoI.

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Manuscript 1

Gulledge, A., Miller, S., & Mueller, M. (2021). Social Support and Social Isolation in Adults with Cystic Fibrosis: An Integrative Review. Manuscript submitted for publication.

Abstract

Background*:* Adults with cystic fibrosis have unique barriers that may decrease their ability to receive adequate social support and socialization, leading to social isolation. Social isolation has been correlated with negative health outcomes in other populations. In those with cystic fibrosis, social isolation may present additional physiological and psychological challenges, potentially interfering with clinical outcomes and quality of life. However, there is a lack of understanding as to how social isolation presents in this population. ***Methods:*** The purpose of this integrative review is to identify and critically analyze how social support and social isolation are reported for adults with cystic fibrosis. PubMed, Scopus, and CINAHL Complete were searched for related publications, resulting in an initial yield of 1,767 articles. After eligibility screening, 21 studies met the criteria for this review, which were all then critically analyzed and synthesized. ***Results:*** There is a scarcity of literature focusing on social isolation and social support in this population. Reduced physical and mental health were the most commonly reported variables associated with reduced social functioning and social support. ***Conclusion:*** Preliminary studies are warranted to understand how adults with cystic fibrosis experience social isolation, as well as its relationship to social support. This knowledge can guide future research focusing on physical and psychological effects of social isolation, along with interventions that facilitate socialization and support.

Introduction

Only four decades ago, children rarely survived past their teenage years when diagnosed with cystic fibrosis (CF), a rare genetic disease causing the body's mucous to become excessively thick.[1-3] Over the past generation, CF therapies have improved dramatically and extended average life expectancy to 44 years; the majority of people living with CF are now over 18.[2] This extended life span presents new challenges for those living with symptoms and comorbidities, including chronic respiratory inflammation and infection, progressive respiratory deterioration, pancreatic insufficiency, malnutrition, liver disease, and psychological illness (i.e. depression and anxiety).[3-5] Given the progressive nature and complexity of CF, care delivery should integrate methods to improve both physical and psychosocial quality of life (QOL) and outcomes over a lifetime.

Among those with chronic diseases, including CF, QOL can be influenced by social support (SS) and social isolation (SoI), two distinct social conditions.[6,7] SS is an expansive term defined as the amount of support and resources an individual receives from others, as well as having people to talk to (definition adapted from Flewelling et al. and Sherbourne).[7,8] In the CF population, higher SS is associated with decreased treatment burden and improved physical and mental health, QOL, vitality, body image, and health perception.[7] Conversely, SoI can be caused by feelings of loneliness or disconnectedness (subjective) or physical separation and limited interaction with others (objective).[9,10] Among older adults, higher levels of SoI have been associated with detrimental effects, including an increased risk for cardiovascular disease, morbidity and

mortality, neuroendocrine dysfunction, inflammation, altered gene expression, poor sleep, depression, and suicidal ideation.[9,10]

While SS and SoI are interrelated, the absence of one does not necessarily imply the presence of the other, nor are they always at opposite ends of a continuum. Whereas SS may help mitigate CF symptoms, SoI can intensify them. Adults with CF face unique barriers that may inhibit their ability to receive adequate SS, such as recurrent hospitalizations, missed school and/or work, disability, and limited functioning from activity intolerance; additionally, increased treatment burden from time-consuming therapies, such as airway clearance methods (i.e. manual percussion, oscillating vests), can take an average of 2-4 hours a day, taking time away from daily living. [3,4,7,11-13] Notably, CF care guidelines recommend that those with CF restrict close contact with other individuals with CF due to the high risk of respiratory cross-infection, which limits opportunities to form face-to-face connections with others who intimately understand the complexities of their disease process.[7,14] New public health guidelines resulting from the SARS-CoV-2 pandemic (i.e. social distancing) may further strain SS resources.[15] These unique challenges may inhibit SS and increase the risk of SoI, thus, requiring the need for tailored interventions.

While the physiologic and psychologic impact of CF is well documented in the literature, there remains insufficient evidence on how SS and SoI present in this population, the connection between the two, and how they affect outcomes. There is a gap in research exploring these concepts in adults with CF, making it difficult to grasp exactly how they are related. As these concepts are interconnected, this review will include both; in doing so, we can explore how these concepts present in this population,

as well as try to establish the relationship between the two. Exploring these multidimensional concepts for a deep understanding will inform future research that ultimately improves care, outcomes, and QOL. The purpose of this integrative review (IR) is to identify and critically analyze how SS and SoI are reported for adults with CF.

Framework

The social ecological model (SEM) served as a framework for this IR because of its focus on systemic factors of health.[16] The SEM highlights 5 levels of interrelated factors that influence health and health-related behavior: 1) intrapersonal; 2) interpersonal; 3) institutional; 4) community; and 5) public policy (Figure 1).[16] The SEM was used to identify how each of these factors influence SS and SoI in adults with CF.

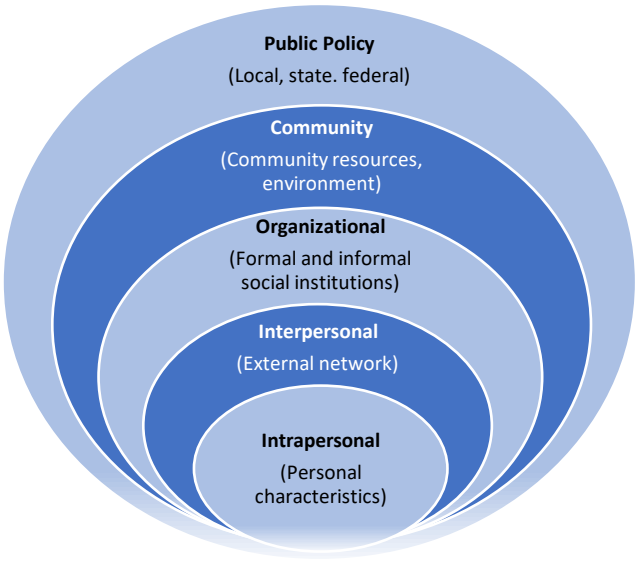

Figure 1. Social Ecological Model[16]

Methods

This IR follows the methodological framework outlined by Whittemore and Knafl as follows: 1) problem identification; 2) literature search; 3) data evaluation; 4) data analysis; and 5) presentation.[17] A comprehensive literature review was conducted in

August 2019 and updated in November 2020 . Relevant studies were identified using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) protocol (Appendix A).

An experienced medical university librarian was consulted before the search to identify the most appropriate databases and search terms. PubMed, Scopus, and CINAHL Complete were searched using the following terms: “adults with cystic fibrosis” OR “adults with CF” OR “adults CF” AND “social isolation” OR loneliness OR “social support” OR “quality of life.” A total of 1,767 articles were identified through these databases. Fourteen additional articles were identified through handsearching. After duplicates were removed, a total of 1,476 articles remained.

Inclusion criteria included studies conducted in adults (≥ 18 years) with CF that had a focus on SS or SoI. Studies that were non-English or used non-human participants were excluded. Studies reported prior to 2009 were also excluded due to changes in CF management. Titles and abstracts were reviewed for inclusion criteria, leaving 97 articles eligible for full text review. Studies were excluded if they did not focus on SS or SoI, not original research, or focused on pediatric populations or caregivers. A total of 21 articles were identified that met the inclusion criteria.

The final 21 articles were evaluated and analyzed using a literature matrix (Appendix B). Critical appraisal was performed on all studies using the following tools as appropriate: The Appraisal Tool for Cross-Sectional Studies (AXIS), the Critical Appraisal Skills Programme (CASP) Cohort Study Checklist for longitudinal studies, the Mixed Methods Appraisal Tool (MMAT) for mixed-methods studies, and the CASP Qualitative Checklist for qualitative studies.[18-20]

Results

Articles reported on quantitative (n = 18), qualitative (n = 2), and mixed-method (n = 1) studies. This IR includes results from a total of 4,190 individuals with CF living in 14 different countries. The majority of the studies took place in an outpatient (OP) setting (n = 14), with other studies taking place in inpatient (IP) settings (n = 2), both OP and IP settings (n = 1), online (n = 3), and mixed OP and online (n = 1).

Only 2 of the studies directly addressed SS as a major concept.[7,21] However, 16 studies assessed health-related QOL (HRQOL) using either a version of the CF Questionnaire (CFQ or CFQ-R) or the CF-QOL questionnaire (CFQoL).[5,7,11,12, 22-33] Given the limited number of studies addressing SS and absence of those exploring SoI, these studies were included because of the instruments' measurement of the social functioning domain, along with the CFQoL's measurement of the interpersonal relationship domain. By examining the social functioning and interpersonal relationships domains as a proxy for SS and SoI, it is possible to learn more about these central concepts.

The social functioning domains of the CFQ/CFQ-R and CFQoL assess one's ability to socialize with friends or go out at night, comfort with discussing CF with others, as well as how the participant feels others view their CF (coughing, are they contagious, etc.)[34,35] The interpersonal relationship domain of the CFQoL assesses how satisfied a person is with their romantic and sex life, social life, relationships with others, how CF changes their ability to relate to others and vice versa, feelings of isolation, and the ability to lead an independent life.[34]

Social Ecological Model

Intrapersonal Factors

Many intrapersonal factors that related to SS or social functioning were identified, including demographic factors, clinical factors, and mental health factors. With respect to demographic factors, females expressed improved perceptions of SS compared to men; however, females tended to have lower social functioning scores.[21,23] As age increased, social functioning scores were found to decrease and interpersonal relationship scores increase.[22,25] Education levels were associated to both the social functioning and interpersonal relationship domains, with the lowest social functioning scores found in those with tertiary education and the highest being in those with secondary education; interpersonal relationship scores increased among those who had more education.[25] Participants of lower socioeconomic status (SES) tended to have lower social functioning scores, which was the case for all other domains of the CFQ-R (physical, vitality, emotional functioning, eating disturbances, treatment burden, health perception, body image, role functioning, weight, and respiratory), except digestive.[24] With respect to race and ethnicity in particular, lower social functioning scores were associated with individuals who were Hispanic or Black.[24] However, in individuals who were Hispanic, ethnicity was not statistically significant after controlling for SES; whereas those who were Black had statistically significantly lower social functioning scores after disease severity and SES were controlled for.[24] Perceived SS was not found to be associated with age, income, education, marital status, or disease severity.[21]

Clinical variables that correlated with lower social functioning scores included having CF (compared to healthy individuals), being on the lung transplant list (compared to post-transplant), requiring oxygen, increased CF exacerbations, higher pain levels, and

decreased pulmonary function.[1,12,26-28] In particular, Ribeiro et al. found that decreased forced expiratory volume for 1 second (FEV_1%) correlated with poorer social functioning scores; no relationships between social functioning and other measures of pulmonary function, such as forced vital capacity, were found.[12] Poor social functioning scores also correlated with increased mental health symptoms and psychological distress, poor sleep quality, fatigue, and greater respiratory symptom burden.[23,30,32]

Several studies identified variables that demonstrated relationships associated with increased social functioning scores, such as being post-lung transplant, not requiring oxygen, higher FEV_1%, pancreatic sufficiency, engaging in active coping skills, and better mental well-being.[5,22,26,33] Improved social functioning scores also correlated with an increase in one's understanding of CF; conversely, those who reported more of an impact on daily from CF tended to have lower social functioning scores.[32]

Interpersonal Factors

Studies explored the interpersonal factors of support, relationships, work, family, friends, and romantic partners. Flewelling et al. investigated SS using the Interpersonal Support Evaluation List (ISEL), measuring 4 areas of SS: instrumental aid, having someone to speak with, having someone to perform activities with, and having someone to relate positively with in regards to self-esteem.[7] Increased levels of SS were correlated with self-reported decreases in physical, mental, and digestive health symptoms, along with improved scores on the following CFQ-R domains: treatment burden, emotional functioning, role functioning, social functioning, vitality, body image, and health perceptions.[7] In contrast, social support did not predict physical functioning, weight gain, or respiratory domain scores.[7]

One's social network proved to be an important factor in many of the studies. Decreased scores on the CFQoL interpersonal relationship domain indicated a higher dissatisfaction with relationships and were correlated with those who were younger, waiting for a lung transplant, experiencing increased anxiety and depression, or had less education.[25,26,29] The cross-sectional study by Havermans et al. discovered that participants who were employed scored higher in social functioning compared to those who did not work; additionally, Flewelling et. al. found those who were not employed had decreased perceptions of SS.[11,21] Qualitative exploration found that relationships with family and friends were important, along with belonging to a social network, desiring social obligations, having a purpose in life, and maintaining a social life.[36-38] Receiving SS from a romantic partner was found to be one of the most important perceived aspects of a romantic relationship.[38]

Organizational, Community, and Public Policy Factors

While only two studies identified organizational or community levels of the SEM, they demonstrated that belonging to a community and access to resources are important. Feeling confident with the care provided by the CF team was the only organizational-level concept identified.[37] For community-level factors, belonging to a social network and the CF community were important.[37] One cross-sectional study found that females who were not able to manage difficult situations as well as others tended to have more social dysfunction, anxiety/depression, and insomnia; this was not true for males.[1] Factors related to the public policy level were not found during this IR.

Discussion

The purpose of this integrative review (IR) was to identify and critically analyze how SS and SoI are reported for adults with CF. Findings include an overall relationship between decreased social functioning scores and decreased physical and mental health, as well as an indication that SS and socialization are important aspects in the lives of adults with CF. Both decreased physical and mental health significantly correlated with decreased social functioning scores across the majority of studies that assessed HRQOL using the CFQ/CFQ-R or CFQoL. Decreased social functioning scores are likely associated with CF-related issues, especially fatigue, treatment burden, hospitalizations, clinic visits, and general feelings of illness that come as physical health declines; mental health is often interconnected to disease severity, presenting challenges that further decrease the desire or ability to socialize. Furthermore, decreased social functioning scores are related to poorer psychological health,[5,7,23,29,32] further hindering one's capacity to socialize and utilize resources that offer SS.

Demographic characteristics, such as age, sex, SES, education, and race/ethnicity had effects on social functioning scores. It may be that the decreased social functioning scores associated with increasing age are related to both CF and age-related changes, therefore, limiting the ability to engage in social activities. Because CF is progressive, older individuals may experience more severe symptoms, such as activity intolerance and fatigue. Additionally, common age-related changes, such as arthritis, may limit mobility and potentially decrease socialization further. Investigating how different age groups manage and cope with the social challenges of CF can help identify the most beneficial social outlets based on age.

Sex has been found to play a complex role in many aspects of CF, with females exhibiting decreased health perceptions, reduced lung capacity, and poorer physical, emotional, and psychological health compared to males; furthermore, females are more likely than males to objectively perceive their health as it compares to their true clinical picture.[1,25,27,39] This IR found differences between females and males that reinforce sex differences. Females demonstrated lower social functioning scores, which may be due to the increased prevalence of anxiety and depression.[40] Supporting this further, females who had difficulty managing stressful events experienced social dysfunction, anxiety, depression, insomnia, and difficulty in managing daily life, which did not hold true for males.[1] However, females reported increased perceptions of SS; whereas males experienced poorer perceptions of SS, consistent with literature suggesting males may not receive SS to the same degree as females.[21,41] Given the lower social functioning domain scores in females, it is possible that a limited support system has a greater effect on females than males.

Another potential explanation for the differences in sex are the societal norms placed on females to simultaneously fulfill various roles, such as being a wife/partner, mother/caregiver, working, and/or running a household. Receiving support from other females who intimately understand these challenges is likely important; females without this support may be more likely to experience SoI. However, it cannot be overlooked that males are juggling multiple similar roles as well, especially as societal norms change, and may be less likely to reach out for support given the poorer perceptions of SS.

Being of lower SES and having less education may limit access to resources due to economic hardship or community limitations, which can reduce the opportunity for SS

and interaction. For example, individuals who struggle financially may not have the capability to use online support groups because of limited free time, limited internet access, or a lack of internet-capable devices. Additionally, in communities of lower SES there may be a lack of resources (i.e. community centers, recreational clubs) that increase socialization and support.

Lower social functioning scores were found for those who were Hispanic or Black, indicating the need for further exploration into how CF affects these populations. Given that CF predominately affects individuals who are White[42], it could be that there are limited resources, outreach, and social support specific to people with CF who are not White. It is also possible that there is hesitancy to reach out for SS because one may not feel a connection or a sense of belonging, meriting a more in-depth examination to develop culturally-relevant resources specific to various populations.

Lower scores on the interpersonal relationship domain were correlated with higher rates of anxiety and depression, less education, and being younger.[25,29] It is anticipated that those with higher rates of anxiety and depression may have difficulty with relationships as a result of symptoms and psychological burden. Interestingly, in the study exploring QOL in Greek adults with CF, those who were 24-33 years had the lowest interpersonal relationship scores compared to the other age groups (18-23 and over 33).[25] It may be that people in this age range are frequently graduating college, having friends move away to begin their careers and/or families, moving away from family and friends to follow their own life goals, and gravitating toward adulthood and independence. In regards to working, employment is related to better perceived SS and social functioning scores, indicating work may offer a source of support and

socialization. Of interest, one study correlated improved mental well-being with working,[5] so it should also be considered that those working may be physically and/or mentally healthier and can tolerate employment better. In addition, working may also provide a sense of purpose and structure, which may account for the improved mental well-being.

One of the studies found results that varied from those of other studies. The study by Stofa et al. conducted in Greece found that adults with CF scored highest on the CFQoL social functioning domain when compared to other domains (physical, treatment, treatment issues, chest symptoms, emotional functioning, concerns for the future, interpersonal relationships, body image, career concerns).[25] Given that these results conflict with other studies reviewed in this IR, it is possible that these participants may have differed in health compared to other samples, or there are socio-cultural differences in Greece (or amongst study participants). Of interest, this same study found overall lower scores for the interpersonal relationship domain, which warrants a deeper understanding of the connection between these multidimensional concepts and how they present among different cultures and countries.[25]

Implications

Practice

Given the relationship between lower social functioning scores and poor physical and mental health, it is worthwhile for clinicians to consider these data when developing a plan of care. FEV_1% is a gold standard for measuring and monitoring disease progression in CF and was found to have a positive relationship with social functioning.[43] Given that decreased FEV_1% scores are associated with increased morbidity and

mortality,[43] clinicians must continue to guide care based upon the conviction that CF is a complex, multisystem process while also addressing concepts of SS and risks for SoI. Those with limited support systems are at higher risk for SoI and potentially will benefit from psychological support.

Addressing how patients utilize support systems may provide additional insight into the physical and mental health needs of adults with CF. Screening patients using the CFQ/CFQ-R or CFQoL questionnaire may elicit beneficial information in developing a holistic approach to care, as well as provide an assessment of how needs may change over time. While more interventional research is needed in this area, referrals to SS groups may offer individuals a way to seek out and virtually connect with other adults with CF.

Research

To our knowledge, this IR is the first to explore SS and SoI in adults with CF. Results from this IR reveal several gaps: 1) Few studies address SS and SoI in this population; 2) There is a lack of diverse methodologies exploring these social-based concepts; and 3) Few studies investigate these concepts using all levels of the SEM or similar frameworks.

It is possible that SS and SoI have not been thoroughly explored in adults with CF because it is a slightly newer population. Additionally, initial research emphasized physiological aspects of caring for adults with CF. While many studies use the CFQ/CFQ-R or CFQoL, these instruments do not directly assess SS or SoI as distinct concepts. Likewise, the interpersonal relationship domain of the CFQoL helps to assess relationships but it does not explicitly measure SS or SoI. While these concepts may not

have a direct linear relationship, it is important to explore the connection in this population. Examining how these concepts present and interact in adults with CF through social-based assessment tools can further expand our knowledge and add to what we know about their QOL.

More quantitative, qualitative, and mixed-method studies are needed to further operationalize and explore the most appropriate ways to measure SS and SoI in the CF population, as well as identify variables with positive and negative relationships to these concepts. Longitudinal studies can help to determine correlations between SS, SoI, and disease progression. With the physiologic and psychologic challenges already faced by this population, it may be possible that these concepts relate to disease progression and outcomes.

SS and SoI may be experienced very differently in those with CF and using a qualitative approach can explore these concepts on a more personal level. Further understanding of SS and SoI can be gained when viewed through a qualitative lens and add a deeper understanding of these concepts. Future investigations should explore what aspects of SS are valuable, connections between SS and physical/mental health, how SoI is perceived, and how SoI is related to SS. These explorations may elicit information that can help us to better understand the unique needs of this population. Other confounding variables that may affect SS and SoI should be explored more in-depth, such as the environment the person with CF grew up in (i.e. parenting styles, etc.), school setting, coping styles, social networks, comorbid conditions, family life, etc.

There is a notable lack of studies testing SS-centered interventions. Considering that increased SS demonstrated positive benefits to physical and mental health, it is

worthwhile to explore ways to improve support that enhances QOL and health perceptions. Because those with CF face the risk of respiratory cross-infection when being around others with CF, specialized interventions must be developed, refined, and tested to accommodate this unique challenge, such as technology-based interventions. Additionally, SS from family and friends without CF cannot be overlooked. A more robust understanding of these support networks may help in developing interventions that increase SS or decrease SoI.

The use of the SEM was beneficial during this review and revealed a gap in studies addressing its different levels. Most of the studies investigated data related to the intrapersonal and interpersonal levels, but very few explored organizational and community-level data. No studies were identified that considered how public policy factors may affect SS and SoI. Using the SEM as a framework for future studies can help uncover variables that may affect what SS and SoI look like among adults with CF.

Limitations

This IR has several limitations. It may be difficult to generalize the results of this review considering participants were from 14 different countries. Ideas and beliefs regarding SS and socialization vary from culture to culture,[44] which may affect how adults with CF view these concepts based on beliefs. It would be beneficial to explore social norms and family structures among different countries and cultures to identify how well this information can be generalized.

Overall, there is a lack of existing studies that address the purpose of this IR. While the information found was useful to establish a basic understanding of this population's social spheres, there remains a vast gap in this area of research. There is a

lack of study methodology diversity, as the majority of studies are cross-sectional, and therefore do not consider the complexity of the long-term needs associated with CF. Dill et al. found a decline in social functioning over time, which supports the need for longitudinal studies.[22]

Both the CFQ/CFQ-R and CFQoL ask questions related to social functioning but they do not explicitly assess SS or SoI. These two concepts are separate from one's ability to socialize, as one can be surrounded by others or attend multiple social events and still feel isolated, while others may have a very small support network or socialize infrequently and not feel isolated. Additionally, 3 of the 4 social domain questions on the CFQoL only consider events during the past 2 weeks.[35] This may limit our ability to truly understand one's social functioning status over a long period of time considering that those with CF may not be able to socialize during times of acute illness or exacerbation. The interpersonal relationship domain of the CFQoL is only included in 3 of the 21 studies in this IR. The 10 questions of this domain elicit information related to how relationships are formed and maintained, as well as feelings regarding relationships with others and isolation.[35] Similar to the social functioning domain, it only offers a glimpse into a small portion of the SS and SoI concepts.

Conclusion

There is a paucity of literature on SS and SoI in adults with CF. However, general relationships among several different variables and social functioning and interpersonal relationship domain scores were established. It is evident that physical and mental health are correlated with social functioning scores and that the need for SS is important to this population. This needs to be further explored through studies that focus on SS and SoI

and how they affect adults living with CF. Having a clear understanding of these concepts can help build a framework for future interventional studies with the goal of decreasing the social roadblocks experienced by this population.

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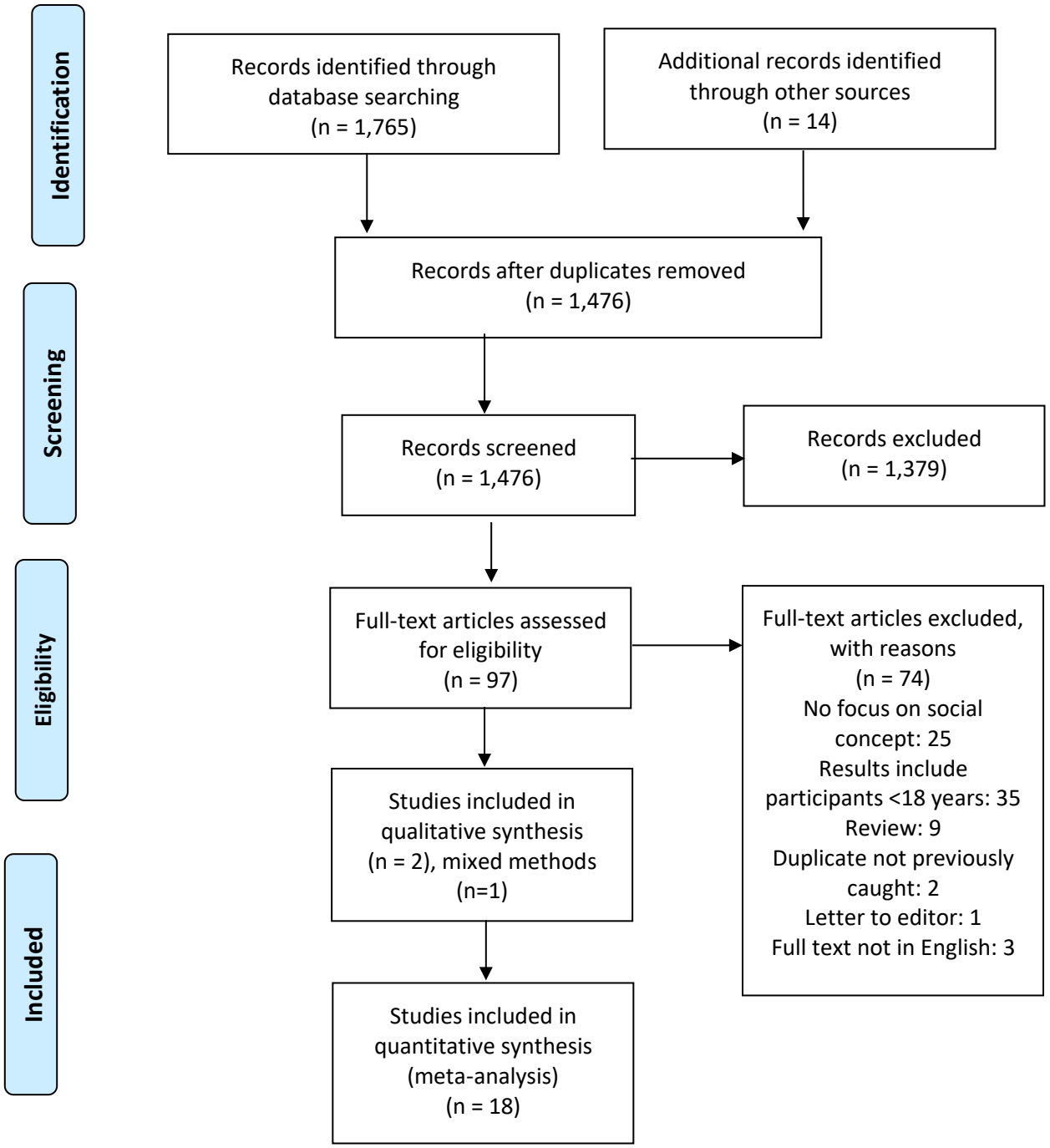
Appendix A

PRISMA 2009 Flow Diagram



Appendix B

Literature Matrix

Article	Purpose	Participants	Instruments	SEM Level/s
Cross-Sectional Studies				
Bouka A, Tiede H, Liebich L, et al. Quality of life in clinically stable adult cystic fibrosis out-patients: Associations with daytime sleepiness and sleep quality. *Respir Med*. 2012;106(9):1244-1249. doi: 10.1016/j.rmed.2012.06.010.	To investigate poor sleep quality and excessive daytime sleepiness and their effects on HRQOL in those with CF.	*N* = 55 Males (*n* = 30) and females 18 years and older (*M* 34.4, SD 7.5) with CF in Germany from an OP CF center.	HRQOL: German version of the revised CFQ-R (CFQ18+R) Daytime sleepiness: The Epworth Sleepiness Scale (ESS) Subjective sleep quality: Pittsburgh Sleep Quality Index (PSQI)	Intrapersonal
Bergsten Brucefors A, Hjelte L, Hochwälder J. Mental health and sense of coherence among Swedish adults with cystic fibrosis. *Scand J Caring Sci*. 2011;25(2):365-372. Accessed Sep 17, 2019. doi: 10.1111/j.1471-6712.2010.00840.x.	To describe mental health among adult Swedish patients with CF and to study if mental health and the salutogene factor sense of coherence correlate with good medical status. *The model of salutogene factor sense of coherence focuses on factors that influence good mental health.[42]	*N* = 59 Males and females (*n* = 26) ages 18-68 with cystic fibrosis (CF) in Sweden from an OP CF center.	Mental health: General Health Questionnaire (GHQ-28) Sense of Coherence: Sense of Coherence Scale (SOC-3). (Consists of 3 subscales: manageability, meaningfulness, and comprehensibility).	Intrapersonal Interpersonal
Cronly J, Duff A, Riekert K, et al. Positive mental health and wellbeing in adults with cystic fibrosis: A cross sectional study. *J Psychosom Res*. 2019;116:125-130. doi: 10.1016/j.jpsychores.2018.11.016.	To assess positive mental health and wellbeing, and associations with physical health and HRQOL in adults with CF.	*N* = 147 Males and females (*n* = 81) ages 18 and older (*M* = 30.5, SD 9.10) with CF from Republic of Ireland from an OP CF center and an online CF community.	Mental Well-being: Warwick-Edinburgh Mental Well-being Scale (WEMWBS) Depression & Anxiety: Hospital Anxiety and Depression Scale HRQOL: CFQ-R	Intrapersonal

Debska G, Cepuch G, Mazurek H. Quality of life in patients with cystic fibrosis depending on the severity of the disease and method of its treatment. *Postepy Hig Med Dosw (Online)*. 2014;68:498-502. doi: 10.5604/17322693.1101598.	To analyze the QOL in CF patients depending on the severity of the disease and methods of its treatment.	*N* = 45 Males and females older than 18 years of age with CF in Poland from an OP CF center. Participants were divided into 3 subgroups: After lung transplantation (*n* = 10), those with poor clinical status requiring oxygen and qualified for lung transplant (*n* = 15) and those in stable clinical status (*n* = 20).	HRQOL: Polish version of the CFQoL	Intrapersonal
Flewelling KD, Sellers DE, Sawicki GS, Robinson WM, Dill EJ. Male gender and unemployment are associated with lower levels of perceived social support in adults with cystic fibrosis. J Psychosom Res 2019;127. doi: 10.1016/j.jpsychores.2019.109858	To examine factors associated with social support in adults with CF in order to identify those who are most likely to experience a lack of support.	*N* = 233 Males and females (60%) ages 19-64 (*M* 33.6, SD 10.2) with CF from OP CF clinics in the United States.	Social support: Interpersonal Support Evaluation List (ISEL)	Intrapersonal
Flewelling KD, Sellers DE, Sawicki GS, Robinson WM, Dill EJ. Social support is associated with fewer reported symptoms and decreased treatment burden in adults with cystic fibrosis. *Journal of Cystic Fibrosis*. 2019;18(4):572-576. doi: 10.1016/j.jcf.2019.01.013.	To examine the self-report of a large panel of adults with CF with regard to social support and examines the relationship between social support and health outcomes.	*N* = 250 Males and females (61%) ages 20-65 (*M* 34.67, SD 10.17) with CF from 10 participating OP CF clinics in the United States.	Social support: ISEL Health assessment: Memorial Symptom Assessment Scale (MSAS) HRQOL: CFQ-R Treatment activity: Tool for Adherence Behavior Screening (TABS)	Intrapersonal
Havermans T, Colpaert K, Vanharen L, Dupont LJ. Health related quality of life in cystic fibrosis: To work or	To investigate whether patients with CF who are studying or	*N* = 57 Males (*n* = 29) and females (*M*	HRQOL: CFQ-R	Intrapersonal Interpersonal

not to work? *J Cyst Fibros*. 2009;8(3):218-223. doi: 10.1016/j.jcf.2009.03.002.	working report a better HRQOL in comparison to non-working/studying patients.	age 26.7, SD 8.1) with CF from an OP CF center in Belgium.		
Kelemen L, Lee AL, Button BM, Presnell S, Wilson JW, Holland AE. Pain impacts on quality of life and interferes with treatment in adults with cystic fibrosis. *Physiother Res Int*. 2012;17(3):132-141. doi: 10.1002/pri.524.	To determine the prevalence, severity and locations of pain in adults with CF during a period of clinical stability and acute illness and to identify the physical and psychosocial consequences of pain, including its effect on HRQOL.	*N* = 73 Males (*n* = 42) and females with a mean age of 29.4 (SD 8.5) with CF from an OP CF center in Australia.	Pain: Brief Pain Inventory and Pain Catastrophizing Scale HRQOL: CFQoL	Intrapersonal
Mc Hugh R, Mc Feeters D, Boyda D, O'Neill S. Coping styles in adults with cystic fibrosis: Implications for emotional and social quality of life. *Psychology, Health & Medicine*. 2016;21(1):102-112. Accessed Sep 26, 2019. doi: 10.1080/13548506.2015.1020317.	To examine which specific coping styles were positively or negatively associated with social and emotional QOL in a CF sample.	*N* = 122 Males and females (70.5%) ages 18-63 (*M* =29, SD = 8.35) recruited through an online support group.	HRQOL: CFQ-R Coping: Brief COPE	Intrapersonal
Nap-van der Vlist, M., Burghard M, Hulzebos HJ, et al. Prevalence of severe fatigue among adults with cystic fibrosis: A single center study. *Journal of Cystic Fibrosis*. 2018;17(3):368-374. doi: 10.1016/j.jcf.2018.03.003.	To investigate the prevalence of severe fatigue among adults with CF and to identify factors associated with fatigue.	*N* = 77 Males (56%) and females ages 19-54 (median 28.4) with CF from an OP CF center in The Netherlands.	HRQOL: CFQ Fatigue: Checklist Individual Strength-20 (CIS-20) Physical activity: Habitual Activity Estimation Scale (HAES)	Intrapersonal
Platten MJ, Newman E, Quayle E. Self-esteem and its relationship to mental health and quality of life in adults with cystic fibrosis. *J Clin Psychol Med Settings*. 2013;20(3):392-399. doi: 10.1007/s10880-012-9346-8.	To explore the predicative value of self-esteem and HRQOL in mental health symptoms in adults with CF.	*N* = 74 Males and females (77%) with mean age of 27.8 (SD 9.2) through an online discussion forum and Facebook page	Mental health symptoms and psychological distress: Clinical Outcomes in Routine Evaluation-Outcome Measures 34 (CORE-OM) Self-esteem: Rosenberg Self-esteem Scale	Intrapersonal

		hosted by a United Kingdom-based CF charity.	HRQOL: CFQ-R	
Quittner AL, Schechter MS, Rasouliyan L, Haselkorn T, Pasta DJ, Wagener JS. Impact of socioeconomic status, race, and ethnicity on quality of life in patients with cystic fibrosis in the United States. *Chest*. 2010;137(3):642-650. doi: 10.1378/chest.09-0345.	To examine the effects of socioeconomic and minority status on HRQOL in patients with CF from childhood through adulthood.	Study included 2,102 adults, 930 adolescents, and 1,719 children, along with 1,826 parents. The data from adults was stratified from the other groups. The adult group consisted of males (54%) and females grouped into two groups: No Medicaid (age *M* 28.5, SD 9.7) and Medicaid (age *M* 24.8, SD 6.7), with CF from an OP CF center in the United States.	SES: median family income for zip code of residence, maternal education, and Medicaid or state health insurance coverage. HRQOL: CFQ-R	Intrapersonal
Ribeiro Moco VJ, Lopes AJ, Vigario Pdos S, de Almeida VP, de Menezes SL, Guimaraes FS. Pulmonary function, functional capacity and quality of life in adults with cystic fibrosis. *Rev Port Pneumol (2006)*. 2015;21(4):198-202. doi: 10.1016/j.rppnen.2014.10.003.	Aimed to evaluate the association between respiratory function, functional capacity and QOL in these subjects.	*N* = 21 Males (57%) and females aged 18 years and older (*M* 25.5, SD 6) with CF from an OP CF Center in Brazil.	Functional capacity: Six-minute walk test (6MWT) QOL: CFQ-R 14 (Brazilian validated version)	Intrapersonal
Sawicki GS, Sellers DE, Robinson WM. Associations between illness perceptions and health-related quality of life in adults with cystic fibrosis. *J Psychosom Res*. 2011;70(2):161-167. doi: 10.1016/j.jpsychores.2010.06.005.	To examine the relationship between illness perception, health status, and HRQOL in a cohort of adults with CF.	*N* = 199 Males and females (63%) with a mean age of 35.8 (SD 10.3) years with CF from an OP CF center in the United States.	Illness perception: Illness Perception Questionnaire – Revised (IPQ-R) HRQOL: CFQ-R	Intrapersonal

Stofa M, Xanthos T, Ekmektzoglou K, et al. Quality of life in adults with cystic fibrosis: The Greek experience. *Pneumonol Alergol Pol*. 2016;84(4):205-211. doi: 10.5603/PiAP.2016.0025.	To report the HRQOL in CF adult patients to correlate findings with patient demographics.	*N* = 77 Males and females (*n* =43) over the age of 18 with CF from an IP CF unit in Greece.	HRQOL: CFQOL	Intrapersonal
Tóth T, Mák E, Galló N, Szabolcs I. Research on the quality of life of adult patients with cystic fibrosis in Hungary. *New Med*. 2016;20(2):53-58. Accessed 30 August 2019. doi: 10.5604/14270994.1206757.	To assess the QOL and nutritional status of adult patients with CF in Hungary and to determine the correlations between nutritional status, lung function and the QOL.	*N* = 57 Males and females over 18 years of age (*M* 28.25, SD 8.95) with CF from OP and IP CF units in Hungary.	QOL: Validated Hungarian translation of the CFQ-R	Intrapersonal
Yohannes AM, Willgoss TG, Fatoye FA, Dodd M, Webb K. Relationship between anxiety, depression, and quality of life in adult patients with cystic fibrosis. Respir Care 2012;57(4):550-556.	To investigate the prevalence and factors associated with anxiety and depression, including QOL, in adult CF patients.	*N* = 121 Males (*n*=65) and females ages 18-70 (*M* = 30, SD 8.8) with CF from an OP CF center in the Northwest region of England.	Anxiety & depression: Hospital Anxiety and Depression Scale (HADS) HRQOL: CFQOL	Intrapersonal
Longitudinal Studies				
Dill EJ, Dawson R, Sellers DE, Robinson WM, Sawicki GS. Longitudinal trends in health-related quality of life in adults with cystic fibrosis. *Chest*. 2013;144(3):981-989. doi: S0012-3692(13)60616-9.	To describe the trajectories of CFQ-R scores over a longer time frame in a non-clinical trial population of adults with CF. Identify factors associated with baseline CFQ-R scores and to examine trends over time among each of the CFQ-R domains.	*N* = 205 – 303 (depending on survey wave) Males and females (55%) ages 19-64 years (*M* 32.5, SD 10.65) with CF from OP CF centers in the United States.	HRQOL: CFQ-R	Intrapersonal
Qualitative Studies				
Bowmer G, Latchford G, Duff A, et al. Adherence to infection prevention and control guidelines: A	To develop previously studied themes related to	*N* = 87 Males and females (*n* =	NA	Intrapersonal Interpersonal

vignette-based study of decision-making and risk-taking in young adults with cystic fibrosis. *Journal of Cystic Fibrosis*. 2016;16(1):146-150. doi: 10.1016/j.jcf.2016.09.001.	decision-making about risks related to infection control precautions in a larger young adult sample for qualitative analysis.	65) ages 18-25 years (*M* 21.4, SD 2.48) with CF from an online CF social media platform in the United Kingdom (UK).		
Broekema K, Weber KM. Disclosures of cystic fibrosis-related information to romantic partners. *Qual Health Res*. 2017;27(10):1575-1585. doi: 10.1177/1049732317697675.	To document CF-related disclosure patterns from persons with CF to a romantic partner using a grounded theory approach.	*N* = 13 Males and females (*n* = 10) ages 24-43 with CF living in Canada and the United States. Interviews conducted over the phone (OP setting).	NA	Intrapersonal Interpersonal
Schmid-Mohler G, Caress A, Spirig R, Benden C, Yorke J. "Thrust out of normality"—How adults living with cystic fibrosis experience pulmonary exacerbations: A qualitative study. *Journal of Clinical Nursing*. 2019;28(1):190-200. doi: 10.1111/jocn.14646.	To explore the experience of pulmonary exacerbation from the perspective of adults with CF.	*N* = 18 Males (11) and females 18 years and older (median age 29.5, range 19-55) with CF in a university hospital in Switzerland.	NA	Intrapersonal Interpersonal Organizational Community

Manuscript 2

Coping in Adolescents and Adults with Cystic Fibrosis: An Integrative Review

Abstract

Background: Adolescents and adults with cystic fibrosis face a multitude of physical and psychological challenges that must be managed simultaneously with potential sources of everyday stress, such as school, careers, and raising children. Developing adequate coping skills are important for both physical and psychological health, especially when living with chronic illness. Identifying coping mechanisms that relate to positive outcomes can potentially improve quality of life. ***Methods:*** The purpose of this integrative review is to identify and critically analyze how coping strategies and associated influential factors are explored for adolescents and adults with CF in the literature. PubMed, Scopus, and CINAHL were searched for related publications, resulting in an initial yield of 1,181 articles. After eligibility screening, 15 studies met the criteria for this review, which were all critically analyzed and synthesized. ***Results:*** Multiple coping styles are utilized by this population; positive reappraisal, seeking guidance and support, taking problem-solving action, and acceptance/resignation were associated with increased quality of life. Coping mechanisms utilized were related to age, sex, social networks, support, severity of illness, and perceived illness. ***Conclusion:*** Further investigations should explore how different coping mechanisms affect short and long-term physical and mental health outcomes. Each coping mechanism comes with both positive and negative effects; it is important to teach coping strategies based on individual needs.

Introduction

Cystic fibrosis (CF) is a progressive, life-limiting genetic disease that causes increased production of thick mucus in multiple organs, resulting in complications such as impaired airway clearance, decreased lung function, and gastrointestinal dysfunction.[1,2] As recently as the 1980s, people diagnosed with CF rarely lived past their teenage years.[3] Now, the median predicated age of survival for those born with CF between 2015 and 2019 is 46 years.[4] This substantial increase in longevity is the result of the advancement and availability of new treatments and approaches to care.[5] However, treatment of CF remains complex and time consuming, typically consisting of airway clearance methods, multiple medications, nutritional therapy, and frequent visits with the care provider.[1,2] In addition to daily treatments, people with CF often have to manage rigorous treatments for complications of CF, such as frequent respiratory infections and CF-related diabetes (CFRD).[1,6]

With increasing life expectancy, people with CF must now manage a longer lifetime of symptoms with complex treatments simultaneously with typical stressors of adolescence and adulthood (i.e. school, relationships, careers, and children).[7,8] These multiple demands may trigger stress, psychological burden, and reduced quality of life (QOL), especially considering the increased anxiety and depression rates in this population.[1,4,9] When confronted with stressful life circumstances, there is the potential to take an active role in adaptation to the particular stressor.[10] Having adaptive coping mechanisms in place may mitigate psychosocial stressors, mental health symptoms, and improve QOL. For example, positive coping strategies (i.e. optimism) are associated with

better QOL, whereas more maladaptive coping strategies (i.e. avoidance or distraction) are associated with poorer disease adaptation.[1,11]

Coping methods for the adolescent and adult CF population may be unique compared to the general population due to a complex interplay of psychological distress, QOL, and management of a chronic condition.[12] However, there is not a thorough understanding of how this population utilizes coping strategies and which strategies best prepare the individual to navigate stressors associated with the multifaceted challenges of CF. Thus, the purpose of this integrative review (IR) is to identify and critically analyze how coping strategies and associated influential factors have been explored for adolescents and adults with CF in the literature. This knowledge can be used to better guide those with CF to cope with their disease process, manage stress, and promote psychological wellness.

Framework

This IR uses the coping skills framework outlined by Moos and Holahan as a way to organize, analyze, and synthesize findings.[13] These coping skills include four general coping domains: cognitive approach, behavioral approach, cognitive avoidance, and behavioral avoidance; each general domain contains two sub-sets (Figure 1).

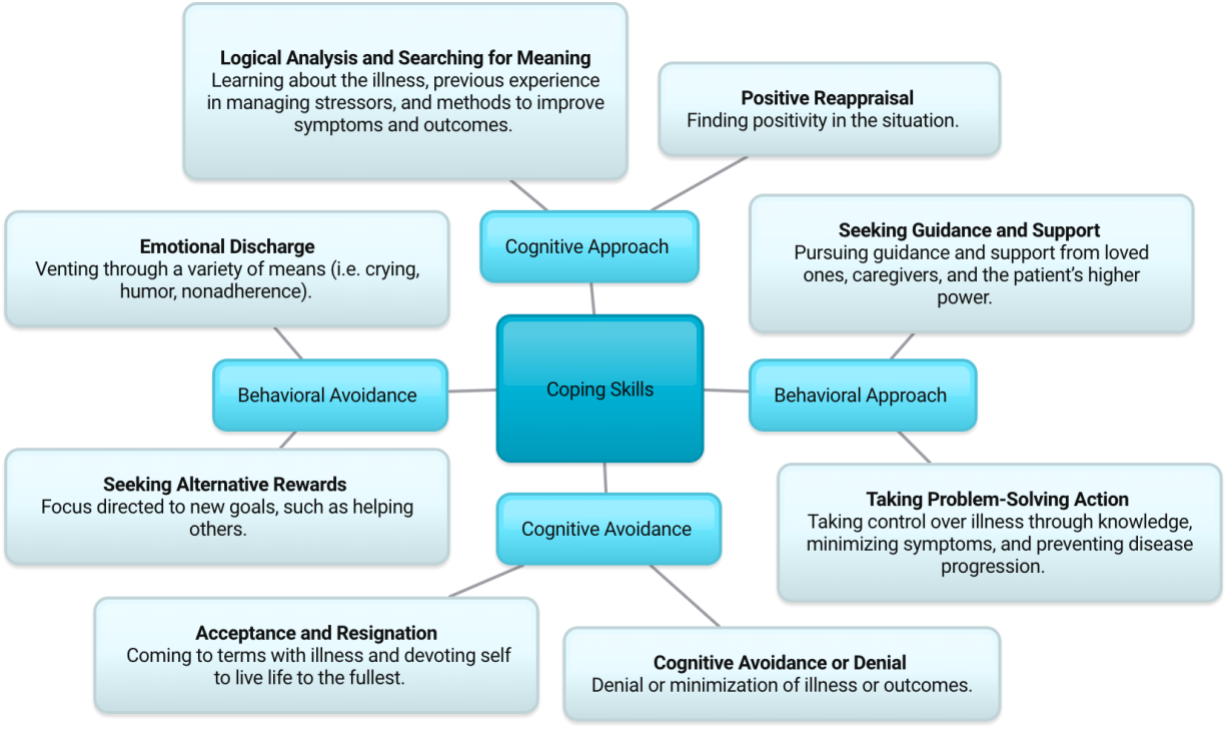


Figure 1: Coping Skills[13]

Methods

This IR follows the methodological framework outlined by Whittemore and Knafl as follows: 1) problem identification; 2) literature search; 3) data evaluation; 4) data analysis; and 5) presentation.[14] A comprehensive literature review was conducted in July 2020. Relevant studies were identified using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) protocol (Appendix A).

An experienced medical university librarian was consulted before the search to identify the most appropriate data bases and search terms. PubMed, Scopus, and CINAHL were searched using the following terms: ("adults with cystic fibrosis" OR "adults with CF" OR "adults CF") AND (cope OR coping OR adapt OR adaptation). A total of 1,181 studies were identified. Inclusion criteria included studies conducted in

adolescents (≥10 years) and/or adults with CF with a focus on coping or adaptation. Studies were excluded if they were non-English, used non-human participants, or were published before 2005. Titles and abstracts were reviewed for inclusion criteria, leaving 56 articles eligible for full text review, of which 15 articles met the inclusion criteria. Data evaluation and analysis of the final 15 articles were conducted using a literature matrix (Appendix B). Critical appraisal was performed on all studies using the Mixed Methods Appraisal Tool (MMAT).[15]

Results of this IR are organized and presented by the aforementioned coping skills. Due to the diverse nature of coping strategies and terminology across studies, coping strategies were coded based upon the definition within the article or context of the study. These definitions were then cross-referenced with coping skills and grouped into segments, which determined the best fit for each coping strategy (Table 1). Many coping strategies have a broad or overarching theme and can belong to various coping skill categories; therefore, consistency was used in the coding approach when determining the most appropriate category based on the best fit given the context of the study. This allowed authors to organize data in a way that could be synthesized in an efficient manner. The data was organized and outlined for analysis and synthesis (Appendix B).

Table 1: Coping Skill Strategies			
Coping Domain	**Coping Skill**	**Coping Strategies**	**Studies (per literature matrix)**
Cognitive Approach	Logical Analysis and the Search for Meaning	NA	None
	Positive Reappraisal	Optimism Optimistic acceptance Positivity	1, 2, 3, 5, 8, 11, 15
Behavioral Approach	Seeking Guidance and Support	Hope/Hopefulness Religion Spiritual	1, 2, 3, 4, 8, 9, 12, 15
	Taking Problem-Solving Action	Active coping Adaptive Cooperation Instrumental Problem-focused Social support-focused	6, 12, 14, 15
Cognitive Avoidance	Cognitive Avoidance or Denial	Avoidance Behavioral disengagement Denial Minimizing Self-isolation	1, 2, 3, 10, 12, 14
	Acceptance and Resignation	Acceptance Accommodative strategies Overcoming limitations Resilience Self-encouragement	5, 10, 11, 12, 13
Behavioral Avoidance	Emotional Discharge	Distraction Emotion-focused Rebellion Substance abuse Tension	1, 2, 5, 6, 12, 15
	Seeking Alternative Rewards	School-based coping	7

Results

Articles reported on quantitative (cross-sectional *n* = 7, short-term longitudinal *n* = 1), qualitative (descriptive *n* = 1, grounded theory *n* = 1, phenomenology *n* = 3), and mixed-method (*n* = 2) studies from 7 different countries (Australia [*n* = 1], Austria [*n* = 1], Brazil [*n* = 1], France [*n* = 1], Israel [*n* = 1], United Kingdom [*n* = 4], and the United States [*n* = 6]). The majority of studies took place in outpatient (OP) settings (*n* = 12);

others took place online (n = 2) or in combined inpatient (IP) and OP settings (n = 1). Results of this IR represent 900 participants (individuals with CF n = 857, family member speaking about a deceased loved one with CF n = 10, partner or spouse of a person with CF n = 33).

Positive Reappraisal

Positive reappraisal coping focuses on remaining positive or using a strategy rooted in positivity.[13] This coping style was found among seven studies which examined coping in relation to age, QOL, health-related QOL (HRQOL), dyadic coping, and end of life care.[1,6,8,12,16,17,18] Positivity and optimism were common mechanisms for those coping with CF as a chronic disease process.[7] Older age appeared to be related to improved coping strategies through the use of positive reappraisal methods.[6,12] One study discussed the use of positive reappraisal coping through optimistic acceptance during the challenging transition from pediatric to adult CF-based care.[12] While the most common strategy in this study was optimistic-acceptance (84%), participants also utilized additional methods, such as avoidance (8.8%), distraction (2.2%), and hopefulness (2.2%); however, these coping methods were used to a minimal extent.[12] Participants in this study reported low levels of anxiety and depression and a positive experience with the complex pediatric to adult care transition.[12] Another study exploring HRQOL found that positive reappraisal coping enhanced HRQOL when measured through a validated CF-specific QOL questionnaire (CFQoL); optimism-based coping was positively associated with the social function, emotional response, interpersonal relationship, and future concern domains of the CFQoL.[1]

Exploration of coping styles among people diagnosed with CFRD found that those who were older at the time of diagnosis used positivity to cope.[6] Additionally, individuals living with CFRD who coped through positivity experienced relief of symptoms due to acceptance of the disease.[6] This qualitative study found that the majority of participants eventually embraced positivity and acceptance to cope with CFRD.[6]

When exploring coping mechanisms among married partners where one partner had CF, positive reappraisal through optimism improved dyadic coping.[17] Similar attitudes within the couples, clear division of roles, focusing on present challenges, open communication, empathy, support, and marital growth improved the use of positive dyadic coping.[17] When using a qualitative approach to explore end of life care in those with CF, optimism and a positive mindset were reported by family members as essential for both the patient and family in creating a more optimistic prognosis.[18] Families later questioned using optimism and positivity because they felt it did not allow them to process their loved one's true condition.[18]

Seeking Guidance and Support

Seeking guidance and support from loved ones, caregivers, or a higher power was found in eight studies, all of which explored the effects of either religious or spiritual coping.[1,5,9,12,16-19] One study reported differences between positive religious coping (RC) (having a secure relationship with a divine power/force) and negative RC (relationship with divine power/force creates negative feelings, such as guilt or abandonment).[5] While participants utilized positive RC more than negative RC, females were more likely to use RC altogether,[5] which was positively associated with emotional QOL.[9] In a study

exploring how coping relates to a connection with God specifically, the age of diagnosis was found to affect this relationship; people diagnosed with CF as children were more likely to feel that their disease was part of their life's divine plan, whereas people diagnosed as adults felt disease management was a collaboration between their ability to manage their disease, the CF team, and God.[16,19] Participants diagnosed with CF late in life used spirituality as a guide to positively reframe their diagnosis and create meaning from the experience.[19]

Seeking guidance and support-based coping using religion was found to have effects on HRQOL. At the baseline of a study exploring effects of RC on depression, anxiety, and HRQOL, positive RC was associated with fewer psychological symptoms and higher HRQOL scores in the vitality, emotion, eating, health, and weight domains of the CF Questionnaire – Revised (CFQ-R), a validated measure for CF-specific HRQOL.[5] During the 3-month follow-up, there was no longer an association found between positive RC and the vitality and emotion domains; a regression analysis found that positive RC could not significantly predict any of the CFQ-R domains.[5] Negative RC was associated with increased perceptions of stress, depression, and anxiety, as well as lower CFQ-R scores in the physical, emotion, treatment burden, social, body image, role, weight, respiratory, and digestive domains at baseline.[5] During follow-up, negative RC was associated with increased anxiety and decreased scores in the physical, vitality, emotional, social, body image, and respiratory CFQ-R domains.[5] Regression analysis demonstrated that negative RC predicted greater depressive symptoms and perceived stress and lower CFQ-R scores in the vitality, social, and digestive domains.[5]

Two studies explored the effects of spirituality-based coping on treatment adherence and disease management. Spiritual beliefs were found to motivate a healthier lifestyle through the belief that proper self-care and disease management were necessary for divine assistance.[16,19] One of these studies specifically explored how spirituality-based coping affected treatment utility (attitude toward treatment), subjective norms (perception of other's expectations), and self-efficacy (perceived ability) on prescribed airway clearance, nebulized medications, and exercise regimens.[16] For airway clearance, treatment utility was positively predicted by self-directed coping (no use of divine assistance) and active surrender coping (participating in self-care and then turning control to a divine power), and negatively by deferral coping strategies (placing disease management into the hands of a higher power); subjective norms were positively predicted by age and negatively by active surrender coping; self-efficacy was negatively predicted by the use of deferral coping.[16] For nebulized medications, treatment utility was positively predicted by collaboration (having a partnership with a divine power), pleading (for divine assistance), self-directed coping, and negatively by deferral coping. Influences affecting subjective norms were inversely predicted by both collaborative and self-directed spiritual coping; self-efficacy was negatively predicted by deferral coping.[16] For exercise, treatment utility was positively predicted by the use of pleading and inversely by mood; subjective norms were positively related to increasing age and negatively to self-directed coping and channeling spiritual constructs.[16]

The use of hope/hopefulness (a behavioral approach strategy where it is believed everything will work out while utilizing support systems)[1] is another coping mechanism rooted in seeking guidance and support. When exploring coping mechanisms among

married partners where one had CF, hope/hopefulness improved dyadic coping.[17] In a study exploring end of life care in those with CF, hope was also reported by the family as essential for both the patient and family during end-of-life stages.[18] However, hope/hopefulness was not found to be associated with HRQOL in those with CF.[1]

Taking Problem-Solving Action

Problem-solving action involves coping by taking control over an illness through knowledge, minimizing symptoms, and preventing disease progression.[13] This coping mechanism was found in four studies which explore dyadic coping among couples where one partner has CF, emotional and social QOL, and coping's relationship to QOL in adults waiting for lung transplants.[9,17,20,21] For dyadic coping, the partners with more severe forms of CF relied on emotional coping and problem-solving and tended to search for social support to enhance coping when compared to those with milder forms of CF.[21] The use of problem-based coping was positively associated with depression and anxiety in the partner without CF.[21] Characteristics that related to negative dyadic coping strategies included discrepancy of illness perception and coping mechanisms between the partners, feeling that CF is disruptive, not seeing the other partner's needs, and a lack of support.[17] When comparing coping styles to emotional and social QOL, instrumental coping (i.e. problem-solving-based coping) was positively correlated to emotional QOL.[9] Active coping (goal-directed effort to minimize stress and its associated physical, psychological, and social effects to problem-solve)[22] was positively correlated to social QOL.[9,20]

Increased use of active coping strategies positively related to both psychological and social QOL.[9,20] In a cross-sectional study exploring coping and QOL among people

awaiting lung transplants for either CF or chronic obstructive pulmonary disease (COPD), participants who used active coping demonstrated a significant improvement in psychological QOL.[20] However, there was only a statistically significant relationship between active coping and improved physical QOL among the COPD group and not the CF participants.[20]

Cognitive Avoidance or Denial

Cognitive avoidance or denial-based coping strategies use denial or the minimization of illness or outcomes.[13] This coping mechanism was explored in relation to HRQOL in five studies, and in another to end of life care.[1,9,12,18,20,23] No significant associations were found between the use of avoidance as a coping method and HRQOL.[1] When exploring coping strategies for pain and disability, passive coping (minimizing and self-isolation) was found to be utilized by participants the least.[23] When exploring QOL and coping in patients awaiting lung transplants, the use of disengagement coping was negatively associated with psychological QOL in people with CF or COPD;[20] whereas disengagement was correlated with decreased emotional QOL in a study exploring coping and QOL in adults with CF.[9] The use of cognitive avoidance and denial-based coping were used by people with CF at the end of life, along with their family members, but this resulted in little or no preparation to talk about expectations for this difficult process.[18]

Emotional Discharge

Emotional discharge-based coping involves venting through a variety of means (i.e. crying, humor, nonadherence, substance abuse, distraction)[13] and was found in six studies.[1,6,9,12,17,21] Coping through substance abuse was associated with decreased

emotional QOL.[9] In a study exploring coping after a diagnosis with CFRD, those younger at diagnosis (ages 10-17) tended to use emotional discharge-based coping (i.e. rebellion, non-adherence) and had greater difficulty adjusting to the new diagnosis.[6] The use of emotion-focused coping (attempting to alter emotions to divert away from a stressor)[9,24] was associated with increased depression and anxiety and decreased marital adjustment in couples where one partner had CF.[21] The use of emotional-discharged based distraction coping (behavioral avoidance strategy where one uses distraction to forget they have CF)[1] was negatively associated with the social function, emotional response, interpersonal relationships, and future concern domains of the CFQoL and the emotional and social domains of the CFQ-R.[1,9]

Acceptance and Resignation

The use of acceptance and resignation coping involves coming to terms with illness and focusing on living life to the fullest.[13] The positive effects of this strategy were explored in three cross-sectional studies and two qualitative studies.[6,8,9,23,25] In the study exploring coping mechanisms following a diagnosis of CFRD, the majority of participants opted for acceptance and positivity.[6] Those using acceptance coping, which was positively associated with QOL,[9] found relief of CFRD-related symptoms.[6] This differed from those who had trouble coping, who experienced difficulties accepting their new lifestyle and therapeutic regimen.[6] Active and accommodative coping through acceptance and self-encouragement was utilized more by those experiencing CF-related pain and disability.[23]

When investigating resilience and intolerance of uncertainty (IU) (negative thought processes resulting from uncertainty) as coping mechanisms for CF, resilience

(personal competence and acceptance) had a positive effect on HRQOL.[25] During bivariate correlations, personal competence was positively associated with the physical, psychological, social, role, body, eating, heath perception, respiratory, and digestion CFQ-R domains, with acceptance positively associated with the psychological, social, and body domains.[25] Linear regression revealed that personal competence predicted the vitality, psychological, health perception, and digestion domains, while acceptance did not offer predictive abilities.[25] Lastly, bivariate correlations revealed that negative thought processes from uncertainty were negatively associated with the physical, psychological, social, and health domains of the CFQ-R but did not offer predictive properties for QOL during regression analysis.[25]

Based on experiences of adults with CF described during a qualitative study, participants reported experiencing CF-related social prejudice, feeling shame and embarrassment around the general public as a result of CF symptoms, such as public coughing or telling others about their disease.[8] Common coping strategies to manage these issues were not letting the disease become the center of their being, utilization of support, and resilience; other coping mechanisms, such as positivity and optimism, were also utilized by these participants.[8]

Seeking Alternative Rewards

One study in this IR addressed seeking alternative rewards to cope, which involves focusing on new goals.[13] This study addressed academic achievement and coping among adolescents with CF, with the potential of academic success as the goal or alternative reward. This study found that adolescent students with CF fell within the average expectations for cognitive and arithmetic functioning and performed well in

school.[7] Participants experienced increased missed school days compared to their peers, which related to lower grade point averages.[7] Average self-efficacy scores, attitude toward school, and depression scores were found to be average when compared to other classmates, with positive feelings about their own abilities and school.[7] Scores on the Role-play Inventory of Situations and Coping Strategies found that the participants in the study had somewhat effective coping mechanisms in place for managing CF-related school stressors.[7]

Discussion

The purpose of this IR was to identify and critically analyze how coping strategies and associated influential factors are explored in the literature for adolescents and adults with CF. Based on these results, positive reappraisal, seeking guidance and support, acceptance and resignation, and seeking alternative rewards offer the most potential, however, each comes with its own risks and may not be appropriate for every individual or for all situations. Taking problem-solving action, cognitive avoidance or denial, and emotional discharge coping mechanisms illustrate both positive and negative effects on physical and psychological QOL, depending on the specific situation, context of the study, and variables explored. This research suggests that the utilized coping strategy and associated outcomes may be dependent upon other variables, such as demographics, severity of illness, mindset, personality, comorbidities, etc. It is important to consider that coping methods are fluid and can change with time.

Participants who are older tended to have different coping mechanisms (i.e. increased use of positivity) than younger participants,[6,16,19,20] suggesting that coping mechanisms may be dependent upon age of diagnosis, maturity level, knowledge, and

disease progression. Positivity was found in younger participants during the complex transition from pediatric to adult care,[12] which may be related to excitement for new chapters in life, such as independence, college, relationships, and family. Additionally, it is possible that age-related differences contribute to improved physical QOL with active coping in those with COPD awaiting lung transplantation,[20] but not in participants with CF,[20] as those with COPD are typically diagnosed much later in life. Enhanced coping may also result from more life experiences and practices with utilizing different approaches throughout the lifespan.

Coping mechanisms using positivity present encouraging outcomes, though these strategies may come with risks. The use of positivity was questioned by families of individuals dying from CF due to the inability to process the impending death.[18] There is the potential that by using positivity, family members and the person with CF create a sense of denial regarding disease progression and death. On the other hand, it is possible that the loved ones of those with CF who use positive coping mechanisms may inadvertently believe their loved one is in denial of their prognosis. Perhaps the positivity resulted in a sense of self-protection by not allowing full acceptance of the prognosis.

Certain coping strategies were found to intersect with other variables, such as sex, social networks, support, and perceived illness.[1,5,8,9,16,21,25] A previous study found that females with CF have better perceptions of social support compared to men[26], which is similar to results from another study suggesting that adult females with congenital heart disease seek out and receive support more than males.[27] This may explain why females with CF utilize RC more;[5] belonging to a religious congregation can provide broader social networks and access to social resources through church. Positive effects of RC

were found for both sexes,[5] and it may be that participants who use religion and/or spirituality to cope felt fulfilled with life and used faith to help navigate their chronic illness. A similar pattern was found when coping was explored in people with sickle cell disease (SCD); participants who used positive RC were less likely to be hospitalized, with religious and spiritual coping being common among adolescents living with SCD.[28,29] However, a potential for negative outcomes exist when using spirituality or religion to cope; for example, putting disease management in the hands of a higher power may lead to nonadherence based on the belief that the higher power will take control, instead of the individual exerting intentional action to engage in self-management.

Social support potentially improves coping mechanisms due to its facilitation of adaptive coping strategies, such as active coping.[30] Additionally, acceptance and resignation-based coping may allow one to live unrestricted by the burden of CF, thereby easing psychosocial challenges and potentially allowing one to develop a broader social circle. A strong support system may aid in the ability to cope with CF, which coincides with extra support derived from a religious congregation in those using RC. This may also apply to a person with CF who receives support from a spouse or life partner; however, the partner without CF can experience psychological burden if they are the primary source of support but do not receive reciprocal support. It is important for couples where one partner has CF to find healthy ways of coping together to ensure both partners have support for managing life with CF or loving someone with CF.

Severity of illness and perceived illness are factors that may affect coping mechanisms and adherence to disease management. Increased severity of illness and perception of disease severity may generate concerns of an earlier decline in condition

and a higher potential for complications, prompting strict adherence to treatment regimens to prevent disease progression. However, these perceptions may lead to a decrease in QOL due to psychological distress, thus increasing the need for appropriate coping mechanisms at different points throughout disease progression. Furthermore, complex management of CF can be time-consuming, further fostering decreased QOL.

On the other hand, cognitive avoidance or denial and emotional discharge are related to negative outcomes. Certain emotional discharge strategies, such as emotion-focused coping and distraction, may provide relief and diversion from acute psychological distress (e.g., distraction to avoid engaging in harmful behaviors such as non-suicidal self-injury) but may not provide long-term sustainable coping for a chronic disease.[1,31] Further, by minimizing perceptions of illness, those with CF may struggle with coming to terms with their chronic disease process, its progressive nature, and the future. This may explain the negative relationship between future concern domain scores and distraction-based coping.[1] Additionally, these concepts may lead to emotional discharge coping through alcohol and/or substance abuse or through acting out from anger or failure to accept CF. These struggles can create difficulties with socialization, emotion, and relationships resulting from hiding or minimizing their illness to friends and loved ones, therefore, limiting the ability to seek support. The use of cognitive avoidance or denial while waiting for a lung transplant may be related to difficulty facing disease severity, leading to little preparation for the challenges of having a lung transplant;[20] additionally, this concept may explain why loved ones of a person who died from CF feel they were not prepared for the loved one's death.[18] These are not surprising findings, as

similar coping strategies (catastrophizing, anger self-statements, isolation) were found to impair QOL in participants with SCD.[32]

Coping is not homogenous, either across different individuals or even within one individual; just because an individual is performing well in one area, does not mean they are in all areas. For example, the study examining academic success demonstrates adolescents with CF have adequate coping capabilities in the school setting, yet they had increased depression scores,[7] indicating difficulty with coping in other areas of life. This potentially illustrates that adolescents may have healthy coping mechanisms in one aspect of life but not others. Additionally, coping strategies may change over time, which perhaps explains why correlations between coping and HRQOL changed over a 3-month timeframe in the study exploring RC, depression, anxiety, and HRQOL.[5]

Implications

Practice

A deep understanding of coping styles and strategies can identify those vulnerable to maladaptive coping mechanisms and redirect them to more adaptive strategies. Understanding that coping skills are fluid based on a person's stressor, personality, and life experiences can help practitioners meet individual needs. Assessing one's social network will help to identify social supports in place, which can determine the strength of their social network and how it may be utilized to improve coping strategies. Coping is not a standardized concept that can be prescribed, but individualized assessments can elicit knowledge to allow providers to educate on the most appropriate coping strategies. These strategies may be integrated into brief interventions performed in clinic as well as for those receiving psychological care, the evidence-based interventions (e.g., cognitive

behavioral therapy, acceptance and commitment therapy) being utilized. Providing appropriate coping strategies to those with CF may have a significant effect on QOL and disease management.

Research

While this IR analyzes multiple coping styles in a variety of settings and specific CF-related modalities, there are still areas that deserve further exploration. Investigating how different coping styles affect clinical outcomes and HRQOL longitudinally can provide data that supports the most effective coping strategies for adolescents and adults with CF. Placing efforts into qualitative studies addressing how coping strategies are developed and utilized while juggling multiple demands of adolescence and adulthood can elicit information that may help with the development of healthy coping strategies early in life. There is also a need for a thorough understanding of exactly what coping means to adolescents and adults with CF, how these coping styles are integrated into everyday life, and how they may affect self-management and self-efficacy to best assimilate coping strategies into the plan of care.

Influences upon coping styles in people with CF have not been explored to our knowledge. Exploration of multiple potentially influential variables would provide a well-rounded picture of coping in this population. For example, the home environment, family life, support system, and parenting style during one's upbringing may exert significant influence on coping skill development. While using spiritual and/or positive RC tended to show benefits,[5] there remains a need to explore how non-religious and non-spiritual support systems can help individuals of varying belief systems. It cannot be assumed that those using RC and spirituality have large support systems or only receive

support from congregations, therefore, exploring all avenues can create a more robust understanding of the connections, if any, between coping and social networks.

Notably, there is a clear lack of interventional studies focused on enhancing coping skills in people with CF, such as cognitive behavioral therapy, to mitigate detrimental coping behaviors and enhance healthy ones. Developing and testing effective interventions specific to this population can allow both researchers and practitioners to fully engage in improvement of the psychological health of adolescents and adults with CF.

Limitations

This IR has several limitations. Multiple studies (n = 9) did not identify if participants were diagnosed as children or adults, which may relate to how coping mechanisms are developed. A few (n = 3) of the quantitative studies have small sample sizes, therefore, the potential for limited statistical power exists. Using Moos and Holahan's coping skills was an appropriate framework for this IR; however, many of the coping mechanisms are appropriate for more than one coping skill category, which has the potential to affect analysis. Future investigations should explore differences of coping strategies based on the age of diagnosis. Considering there were differences between how those diagnosed as children and adults approached their relationships with a higher power through religion or spirituality, this warrants a closer look to identify how coping mechanisms are developed.

Future investigations should focus on assessing coping strategies through different stressors, along with longitudinal studies to see if, and how, coping strategies change over time as they relate to age and disease progression. The use of other coping

skills, such as self-compassion or humor, deserve exploration into their ability to provide adaptive coping in the CF population. It would be beneficial to investigate how coping terminology is used in chronic illness populations; the use of Moos and Holahan's coping skills was advantageous for this review but there remains a great deal of overlap of coping terminology. This may cause confusion to how coping mechanisms relate to each other across similar populations.

Conclusion

Findings from this IR revealed many adaptive and maladaptive coping skills related to the adolescent and adult CF population in the current literature. There are multiple opportunities for future studies to extensively explore effects of each coping skill in depth, especially how they relate physical and psychological health for people with CF. As healthy coping mechanism assessment and education become more embedded into the complex interdisciplinary management of CF, the greater the opportunity to further improve the overall QOL of adolescents and adults with CF.

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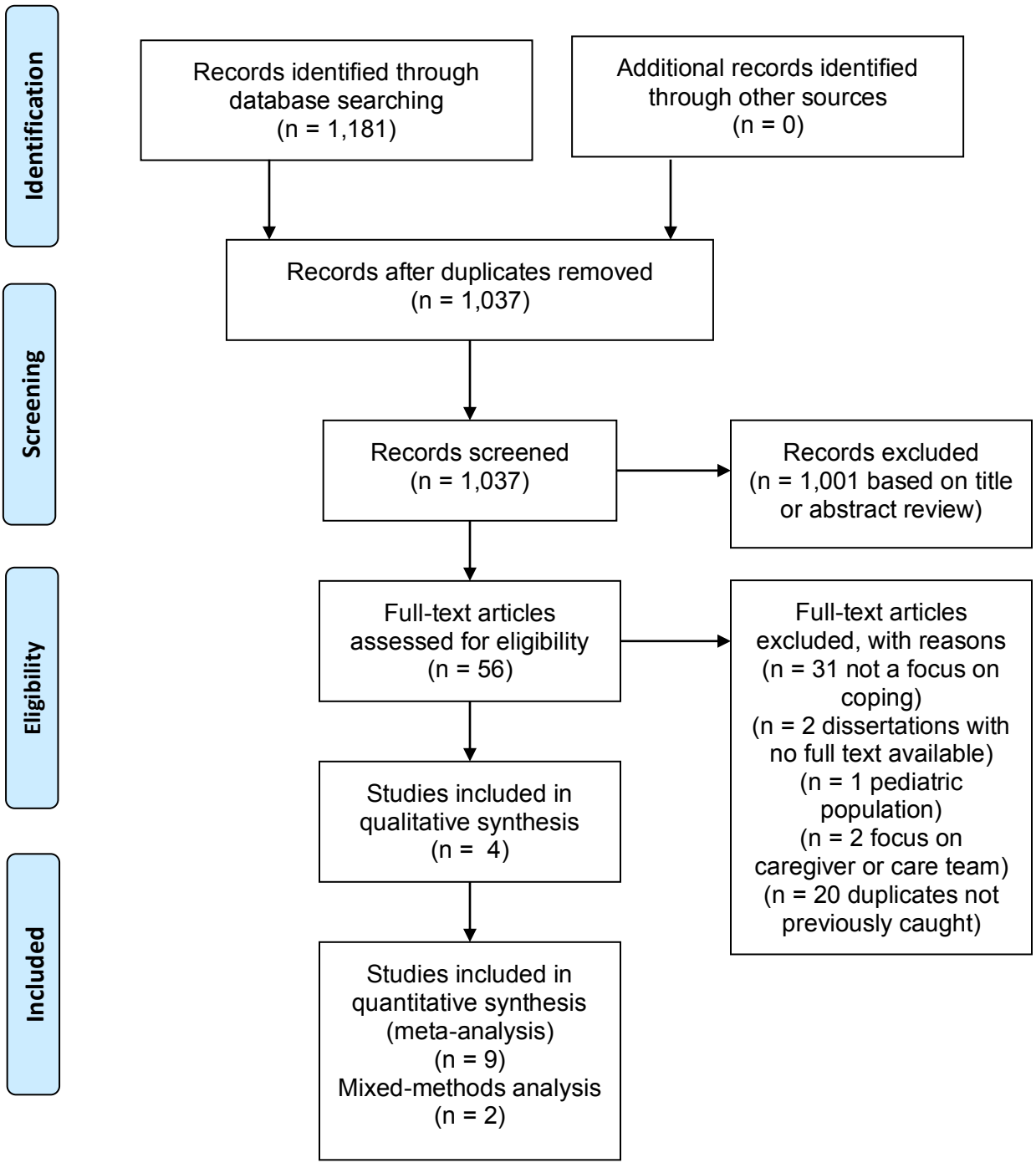
Appendix A

PRISMA 2009 Flow Diagram



Appendix B
Literature Matrix

Article	Study Design/Purpose	Participants/Setting	Instruments	Coping Skill and Method/s Explored	Results
1. Abbott J, Hart A, Morton A, Gee L, Conway S. Health-related quality of life in adults with cystic fibrosis: the role of coping. J Psychosom Res 2008 February;64(2):149-157.	Cross-sectional To examine the associations between ways of coping and QOL domains using CF patient-derived and validated measures, considering key demographic and clinical factors in explaining HRQOL in CF.	*n* = 116 Age range: 16-50 years (*M* 25.4, *SD* 6.8) Females *n* = 72 Males *n* = 44 Regional Adult CF Unit in Leeds, UK	CF Coping Scale CF QOL Questionnaire (CFQoL)	<u>Positive Reappraisal:</u> Optimism <u>Seeking Guidance and Support:</u> Hopefulness <u>Cognitive Avoidance or Denial:</u> Avoidance <u>Emotional Discharge:</u> Distraction	- Regression analyses and path analyses were consistent. No significant associations were found between hopefulness or avoidance. *Optimism* - Positively associated with social function, emotional response, interpersonal relationships, and future concern domains. *Distraction* - Negatively associated with social function, emotional response, interpersonal relationships, and future concern domains.
2. Askew K, Bamford J, Hudson N, Moratelli J, Miller R, Anderson A, et al. Current characteristics, challenges and coping strategies of young	Mixed Methods To determine the following for young adults with CF: Current health and	*n* = 45 Age range: 17-24 (*M* 20.7) Male *n* = 27 Female *n* = 18	Hospital anxiety and depression scale (HADS) Ways of Coping Scale	<u>Positive Reappraisal:</u> Optimistic acceptance Hopefulness	- Overall mean for anxiety was 4.02 (range 0-18, *SD* 4.2) on the HADS, indicating the majority of participants reported lower levels of anxiety. - Overall mean for depression was 2.18 (range 0-15, *SD* 0.48) on the

people with cystic fibrosis as they transition to adulthood. Clin Med J R Coll Phys Lond 2017;17(2):121-125.	psychological status, identify their perception of the challenges they face and to assess their needs and coping strategies during transition to adulthood	Outpatient Adult CF Center in England		<u>Seeking Guidance and Support:</u> Hopefulness <u>Cognitive Avoidance or Denial:</u> Avoidance <u>Emotional Discharge:</u> Distraction	HADS, indicating the majority of participants reported lower levels of depression. - Multiple coping strategies were identified by participants (praying, ETOH/drug use, crying, etc.) but the most common ones used as the main mechanism to cope were: - Optimistic acceptance (84%) - Avoidance (8.8%) - Distraction (2.2%) - Hopefulness (2.2%)
3. Braithwaite M, Philip J, Tranberg H, Finlayson F, Gold M, Kotsimbos T, et al. End of life care in CF: patients, families and staff experiences and unmet needs. J Cyst Fibros 2011 July;10(4):253-257.	Qualitative To explore the unmet needs and key issues for CF patients, their families and the staff providing their care whilst awaiting organ transplantation.	CF Patients *n* = 12 Ages 26-53 years (*M* 35) Male *n* = 58% Family members of CF patients that passed away in the past 4 years *n* = 10 Ages 27-58 years (*M* 45) Male *n* = 50%	Single-occasion interview	<u>Positive Reappraisal:</u> Optimism/ Positivity <u>Seeking Guidance and Support:</u> Hope <u>Cognitive Avoidance or Denial:</u> Denial	Themes: - *Knowledge of palliative care (PC)* - Many did not want to discuss PC due to fear of bringing death closer - *Psychological frame* - Family and patients felt a positive attitude would have a positive impact on prognosis. - Many families felt this positivity caused later regrets. - Patients had difficulty confronting the reality of death. - Hope and positive psychological mindset was essential for coping but

		CF Clinic in Australia			it may not allow for the processing of information. - Denial as a coping strategy resulted in a lack of preparation for a deterioration in health.
4. Burgess BE, Gresham BL, Mrug S, Bray LA, Leon KJ, Troxler RB. Religious coping and psychosocial adjustment in patients with cystic fibrosis. J Health Psychol 2020:1359105320935979.	Short-term longitudinal (Baseline with a 3-month follow up) Evaluating the direct effects of positive and negative RC on depressive anxiety symptoms and HRQoL domains and to examine the moderating effects of positive and negative RC on the relationship between perceived stress and symptoms of depression and anxiety.	*n* = 123 Ages ≥18 years Inpatient and outpatient pulmonary clinics in Alabama, USA	Religious Coping: Brief RCOPE Depression and anxiety: Brief Symptoms Inventory Perceived Stress Scale HRQoL: CFQ-R	<u>Seeking Guidance and Support:</u> Religious	- Overall, participants used positive religious coping (RC) more than negative RC. *Positive RC* - Females reported higher rates of RC and scored better in the CFQ-R weight domain. - At baseline, positive RC was associated with lower perceived stress and depressive/anxiety symptoms scores, higher HRQoL scores in the following CFQ-R domains: vitality, emotion, eating, health, and weight. - At follow-up, positive RC was associated with decreased depressive/anxiety symptoms, and higher CFQ-R scores in the eating, health, and weight domains but was not a significant predictor of these domain scores. *Negative RC* - At baseline, negative RC was associated with increased perceived

					stress, depression, and anxiety, and lower CFQ-R scores in all domains except vitality, eating, and health. - At follow-up, negative RC was associated with decreased anxiety symptoms, and decreased scores in the following CFQ-R domains: physical, vitality, emotional, social, body image, and respiratory. - Negative RC predicted a decrease in CFQ-R scores for the vitality, social, and digestive domains.
5. Collins S, Reynolds F. How do adults with cystic fibrosis cope following a diagnosis of diabetes? Journal of Advanced Nursing 2008 Dec;64(5):478-487.	Qualitative with Interpretive Phenomenological Analysis To examine the experience of adults with CF in adapting to the diagnosis of diabetes, a second chronic illness.	*n* = 22 Ages 24-55 years Male *n* = 12 Female *n* = 12 National Health Service CF database in London and Southeast England	Single-occasion interview	<u>Positive Reappraisal:</u> Positivity <u>Acceptance and Resignation:</u> Acceptance <u>Emotional-Discharge:</u> Rebellion	- Participants were now confronting feelings about two chronic illnesses. *Positivity and Acceptance* - The majority of participants eventually approached the diagnosis of CFRD with positive attitudes and acceptance. - Acceptance of the new diagnosis seemed to relate to the relief of CFRD-related symptoms. - Living with positivity was associated with being older, having a stable CF treatment regimen, and treating illness as a problem to be managed in a depersonalized way. *Difficulty Coping*

					- Those who described difficulty adjusting to CFRD were younger, living alone, longing for a more active lifestyle, and not having the skill required for blood glucose control. - Barriers to acceptance included adjusting to insulin injections, prioritizing a normal lifestyle, and conflicting dietary demands of having both CF and CFRD. - Participants that were diagnosed at a younger age (10-17 years) used rebellion against CFRD to cope by not injecting insulin or adhering to the proper diet.
6. Delelis G, Christophe V, Leroy S, Vanneste J, Wallaert B. The effects of cystic fibrosis on couples: Marital satisfaction, emotions, and coping strategies. Scandinavian Journal of Psychology 2008 Dec;49(6):583-589.	Cross-sectional To point out the emotional experiences, marital satisfaction, and coping strategies of CF patients and their partners and to determine 1) whether patients and partners exhibit the same	Participants with CF *n* = 16 Age *M& SD* 28(4.56) Partners *n* =16 Age *M& SD* 29(5.41) CF Center of a hospital in Northern France	Spanier's Dyadic Adjustment Scale (SDAS) State-Trait Anxiety Inventory Centers for Epidemiologic Studies - Depression Scale	<u>Taking Problem-Solving Action:</u> Problem-focused Social support-focused <u>Emotional Discharge:</u> Emotion-focused	*Marital Adjustment* - All couples reported a basically satisfying relationship. - Only 2 of the 16 healthy partners reported a different level of marital adjustment based on the SDAS than their partner with CF - SDAS scores of men were better when they were the partner with CF with the reverse being the case for female partners with CF *Coping*

	response profile, and 2) whether the severity of the disease and its treatment have an effect on these variables.		Ways of Coping Checklist		- Coping strategies are employed less among participants compared to the healthy control group - No significant associations were found between participant status (CF or non-CF), sex, and coping mechanism. *Coping Strategies* - Partners with CF who used emotional-focused coping had more depressive and anxious symptoms and poorer marital adjustment. - For partners without CF, increased depression and anxiety levels were positively correlated with problem-focused and support-focused coping. - Participants with a more severe form of CF tended to use emotion- and problem-focused coping and search for social support coping strategies compared to participants with a milder form of CF.
7. Grieve AJ, Tluczek A, Racine-Gilles CN, Laxova A, Albers CA, Farrell PM. Associations between academic achievement and psychosocial variables in adolescents	Cross-sectional study of a longitudinal investigation To investigate the extent to which self-reported	*n* = 40 Ages 16-21 (*M* 18.6) Male *n* = 22 Female *n* = 18	Self-Efficacy subscale of the Resiliency Scales for Adolescents The Role-play Inventory of	<u>Seeking Alternative Rewards:</u> School-based coping	*Academic Performance* - Participants scored within the average range for cognitive functioning and arithmetic performance and generally performed well in school. *CF-related School Issues*

with cystic fibrosis. J Sch Health 2011 November;81(11):713-720.	psychosocial variables of depression, self-efficacy, school coping effectiveness, and attitude to school were associated with actual academic outcomes.	2 Midwest CF centers	Situations and Coping Strategies The Behavior Assessment for Children – 2nd Ed. Wide Range Achievement Test – 3rd Ed. Wechsler Abbreviated Scale of Intelligence		- Those with CF missed more school days (86.9% attendance rate) compared to their peers (92.7-93.3% attendance rate). More school absences were related to a lower GPA. - Scores were average for self-efficacy, attitude toward school, and depression. *Coping* - Positive feelings about abilities and school with few depressive symptoms were found - Mean score of 2.97 on the RISCS indicates somewhat effective coping strategies with CF-related school stressors. - An increase in depression scores were associated with more effective school coping strategies.
8. Grossoehme DH, Cole AG, Lewis K, Stamper SM, Teeters A, Joseph PM. Adults with cystic fibrosis: spiritual coping with lifelong disease. Journal of Health Care Chaplaincy 2020 Apr 2,;26(2):45-57.	Mixed-Methods To qualitatively describe how adults diagnosed with CF as children use spirituality to construct meaning and to	*n* = 58 Ages 20-54 (median age 29) Male 53% Adult CF center in the Midwestern US	International Physical Activity Questionnaire (IPAQ) World Health Organization Well-being	<u>Positive Reappraisal:</u> Optimism <u>Seeking Guidance and Support:</u> Spiritual (self-directed, active	Qualitative Themes - *Reframing CF as part of God's plan.* Adults diagnosed as children felt their disease was part of a Divine plan. Participants diagnosed as adults saw disease management as a collaboration between God, their treatment team, and self-care. - *Spiritual beliefs motivated healthy behaviors.* God's assistance was

	cope, to compare these qualitative results with how adults diagnosed with CF as adults described their use of spirituality in a prior study, and to determine the feasibility of collecting questionnaire and daily behavioral data in order to explore the impact of spiritual and psychosocial factors on adherence to prescribed pulmonary treatments in a subsequent, adequately powered study.		scale (WHO-5) Profile of Mood States (POMS) Brief spiritual coping (Brief R-COPE) Sanctification of the Body Treatment Utility Self-efficacy Perceived Behavioral Norms	surrender, deferral, collaborative, pleading) Hope	based on how well they were self-managing/caring for themselves. - *Church support mediated by relationships and material intervention.* Belonging to a congregation provided additional support. Quantitative Analysis - *Airway clearance:* - Treatment utility: Predicted by 3 forms of spiritual coping (self-directed, active surrender, and inversely by deferral). - Subjective norms: Predicted by age and inversely by active surrender coping. - Self-efficacy: Inversely predict by deferral coping and mood. - *Nebulized Medications:* - Treatment utility: Predicted by four methods of coping (positively by collaborative, pleading, self-directed coping, and negatively by deferral coping). - Subjective norms: Inversely influenced by collaborative coping and self-directed coping.

					- Self-efficacy: Inversely predicted by deferral spiritual coping. - *Exercise:* - Treatment utility: Predicted by collaborative coping and inversely by mood. - Subjective norms: Positively associated with increasing age and inversely predicted by self-directed coping and imbuing the body with sacred qualities.
9. Grossoehme DH, Ragsdale JR, Cotton S, Meyers MA, Clancy JP, Seid M, et al. Using spirituality after an adult CF diagnosis: cognitive reframing and adherence motivation. J Health Care Chaplain 2012;18(3-4):110-120.	Grounded Theory To determine whether persons diagnosed with CF as adults use spirituality to cope and influence disease management.	*n* = 12 Age in years, *M*(*SD*) 47(13) Female *n* = 10 Pediatric and Adult CF center in the Midwestern US	Single-occasion interviews	<u>Seeking Guidance and Support:</u> Spiritual	- Emergent theory: Those diagnosed later in life with CF related spirituality to health in terms of relationships between themselves, care team, and God. Supportive themes - *Spirituality guides the care of the body and treatment adherence.* Motivation for caring for themselves was found through faith. They believed that self-management was necessary for God's help. - *Adults coped with their adult CF diagnosis by making meaning.* Spiritual growth was related to ongoing personal development unrelated to CF. One participant

					reported a loss of previous faith after prayers for better health went unanswered. - Some participants stated their spiritual growth was unrelated to CF but instead their personal growth.
10. Hubbard PA, Broome ME, Antia LA. Pain, coping, and disability in adolescents and young adults with cystic fibrosis: a Web-based study. Pediatr Nurs 2005;31(2):82-86.	Cross-sectional To develop a web-based education program tailored to patients with CF who may be experiencing pain, and to investigate, via the website, the pain experiences of those patients by studying their pain reports, disability, and coping strategies.	*n* = 18 Ages = 33% less than 22 years, 67% greater than 23 Female *n* = 12 Male *n* = 5 No response *n* = 1 Online	Pain Disability Index Pain Coping Questionnaire	<u>Acceptance and Resignation:</u> Acceptance and self-encouragement. <u>Cognitive Avoidance or Denial:</u> Minimizing, self-isolation, and behavioral disengagement	*Coping for Pain and Disability* - Participants used a variety of coping strategies. - Active and accommodative strategies (problem-solving, acceptance, and self-encouragement) were reported most frequently. - Passive strategies (minimizing pain, self-isolation, and behavioral engagement) were reported the least. - No significant associations were found between pain and pain intensity, duration, or disability.
11. Macedo Cordeiro S, Pinto de Jesus, Maria Cristina, Evangelista Tavares R, Moura de Oliveira D, Barbosa	Qualitative social phenomenology To understand the experience of	*n* = 12 Age = *M* 26 years Male *n* = 6	Single-occasion interview	<u>Positive Reappraisal:</u> Positivity Optimism	Themes: - *Biopsychosocial impact of the disease on daily life* - Fatigue, performing activities of daily living, and treatment regimen

Merighi MA. Experience of adults with cystic fibrosis: a perspective based on social phenomenology. Rev Brasil Enfermagem 2018 November;71(6):2891-2898.	adults living with CF.	Female *n* = 6 CF Organization in São Paulo, Brazil		<u>Acceptance and Resignation:</u> Resilience Searching for ways to overcome limitations	makes it difficult to work, finish studies, have leisure time, and isolates them. - *Social prejudice as a source of embarrassment* - Feelings of shame and embarrassment due to coughing when in public. - Avoiding telling others about the disease. - *Coping strategies* - Try to not live for the illness/treatment and not let CF become the center of who they are. - Positivity, optimism, resilient, and searching for ways to overcome challenges were common among the participants. - Having support helps them to face difficulties.
12. McHugh R, McFeeters D, Boyda D, O'Neill S. Coping styles in adults with cystic fibrosis: implications for emotional and social quality of life. Psychol Health Med 2016;21(1):102-112.	Cross-sectional To examine which specific coping styles were positively or negatively associated with social and	*n* = 122 Ages 18-63 (*M* 29, *SD* 8.3) Female *n* = 86 Male *n* = 36	HRQOL: CFQ-R Brief COPE Scale	<u>Seeking Guidance and Support:</u> Religion <u>Taking Problem-Solving Action:</u>	*Coping and QOL Domains* - Emotional and social QOL domains had a negative association with distraction coping. - Increased substance use and disengagement were associated with decreased emotional QOL. - Greater religious coping, instrumental support, and acceptance

	emotional QOL in a CF sample.	Online support group		Instrumental Active coping <u>Emotional discharge:</u> Substance abuse Distraction <u>Cognitive Avoidance or Denial:</u> Disengagement <u>Acceptance and Resignation:</u> Acceptance	were positively associated with emotional QOL. -Social QOL was positively associated with active coping. -Active coping was associated to increased social QOL.
13. Mitmansgruber H, Smrekar U, Rabanser B, Beck T, Eder J, Ellemunter H. Psychological resilience and intolerance of uncertainty in coping with cystic fibrosis. J Cyst Fibrosis 2016;15(5):689-695.	Cross-sectional To explore associations of intolerance of uncertainty (IU) and resilience variables with QOL in CF patients and to investigate the relationship between IU and	*n* = 57 Ages 18-58 (*M* 28.49) Male 54.4% Female 45.6% OP CF clinic visits in Austria	HRQOL: CFQ-R Intolerance of Uncertainty Scale (IUS) Resilience Scale	<u>Acceptance and Resignation:</u> Resilience (personal competence and acceptance) Intolerance of uncertainty	*Resilience* - The majority of the CFQ-R domains were associated with resilience and some with IU. - Within the Resilience Scale, the personal competence subscale was the most consistently associated with CFQ-R scales. - The use of high subjective competence was associated with increased QOL. - Acceptance was associated to a lesser degree to QOL.

	the resilience variables importance in predicting QOL and patterns that shed light on processes in emotion regulation and coping with CF.				-During regression analysis, competence was shown to positively predict vitality, psychological well-being, health perception, and digestion. -During regression analysis, acceptance did not have any significant predictive power. - *Intolerance of uncertainty* (IU) - IU-related stress was negatively associated to QOL. - During regression analysis, IU scales did not offer much predictive power.
14. Taylor JL, Smith PJ, Babyak MA, Barbour KA, Hoffman BM, Sebring DL, et al. Coping and quality of life in patients awaiting lung transplantation. J Psychosom Res 2008 July;65(1):71-79.	Cross-sectional To examine the relation between coping and QOL and to determine whether this relation is affected by the nature of the lung disease. Of note, this study included participants with CF or chronic	*n* = 187 (CF *n* = 48) Age *M* 30.9 (*SE* 8.7) Female *n* = 32 Male *n* = 16 Patients listed for lung transplantation at Duke Medical Center and Washington University	Short Form-36 Health Survey: Mental and Physical Health Components Pulmonary-Specific Quality of Life Scale: Psychological and Physical Functioning Components	<u>Taking Problem-Solving Action:</u> Active coping <u>Cognitive Avoidance or Denial:</u> Disengagement	*Active Coping* - Increased active coping are positively related to better psychological QOL. - Active coping was not significantly related with physical QOL in the CF group but was for the COPD group. This finding suggests that how coping influences health may depend on the disease process and age of diagnosis. *Disengagement* - Higher levels of disengagement coping is negatively related to psychological QOL.

	obstructive pulmonary disease (COPD). Only the CF participant data is considered in this review.		Beck Depression Inventory II (BDI) Spielberger State and Trait Anxiety Inventory (STAI) General Health Questionnaire (GHQ) Perceived Stress Scale (PSS) Perceived Social Support Scale (PSSS) University of California, San Diego, Shortness of Breath		- Overall, CF participants waiting for lung transplant demonstrated higher psychological and physical QOL compared to the COPD participants. - The authors note the link between the younger age of participants with CF (compared to the older age of COPD participants), which may influence coping.

			Questionnaire (SOBQ) COPE Inventory		
15. Werner S, Hochman Y, Rosenne H, Kurtz S. Cooperation or Tension? Dyadic Coping in Cystic Fibrosis. Fam Process 2020.	Qualitative hermeneutic phenomenological approach To expand our knowledge of couple relationships in case of CF in adulthood, in particular, dyadic coping.	17 married Jewish couples *n* = 34 Age 25-69 (*M* 38.1) Two largest CF clinics in Israel	Couples were interviewed separately.	<u>Positive Reappraisal:</u> Optimism <u>Seeking Guidance and Support:</u> Hope <u>Taking Problem-Solving Action:</u> Cooperation Adaptive <u>Emotional Discharge:</u> Tension	- An overall pattern of cooperation was found between 11 couples but with recognized periods of tension and vulnerability. *Methods to improve dyadic coping strategies:* - Similar attitudes on illness on how it should be addressed - The CF patient is responsible for disease management - Division of roles - Optimism and hope - Focusing on present challenges - Communication - Mutual empathy (including understanding, validating, and caring) - Instrumental and emotional support - Marital growth - Many couples identified that aspects of the illness are downplayed so the disease 'does not take over'.

					- Optimism and hope were a focus of the coping process *Methods related to negative dyadic coping strategies:* - Themes found among these couples included: - Discrepancy in illness perception and coping mechanisms - Perceptions that CF is disruptive - Inability to see each other's needs and communicate - Inability to provide each other with support

Manuscript 3

The Experience of Social Isolation in Adults with Cystic Fibrosis: Results of a Mixed-Methods Feasibility Study

Abstract

Background: Adults with cystic fibrosis face unique challenges that potentially contribute to increased risk for social isolation, including complex treatment regimens, fatigue, pulmonary exacerbations, and infection control guidelines limiting face-to-face interactions with others with cystic fibrosis. Social isolation is associated with detrimental health outcomes, yet has not been explored in this population. This study aims to explore the feasibility of a mixed-methods approach to gain a preliminary description of if, and how, this population experiences objective and subjective social isolation using Cornwell and Waite's Model of Social Isolation. ***Methods:*** Participants were recruited from a large Southeast academic medical center adult cystic fibrosis clinic. Quantitative data on demographics, health information, objective and subjective social isolation, effects related to COVID-19, and cystic fibrosis health-related quality of life outcomes were collected via an online survey. Qualitative interviews elicited a deeper exploration into feelings of isolation, social support, and COVID-19-related effects. Quantitative and qualitative data were collected and analyzed separately and then triangulated for a robust picture of social isolation. ***Results:*** This study found the methodology feasible for future studies and elicited ways to improve future work. As a whole, this sample had adequate support systems in place, reported low levels of social isolation, and did not experience negative COVID-19-related effects. Preliminary data reveals potential predictors of social isolation, including sex, martial/relationship status, social network size, and cystic-fibrosis health-related quality of life outcomes.

Conclusion: This study provides a preliminary insight into social isolation in adults with cystic fibrosis. The mixed-methods approach is feasible for future work, which is warranted to confirm findings of this study and explore social isolation in a more diverse sample size.

Introduction

As recently as the 1980s, infants diagnosed with cystic fibrosis (CF) rarely survived into adulthood.[1] Advancements in therapies have since increased life expectancy dramatically; more than half of the CF population are adults (≥ 18 years) with a median predicated age of survival of 46 years for those born with CF between 2015 and 2019.[1-3] Despite these advances, CF remains a progressive disease that results in impaired airway clearance, respiratory infections, digestive dysfunction, fatigue, activity intolerance, and a higher incidence of psychological illness.[1,4,5] With this increased longevity, adults with CF now have a longer lifetime to navigate diverse symptoms and complex, time-consuming regimens that may take 2-4 hours a day.[6,7] CF-related symptoms, treatments, multiple hospitalizations, and infection control guidelines limiting face-to-face interactions between people diagnosed with CF may limit the ability to socialize.[8] Additionally, beginning in the Spring of 2020, social distancing guidelines resulting from the SARS-CoV-2 (COVID-19) pandemic further limit the potential for socialization.[9] This limitation potentially decreases social support received from the support network.

Social support is a broad concept that includes the amount and quality of support and resources an individual receives from others, as well as having people to talk to (definition adapted from Flewelling et al. and Sherbourne).[10,11] While social support may act as a protective health factor, potentially mitigating symptoms of CF, the lack of support may have the opposite effect, causing social isolation (SoI).[12] SoI can result from loneliness, disconnectedness, or physical separation from others and is associated with detrimental health effects.[13-15] Grim evidence on SoI among older adults reveals it is as comparable to risks noted in detrimental health behaviors, such as cigarette smoking

dangerous and obesity, causing an increase in morbidity and mortality, cardiovascular disease, neuroendocrine dysfunction, inflammatory regulation, and adult clustered risk factors (i.e. hypertension, increased body mass index, and hyperlipidemia).[13-18]

Theoretical Framework

SoI is a multidimensional concept that exemplifies various properties, from feelings of isolation or loneliness to a reduced social support network. The literature frequently describes two elements of SoI: objective and subjective.[19] Objective SoI includes the number, frequency, and quality of social contacts, whereas subjective SoI refers to individual feelings of isolation from others or loneliness from a lack of social needs being met.[19] The conceptual model of SoI presented by Cornwell and Waite (Figure 1) was used to guide this study. This model approaches SoI using the aforementioned objective and subjective dimensions. Cornwell and Waite refer to objective SoI as social disconnectedness from a limited number and frequency of social network contacts and/or a decreased ability to participate in social activities.[19] Subjective SoI refers to individual feelings of perceived isolation, including feelings of loneliness and lack of support.[19]

To our knowledge, Cornwell and Waite's model has not been used to explore the CF population. However, its use among older adults[19] and after spinal cord injury (SCI)[20] demonstrates an appropriate fit for this study, as it will provide a description of objective and subjective SoI as experienced by adults with CF and provide preliminary data about the relationship between these interconnected concepts.

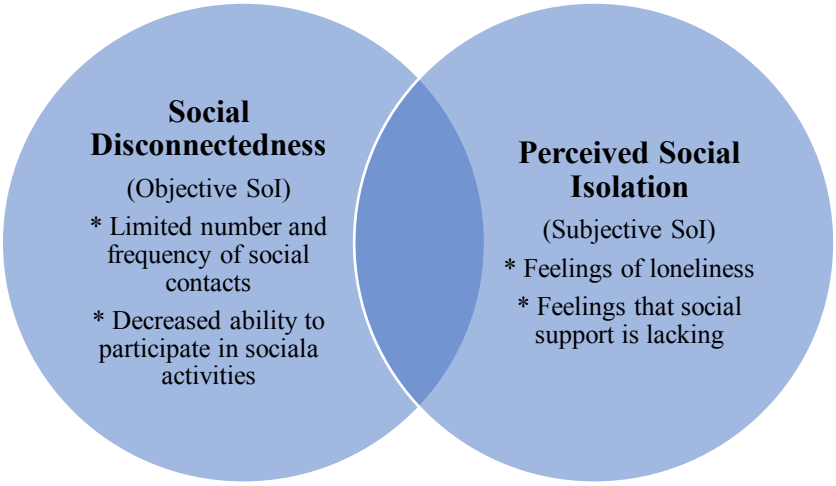


Figure 1. Cornwell and Waite's Model of Social Isolation[20]

Current Study Aims

While evidence on the effects of SoI is rapidly emerging in the literature, SoI in adults with CF has received little attention. Given the unique needs of this population, it is worthwhile to understand how this population experiences SoI. This knowledge may translate to the identification of those at high risk for SoI and guide future interventions specific to the challenges faced by adults with CF. Therefore, the main goals of this study were to 1) To evaluate the process and resources of the proposed study methodology using Tickle-Degnen's feasibility model[21] in preparation for future large-scale studies of SoI in adults with CF and 2) To develop a preliminary characterization of SoI in adults with CF using a parallel convergent mixed methods approach[22] by a) measuring objective and subjective SoI, b) identifying preliminary signals of predictors to objective SoI, subjective SoI, c) elucidating experiences and perceptions of objective and subjective SoI, and d) comparing and contrasting the relationship between objective and subjective isolation.

Methods

Ethics approval

Approval was obtained from the Institutional Review Board (IRB) at the Medical University of South Carolina. This study was eligible and approved for a waiver of signed consent. A statement of research was provided to all potential participants who accessed the survey link. Only study personnel listed on the IRB form had access to data. Data was deidentified to maintain confidentiality of participants.

Design

A convergent parallel mixed-methods research (MMR) design was used to gain a preliminary understanding of the feasibility of implementing research with this population to inform future studies, and generate a preliminary characterization of objective and subjective SoI in adults with CF.[22] This design facilitated the independent collection and analysis of quantitative and qualitative data concurrently, allowing for the consequent merging and triangulation of results for collective interpretation.[22]

Participants and Recruitment

A total of 153 participants were recruited using convenience sample through an adult CF clinic. To be eligible, individuals were required to be 18 years of age or older with a confirmed diagnosis of CF, have internet access for online survey completion, and have the ability to read and speak English. Individuals completed a self-screening questionnaire at the beginning of the survey. Potential participants on the clinic's email listserv were sent an email by a clinic provider, which included a letter explaining the purpose of the study and link to the study survey. Additionally, potential participants were provided with a study letter by clinic personnel during in-person clinic visits. Our goal was to recruit 50% of participants receiving recruitment materials for the study.

Data Collection

Following consent, participants completed an online REDCap[23] survey that included measures of feasibility, demographic and clinical characteristics, validated measures for subjective and objective social isolation, a validated CF-specific quality of life (QOL) measure, and COVID-19-related questions. Within the survey, participants had the option to indicate if they were interested in participating in a subsequent interview for the current study within the survey. A descriptive qualitative approach was used to develop the interview guide (Table 1), which elicited perceptions of SoI and social support in relation to CF.

Measures

Feasibility Measures. Feasibility measures were guided by Tickle-Degnen's feasibility model.[21] To evaluate feasibility of study processes, recruitment and drop-out rates were monitored, and participants were queried about interest in future similar studies through the survey. During qualitative interviews, data were collected regarding participants' perceptions of how well the study adequately captured the experience of the adult with CF. To evaluate feasibility of study resources, data was collected on the length of time to complete the interview to assess time commitment.

Demographic and Clinical Characteristics. Demographic information consisted of age, sex, race/ethnicity, marital/relationship status, education level, work status, insurance status, and zip code. Zip code was used to determine metropolitan and non-metropolitan status was based on the 2013 Vital and Health Statistics Urban-Rural Classification Scheme.[24] Clinical characteristics included forced expiratory volume (FEV_1), oxygen use, transmembrane conductance regulator (CFTR) medication use, number of CF-related

hospitalizations in the past year, and if they had a history of lung transplantation status or were on the lung transplant list.

PROMIS Social Isolation Short Form 8a (subjective isolation). The PROMIS SoI scale measures subjective SoI, such as feelings of being avoided or excluded, along with feeling disconnected or detached from others.[25] This is an 8-item scale instrument derived from the original 14-item scale; each question has a 5-point Likert scale rating from never to always. Instrument scores are converted to T-scores using the PROMIS measure-specific scoring guide.[26] T-scores range from 33.9 – 76.9, with higher scores indicating increased SoI.[26] The original 14-item scale indicates an average score is 50 when tested in the general population; however, the PROMIS SoI short form instrument's average score of 50 is from a population more representative of people with chronic health issues.[26] The original 14-item PROMIS SoI scale has a construct validity effect size of 0.45 (p <0.001) and a confirmatory factor analysis model fit of 0.99.[27] The instrument used for this study has a strong correlation (α = <0.95) with the original full item bank.[27]

Lubben Social Network Scale – Revised (objective isolation). The LSNS-R is a 12-item instrument updated from the original 10-item scale and measures one's social network, including that of family, friends, and neighbors.[28] Answers are on a 5-point Likert scale with varying responses per question. Scores range from 0-60, with higher scores representing broader social networks, indicating less objective SoI. Participants scoring under 20 are at high risk for SoI due to a limited social network.[28] The LSNS-R has a strong internal consistency (α = 0.78) and a correlation of 0.68 with the original LSNS.[28] While this instrument has not been validated in a population outside of older adults, it was selected due to its ability to capture objective SoI.

Cystic Fibrosis Questionnaire – Revised (CFQ-R). The CFQ-R is a CF-specific measure that assesses HRQOL in the following 12 domains: physical function, vitality, emotional functioning, eating problems, treatment burden, health perceptions, social functioning, body image, role perceptions, weight, respiratory symptoms, and digestive symptoms.[29] This instrument contains 50 questions with a variety of formats. For each domain, scores range from 0-100, with lower scores indicating poorer QOL.[29] Psychometric evaluation demonstrates appropriate reliability for each domain, ranging from $\alpha = 0.51$ (treatment burden) to $\alpha = 0.94$ (physical functioning), with $\alpha = 0.88$ for all scales.[29]

COVID-19 Impacts. Due to the novelty of COVID-19 at the time of study, there were limited instruments assessing potential COVID-19 impacts to consider for this population. We used questions from two different newly developed instruments: 1) From the COVID-19 Community Response Social Distancing Impact Survey we selected two questions: *"How many relatives or friends do you see or hear from at least once a month?"* and *"How often do you see or hear from the relative or friends with whom you have the most contact?"*[30] The questions were taken from the LSNS-R scale, therefore, it was fitting to use these questions to assess COVID-19 effects on SoI, and 2) From the Osteoporotic Fractures in Men (MROS) COVID-19 Social Impact Questionnaire we selected one question: *"Who is providing you with social support during the outbreak?"*[31] Additionally, we developed a question assessing the severity of COVID-19's effects on the ability to socialize and interact with others: *"Has the coronavirus (COVID-19) pandemic had a significant impact on your ability to socialize or interact with others?"*

Qualitative Interviews

Qualitative description methodology guided collection and analysis of qualitative data. Participants were read a statement of research outlining the purpose and risks of participating in the interview (Appendix A). The interview protocol contained six questions (Table 1) that were designed to facilitate dialogue about experiences regarding social support and SoI. Interviews were semi-structured; therefore, questions and prompts were modified based on participant responses to elicit further understanding of experiences of social support and SoI. The last question prompted participants' thoughts regarding the appropriateness of the survey and interview questions for feasibility data and future study improvement. All interviews were conducted via phone and audio recorded. A third-party transcription service (Rev)[32] was utilized and all transcripts were checked for accuracy by the primary investigator.

Table 1. Interview Questions

1) What does socialization and the ability to interact with others you care about mean to you?
2) Tell me what it is like to live with cystic fibrosis, in terms of how it affects your relationships, social life, and ability to interact with those who you care about.
3) Tell me about your support system.
4) Tell me about your relationship with the cystic fibrosis community.
5) Tell me about how the COVID-19 pandemic has affected your ability to socialize and spend time with those you care about?
6) Post-interview: How well do you feel the survey and the interview appropriately captured your experience as an adult with CF?

Quantitative Analysis

The final data set was checked for missing data; incomplete surveys were excluded. Scores were manually calculated for LSNS-R.[28] PROMIS SoI scores were calculated manually and converted to t-scores.[26] CFQ-R scores were calculated using a

validated online scoring application.[33] All statistical data was computed using IBM SPSS (v25) statistical software.[34]

Descriptive statistics were obtained for survey-related feasibility data (interest in future studies, willingness to participate in an interview), demographic, clinical data, and COVID-19-related questions. Categorical data was examined using frequencies. Mean, median, standard deviations, and interquartile ranges (where appropriate) were calculated for continuous variables. Continuous data was examined for normality. Due to non-normality of data and a small sample size (n = 34), appropriate non-parametric tests were utilized. Relationships between subjective SoI, objective SoI, age, and CFQ-R domains were explored using Spearman's rho with 95% confidence intervals. The mean, standard deviation, median, and interquartile ranges were calculated for subjective (PROMIS-SoI) and objective (LSNS-R) SoI scores and for each of the CFQ-R domains. Differences between sex, marital/relationship status, work status, insurance status, geographic area, oxygen use, lung transplant status, and who is providing social support during COVID-19 were compared with Mann-Whitney U testing. Education level, FEV_1, taking a CFTR, number of hospitalizations over the past year, the number of relatives, friends, or neighbors the participant sees/hears from at least once a month during COVID-19, and the frequency of seeing/hearing others during COVID-19 were compared using Kruskal-Wallis H testing. Alpha was set at $p = 0.05$ to determine significance.

Qualitative Analysis

Interviews were conducted until data saturation was reached (n = 17). Qualitative analysis of interview data using inductive content analysis was done through manual coding.[33] The investigator checked every transcript for accuracy by listening to each

recording and comparing to the transcript. Any inconsistencies were corrected. Interviews were coded line-by-line and analyzed for significant words and statements, which were then condensed to smaller statements. A codebook was developed for consistency in theme development (Appendix B). These condensed statements were transferred to a spreadsheet to determine commonalities that assisted in the development of major themes and sub-themes. Qualitative experts reviewed these themes for consistency and accuracy.

Mixed-Methods Analysis

Quantitative and qualitative data were collected and analyzed individually for preliminary data pertaining to SoI. An MMR design was utilized to deliver an initial description and understanding of how SoI presents in adults with CF. To accomplish the merging of quantitative and qualitative data, data streams were collected using a parallel approach, allowing for two distinct dimensions of SoI to be analyzed for an in-depth examination (Figure 2).[22] The goal of this approach was to develop a complex understanding of SoI. Quantitative and qualitative data were collected concurrently throughout the study yet analyzed independently. Quantitative data provided a description of SoI among the participants through the use of the survey results; qualitative data provided deeper explorations through interviews that either converged or diverged with the quantitative data. Experts reviewed the merging of data streams for consistency and accuracy.

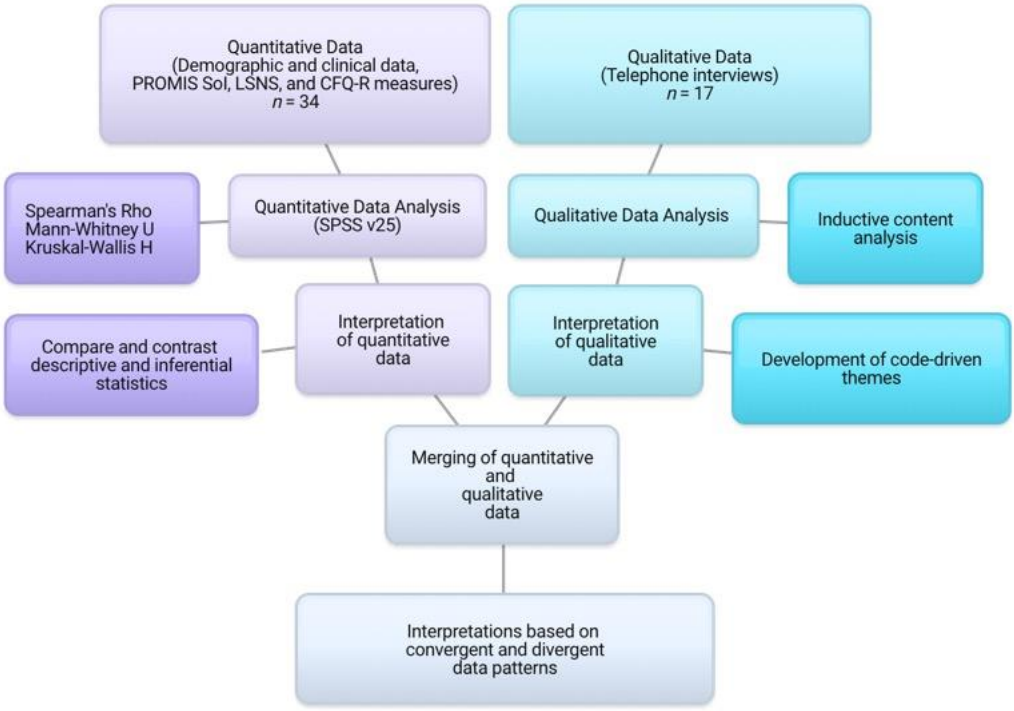


Figure 2 Mixed-Methods Analysis

Results

Sample

Potential participants (n = 153) received the recruitment letter and survey link through the CF clinic listserv, which was sent out three times over a 5-week period. Individuals were also approached during clinic visits and provided with study information by clinic personnel. 46 individuals were initially enrolled in the study with a total of 34 completing the study (22.2% of the potential patients receiving the online survey via email); demographics are presented in Table 2. The majority of participants were female (73.5%), White (94.1%), married or with a partner (61.8%), had a college degree (32.4%), were employed (55.9%), had private/employer insurance (70.6), and lived in metropolitan areas (85.3%). The majority appeared clinically stable, with an FEV_1 range of 70-90% being the most common (35.3%), did not require oxygen (94.1%), were taking a CFTR modulator medication (73.5%), the majority not requiring a CF-

related hospitalization over the past year (55.9%) or having a lung transplant (91.2%). More detail is provided in Table 2.

Table 2. Demographic and clinical characteristics of participants (*n* = 34)	
Demographics	
Age (years), mean (*SD*)[1]	35.3(10.42)
Sex[2], *n*(%)	
Female	25(73.5)
Race, *n*(%)	
White	32(94.1)
Prefer not to answer	2(5.9)
Marital status, *n*(%)	
Not married or not with a partner	13(38.2)
Married or with a partner	21(61.8)
Educational Attainment, *n*(%)	
High school/GED or less	5(14.7)
Some college	8(23.5)
College degree	11(32.4)
Professional or graduate degree	10(29.4)
Employment, *n*(%)	
Not working full or part time	15(44.1)
Working full or part time	19(55.9)
Insurance status, *n*(%)	
Medicaid/Medicare	10(29.4)
Private/Employer Insurance	24(70.6)
County type[3], *n*(%)	
Non-metropolitan	4(11.8)
Metropolitan	29(85.3)
Clinical Characteristics	
FEV_1[4], *n*(%)	
>90%	5(14.7)
70-90%	12(35.3)
40-69%	9(29.0)
<40%	3(8.8)
Do not know	2(5.9)
Uses oxygen[5], *n*(%)	
No	32(94.1)
Taking a CFRT medication, *n*(%)	
No	7(20.6)
Yes	25(73.5)
Does not know	2(5.9)
Number of inpatient hospitalizations related to CF in the past year, *n*(%)	
0	19(55.9)
1-3	10(29.4)
4-6	1(2.9)
7-9	1(2.9)
10 or more	1(2.9)
Does not know	2(5.9)
Has had a lung transplant, *n*(%)	
No	31(91.2)
On lung transplant list, *n*(%)	

No	31(91.2)
1 – 1 participant did not provide age 2 – 1 participant did not provide sex 3 – Unable to determine county type of 1 participant 4 – 3 participants did not provide FEV_1 5 – 2 participants did not provide oxygen use	

Feasibility Measures

For resource assessment, a total of 46 participants accessed the survey, however, 12 participants either opened the survey without answering questions (n = 7) or did not complete the survey (n = 5), leaving a total of 34 participants enrolled in the study. With a recruitment rate of 22.2%, we did not meet the recruitment goal of 50%. To recruit for the qualitative portion, participants selected an option to indicate interest in participating in a subsequent interview. Twenty-seven (79.4%) of the 34 participants expressed willingness to take part in the interview portion. Two of the participants that agreed to an interview could not be reached to schedule a time and two did not answer the phone at the scheduled interview time. Depending on the participants' preferred contact method, these participants were either called or emailed two additional times without success. Thirty-two (94.1%) indicated an interest in participating in future similar studies. All interview participants felt the survey and interview questions captured their experience as an adult with CF but provided recommendations for future studies, including assessment of emotional state and mindset, coping strategies, difficulties with romantic relationships, questions to help pinpoint origins of feelings of SoI, and family dynamics. For resource assessment, the mean(*SD*) interview time was 29.6(10.5) minutes with a range of 15 – 53 minutes.

Subjective and Objective Social Isolation Scores

Nine (26%) participants had PROMIS SoI scores over 50, indicating higher levels of subjective SoI compared to others with chronic illness; scores ranged from 33.9 – 76.9,

with a mean(*SD*) of 45.5(11.2). Two (6%) participants had LSNS-R scores under 20, indicating a high risk for SoI and a poor support system; scores ranged from 8 – 55, with a mean(*SD*) of 38.2(11.2). Additional details are reported in Table 3. Spearman's rank-order correlation assessed the relationship between subjective isolation (PROMIS SoI) and objective isolation (LSNS-R) scores. There was a statistically significant negative correlation between subjective isolation scores and objective isolation scores ($r_s(32) = -.65$, $p = <.001$) (Table 4).

Table 3. Mean Instrument Scores ($n = 34$)		*IQ Range*		
	M(*SD*)	25%	50%/Median	75%
PROMIS SoI (Subjective SoI)	45.5 (11.2)	33.9	44.4	53.1
LSNS-R (Objective SoI)	38.2 (11.2)	31	38	47.5
CFQ-R domains				
Physical	72.2 (28.6)	40.6	85.4	95.8
Vitality	61 (21.7)	41.7	66.7	75
Emotion	73.3 (20.8)	60	80	86.7
Eat	87.9 (19.2)	77.8	100	100
Treatment burden	76.1 (22.1)	63.9	77.8	100
Health perception	72.5 (24.8)	52.8	77.8	100
Social[1]	62.8 (21.6)	41.7	66.7	77.8
Body image	75.5 (21.3)	55.6	77.8	91.7
Role	80.9 (24)	66.7	91.7	100
Weight	81.4 (35)	66.7	100	100
Respiratory	81.9 (19)	72.2	86.1	100
Digestive	73.9 (22.4)	66.7	77.8	88.9
1 – Unable to score 1 participant's social domain due to missing data				

Preliminary Signals of SoI Predictors

Mann-Whitney U tests were performed to determine differences between subjective and objective SoI scores across sex, marital status, work status, insurance status, metropolitan/non-metropolitan status, oxygen use, lung transplant status, and COVID-19 support (Appendix C). All values are reported as medians. PROMIS SoI scores were significantly higher in those who were not married or with a partner (50) than those who were married or with a partner (43.1), (U 72.5, $p = .022$). LSNS-R scores were

significantly higher in females (43) than in males (28), (U 167.5, p = .003); among those who had support from relatives, friends, or neighbors coming by their place during COVID-19 (46.5) compared to those who did not (35), (U 191, p = .006); and in those who had a relative, friend, or neighbor they could talk with on the phone during COVID-19 (46) compared to those who did not (36), (U 201, p = .022).

To tests for differences among subjective and objective SoI scores between groups for education, FEV_1, use of CFTRs, number of CF-related hospitalizations over the past year, COVID-19 family support, how many people the participant sees and hears from during COVID-19, and COVID-19 impact, Kruskal-Wallis H tests were conducted (Appendix D). For how often do you see/hear from others during COVID-19 and PROMIS SoI scores, frequency distributions were significantly different between groups (less than monthly [n = 2], monthly [n = 1], weekly [n = 9], few times a week [n = 7], and daily [n = 14]), $H(4) = 10.3$, p = .036. Post-hoc testing shows significant differences between the few times a week (33.9) and less than monthly (71.6) groups (p .043). Differences were also noted for LSNS-R scores ($H(4) = 12.0$, p = .017) but no significant pairwise comparisons were found. Frequency distributions of LSNS-R scores were statistically different among how many family members the participant is receiving support from during COVID-19 (none [n = 2], 2 [n = 1], 3-4 [n = 14], 5-8 [n = 12], 9 or more [5]), $H(4) = 10.5$, p = .033, with pairwise comparisons reporting significances between the none (13) and 5-8 persons (44.5) groups (p = .009) and the none (13) and nine or more persons (47) groups (p .010).

Spearman's rank-order correlations were used to explore potential preliminary signals of relationships between subjective SoI, objective SoI, and CFQ-R scores (Table

4). There was a statistically significant negative correlation signal between PROMIS-SoI scores and the following CFQ-R domains: physical ($r_s(34) = -.40$, $p = .021$), emotion ($r_s(34) = -.61$, $p = <.001$), treatment burden ($r_s(34) = -.40$, $p = .020$), health ($r_s(34) = -.52$, $p = .002$), social ($r_s(33) = -.53$, $p = .001$), body ($r_s(34) = -.44$, $p = .009$), and role ($r_s(34) = -.56$, $p = .001$). A significantly positive correlation signal was found between LSNS-R scores and the CFQ-R emotion domain ($r_s(34) = .39$, $p = .024$).

Table 4. Spearman's rho (r_s) correlations ($n = 34$)

	PROMIS SoI		LSNS-R	
	r_s(95% CI)	*P value*	r_s(95% CI)	*P value*
PROMIS SoI	-	-	-.65(-.81/-.40)	<.001
LSNS-R	-.65(-.81/-.40)	<.001	-	-
Age[1]	-.07(-.40/.28)	.709	.07(-.28/.40)	.717
CFQ-R Domains				
Physical	-.40(-.65/-.07)	.021	.15(-.20/.46)	.406
Vitality	-.23(-.53/.117)	.186	.04(-.30/.37)	.837
Emotion	-.61(-.79/-.34)	<.001	.39(.06/.64)	.024
Eat	-.27(-5.6/.08)	.129	.28(-.06/.56)	.112
Treatment	-.40(-.65/-.07)	.020	.17(-.18/.48)	.326
Health	-.52(-.73/-.22)	.002	.29(-.05/.57)	.099
Social[2]	-.53(-.74/-.23)	.001	.32(-/03/.60)	.074
Body	-.44(-.68/-.12)	.009	.32(-.02/.59)	.065
Role	-.56(-.76/-.27)	.001	.19(-.16/.50)	.285
Weight	-.10(-.42/.25)	.756	.09(-.26/.42)	.609
Respiratory	-.32(-.59/.02)	.063	.12(-.23/.44)	.517
GI	-.26(-.55/.09)	.140	.14(-.21/.46)	.424

1. One participant is missing age.
2. One participant is missing social domain score due to missing data.

Qualitative Description of SoI Among Adults with CF

Five main themes were elicited from the qualitative portion of this study: the importance of socialization and social support, the effect of CF on socialization, feelings of isolation, importance of CF-specific support, and COVID-19-related socialization and support. Definitions of qualitative themes can be found in Appendix B.

Theme #1: The importance of socialization and social support

Socialization. The majority of participants ($n = 16$ [94%]) discussed the importance of socialization. A variety of activities were considered within the construct

of ‘socializing’: hanging out with friends and/or family, face-to-face, virtual, and mobile communication, participating in church, going to parties, networking, entertaining, having meals with others, and interacting with others. Only one participant did not feel socialization was important but stated it is because he considers himself a homebody. Socialization was highly valued by the other 16 participants.

- *“I feel like we were created to interact with others and have friends and have family.”* – 32-year-old female with CF
- *“It's* [socialization] *very high on my list of priorities in terms of being able to have what I call normal interactions.”* – Adult female of unknown age with CF
- *“It* [socialization] *means a lot. It just kind of helps life go by smoother.”* – 57-year-old male with CF
- *“Well, the interaction with others helps me mentally to feel positive, to feel like a part of the group and a part of the world and a part of humanity. CF can certainly make you feel like a non-human at times and having friends and getting together with people and doing things and doing quote-unquote typical, normal activity makes me feel good about myself and good about the things that I'm able to accomplish.”* – 50-year female with CF

Social Support. Participants reported the importance of receiving social support from their family, spouse or significant other, friends, children, the CF care team, and CF support groups. All participants (100%) spoke about receiving social support, which included others being available and dependable, others understanding CF and related symptoms, others being protective of the participant’s health, the feeling of being able to

confide in someone, receiving encouragement from others, having others remain involved in their CF care, and not feeling embarrassed about CF-related symptoms among members of their support team. While participants reported having a positive support system in place, some reported negative experiences within the support system as well. These included the perception of a lack of concern from others, members of their support system making negative comments about the participant's body or health, having no local support, or feeling there was dysfunction within their support system. Overall, social support was an important aspect of the participants' lives.

- *"Thankfully, I found someone who does* [accepts her for who she is] *and supports me in whatever I do and everything, and goes to appointments with me and helps me with my meds and all that good stuff."* – 24-year-old female with CF
- *"I mean, because socialization is a big part of having CF, because, if you don't have a support system (...) there's not really more of a reason to take care of yourself and make sure that you're healthy. Because sometimes you feel like, "Well, what's the point?"* – 28-year-old female with CF
- *"My sister (...) doesn't communicate or show any concern with my CF, or getting to know what I've experienced."* – 54-year-old female with CF

Theme #2: The effect of CF on socialization

The majority of participants (*n* = 13 [76%]) reported some form of CF-related socialization challenges, such as interference due to treatment regimens, fatigue, difficulty making friends, fear of catching illnesses from others, environmental factors (i.e. cigarette smoke, air quality) and anxiety about going out. Of these, three (18%)

reported that challenges and interferences with socialization decreased with age as a result of becoming more comfortable and verbal about limitations.

- *"I didn't have the typical social interactions with girls and I had to learn that typical middle school social interaction in my 40s because if you don't learn it then, you get to learn it later in life, at least that's what I've found. And so, I was very delayed socially, but I made up for it in college."* – 50-year-old female with CF

Participants that expressed little (n = 6 [35%]) or no (n = 4 [24%]) CF-related social interference tended to verbalize they had milder disease or minimal symptoms and/or treatments.

- *"So, my CF is extremely mild, so it really hasn't had any effect on being able to socialize with people."* – 29-year-old female with CF

Participants reported embarrassment from CF-related symptoms, such as coughing, sputum production, and malodorous bowel movements. Reports of CF's interference with socialization ranged from not changing their socialization patterns to having significant effects on their socialization, with many participants describing detailed accounts of their challenges related to socialization.

- *"I just was coughing up stuff all the time. And I felt very insecure being around others because I know when I hear someone, you know, make a productive cough, it grosses me out and I don't want to be around that, so that fact that I was doing that all the time it's made me feel like not wanting to be in a social setting during that time."* – 32-year-old female with CF

- *"A girl who I was in school with (…), her family knew that I had CF and her dad said something to her at one point about being cautious about not becoming too close friends with me because I was likely to die and he didn't want her to have to cope with the loss of a friend."* – Adult female of unknown age with CF
- *"I get bad anxiety* [when planning an outing]. *Usually I just cancel before I even can tell if something's legitimately wrong because I think (…) "Okay, what if something happens or I can't hang out that long?" (…) It's really, really hard."* – 29-year-old female with CF
- *"Sometimes I just feel like I hardly have the energy to do anything, so being out for more than about 30 minutes is really weary on me."* – 24-year-old female with CF

Theme #3: Feelings of Isolation

Three subthemes were noted under the theme 'Feelings of Isolation.' These include SoI resulting from CF, a lack of understanding from others regarding CF symptoms and the limited ability to participate in social activities, and invisible illness from participants expressing that others do not understand they may feel sick because they do not outwardly appear ill.

Subtheme: Social isolation resulting from CF

For some adults with CF (n = 6 [35%]), feelings of SoI were present as a result of not being able to reach out to others or having a small support system, infection control guidelines in place for people with CF, being hospitalized without visitors, being the only person in the family with CF, not being able to participate in activities due to CF, and the

perception that others were inconsiderate or not understanding. Some participants denied feeling isolated from others and attributed this to positive thinking and/or large support systems (including CF-specific support systems); others described that feelings of isolation improved as they got older.

- *"It was very, very isolating* [having CF]. *I did not know a single person with CF growing up, and I still don't really personally know anybody with CF."* – Adult female of unknown age with CF
- *"Kind of hard to explain because I'm just so used to it* [feeling isolated]. *It doesn't strike me as odd or abnormal. But yes, it's very lonely anyway. Especially if you're the only person in the family that has it* [CF]*."* – 32-year-old male with CF
- *"I would say that when I was a child, I felt extremely isolated. As an adult, I have not felt as isolated. As a married person, before I had a child, I felt very isolated. But having a child really didn't help me to bond with other people in my age and my stage of life, so there's times I have felt isolated (…) But in general, I don't as much anymore."* – 50-year-old female with CF

Subtheme: Lack of understanding from others

Participants often perceived a lack of or unwillingness of others to understand multiple aspects of CF (n = 8 [47%]), including the disease process, symptoms such as fatigue or coughing, treatment regimens, and how dangerous a simple viral infection can be for them. Participants spoke to how frustrating this lack of understanding could be:

- *"They don't understand why I can't walk as fast as them or do certain things."* – 24-year-old female with CF

- *"Well I feel like with my family it's definitely a challenge because I have two sisters and they don't have CF. I think it's hard to get them to understand when I don't have energy or the time that I do have energy just how much that time means to me to actually hang out and socialize and interact. I guess with my friends it's kind of the same concept."* – 29-year-old female with CF.
- *"But they don't always understand I think, that being in that large of a crowd, isn't always the best for me."* – 32-year-old male with CF

Subtheme: Invisible Illness

Some (*n* = 5 [29%]) participants felt as if others did not see them as ill because they do not physically appear ill ("invisible illness"). These feelings have caused withdrawal of the person with CF or feeling as if they could not express how they are feeling to loved ones. Looking physically healthy has led to misunderstandings or unrealistic expectations for the participants:

- *"Yeah, I feel like I have to have oxygen or wear a mask or not put myself together for people to realize like, this is how I feel."* – 29-year-old female with CF
- *"You know, sometimes there's things I can't do, and if you saw me, I do not look sick at all. I do not look like anything anybody would look like that's sick and that's hard for people to comprehend, but at the same time, I can do other things, but I can't do that, and that's also hard for people to understand. (...) I mean, people just don't understand."* – 50-year-old female with CF
- *"I don't look sick therefore, I must have the same energy level as they do."* – 54-year-old female with CF

Theme 4: Importance of CF-Specific Support

The majority of participants (*n* = 13 [76%]) were involved in some form of CF-specific support group, either from an online support forum or social media (SM) platform. Participants found the support group or SM sites comforting because they were able to connect with others who they felt could relate to them and understood the challenges from CF, so they did not feel as alone and found the experience to be uplifting and encouraging.

- *"Whenever your health has declined, like when there are health issues I think that it is helpful to have support* [from others with CF] *when you need it."* – 32-year-old female with CF.
- *"Seeing and finding other people* [with CF] *and following their pages and just seeing their experience and feeling like there's some degree of community around it and it's not quite so isolating."* – Adult female of unknown age with CF
- *"I do think it helps having somebody who knows exactly how you feel. Who has the same symptoms, and the same problems, because if you don't really go through it, you don't really understand."* – 46-year-old female with CF

Two participants stated they had undesirable experiences on the SM sites due to negativity, foul language, harassment, and bullying, but the majority reported positive experiences. A small number of participants (*n* = 4 [24%]) no longer used the support groups or never have accessed them.

- *"There are a few people that just make you want to get off of it* [online CF-specific support group]. *They're very negative. They use the worst language.*

They make jokes of serious issues, things like that." – 46-year-old female with CF

Theme 5: COVID-19-related socialization and support

While almost half of the participants (*n* = 8 [47%]) reported negative effects on their social lives from COVID-19, the majority (*n* = 9 [53%]) reported either no or minimal change or felt neutral toward how COVID-19 has changed their socialization. No participants reported changes in support, but some noted the means of receiving support changed (i.e.changing to video chats versus in-person support). Negative effects reported included feeling isolated or feeling cut off from socialization, missing face-to-face interactions with family and friends, concern about children having to isolate from friends, increase in depression or anxiety, feeling scared, frustration with others not wearing masks, and feeling stuck at home.

- *"Post-COVID it's been kind of depressing, because we have all been trying to stay away from each other, just because my sister and I do have CF."* – 46-year-old female with CF
- *"I was wanting to actually go out and do more things. I felt like I wanted to really push myself socially since I do have bad anxiety. Even being in a relationship, just actually wanting to go out with him whether it's simple, just like going to dinner somewhere and sitting or going to a movie or whatever. Just being outside and I definitely can't do that now so that's been, kind of it feels almost really not fair because I have to stay isolated."* – 29-year-old female with CF

- *"It's scary. I definitely want to go out and do something, but the moment I see people aren't wearing masks, or there's a stranger being really close, I feel there's no point of going out anywhere."* – 24-year-old female with CF
- *"Oh, cut it* (socialization) *off completely, almost completely. I mean, (...)* it's *been terrible."* – 50-year-old female with CF

Participants that reported minimal or no changes or were neutral toward COVID-19-related effects on socialization stated they were cautious but continued to socialize face-to-face. Social distancing guidelines and wearing masks were not novel practices to participants, as they have been living with infection control precautions for much or all of their lives to limit infections exposure. They also reported finding relief with not having to meet other's expectations, wanting to remain positive, or that COVID-19 was not yet affecting their location at the time of the interview, which took place toward the beginning of the pandemic.

- *"As far as like some of the other things that happened, like no more handshaking, that did not bother me (...),wearing a mask in public, that wasn't new. I didn't do it in public. But just wearing a mask when you walk around, that was not a major change for me either. In some ways I think it's maybe gave people a little bit of introspection about what it's like to maybe live with a compromised immune system."* – 32-year-old male with CF
- *"Oh yeah, this is all just like normal to me."* - Adult female of unknown age with CF
- *"I'm lucky that we're locked in and doing virtual things, because the expectation of physically going in can be difficult, with stairs and all, and*

worrying about being around other people that might get me sick somehow. So, it's just a lot more convenient to do everything virtually right now." – 24-year-old female with CF

Triangulation of Mixed-Methods Data

Overall, results of the MMR analysis shows little divergence. Results indicate that as a whole, participants did not experience high levels of SoI and had good social support systems in place. Many participants denied feelings of SoI or voiced that they experienced these feelings when they were younger, but as they got older feelings of isolation disappeared; this was not reflected in the quantitative data. Participants reporting satisfaction with their support system and having minimal or no feelings of subjective SoI had lower PROMIS-SoI scores and higher LSNS-R scores, indicating less subjective and objective SoI. Those who spoke about dissatisfaction with their support systems also tended to verbalize feelings of SoI during interviews. These participants had higher PROMIS-SoI scores and lower LSNS-R scores, indicating higher levels of objective and subjective SoI. Data triangulation examples with quotes, PROMIS-SoI, and LSNS-R scores can be found in Appendix E.

Discussion

This novel study explores the feasibility of a parallel mixed-methods approach to develop a preliminary characterization of SoI in adults with CF. Through analysis of quantitative, qualitative, and triangulated data, we were able to determine the feasibility of this study to aid in the design of future studies on a larger scale, as well as gain an initial description of how SoI is experienced by this population.

Feasibility of the study

The response rate of 22.2% did not meet our initial goal of 50%. This may be a result of the short recruitment period (three months); additionally, recruitment began only three months after the start of the COVID-19 pandemic. There is potential that with a longer recruitment period, higher recruitment rates will be reached. It may be beneficial for the investigator to have an in-person presence at the clinic to speak to potential participants about the study. With 94.1% indicating an interest in future, similar studies and 79.4% willing to take part in an interview, there seems to be an interest in this ongoing research.

Given 12 potential participants opened the survey and did not begin or complete the survey, consideration will be given to providing shorter surveys in different waves instead of one long survey. Physical and mental fatigue and busy schedules may create difficulty with completing longer surveys; breaking the survey into various parts may improve recruitment.

During the qualitative portion, participants did not report feeling the survey or interview was too long. Participants provided beneficial feedback that will be useful for revising the survey and interview guide for future studies. While all participants felt the survey and interview questions were appropriate, the feedback they provided will help to strengthen future studies.

Subjective and Objective Social Isolation

Participants with more subjective SoI tended to have more objective SoI as demonstrated through a smaller social network or decreased interactions with the network. Overall, this sample did not demonstrate high levels of either subjective or objective SoI. While there are outliers who have significant SoI, these participants did not

agree to take part in the interview process. Based on the clinical characteristics and statements made during interviews, study participants represent a sample of the CF population with fewer health complications when compared to the CF Patient Registry.[3] In 2019, people with CF in the CF Patient Registry had a mean FEV_1 of 78.7, a mean of 18.3 hospital days related to pulmonary exacerbations (in those with hospitalizations), 10.9% required oxygen, and 52% were working full or part time.[3] Not all participants were able to report their last FEV_1 actual value, so we were unable to obtain a mean for this sample, but 50% had a FEV_1% of ≥ 70%. The majority (55.9%) of participants were not hospitalized in the past year, 5.9% required oxygen, 55.9% were working full or part time, and 91.2% have not required a lung transplant or placement on the waitlist for one. Those with moderate or severe illness may have been less likely to take part in this study due to fatigue, illness, time restrictions, or COVID-19-related issues. It is possible that those with more severe illness experience higher levels of SoI, but it cannot be determined from this small sample.

During interviews, participants voiced feelings of SoI, not being understood by others, and not being taken seriously because they "do not look sick". This phenomenon has been found in other chronic illness populations who may not outwardly appear sick, including people with systemic lupus erythematosus, chronic headache, and chronic fatigue syndrome.[35-37] Participants felt less isolated when having a strong support system in place and/or connecting with others who have CF through online social support groups. Strong support systems in people with CF have demonstrated its benefit by increasing QOL and decreasing physical and mental health symptoms.[10] Even when COVID-19 social distancing guidelines are reduced, individuals with CF will continue to

have restrictions face-to-face social support from one another; technology may be a bridge to provide these connects in a safe fashion. Future research should focus on technology-based support interventions to reduce SoI, as they have been found to significantly decrease SoI in those with chronic illness.[38]

Preliminary Signals of SoI Predictors

We were able to explore preliminary signals of SoI predictors; however, this data is considered cautiously given the small sample size. While age was not correlated with subjective or objective SoI, age emerged as a potential predictor during interviews, as decreased feelings of SoI with age was verbalized among older participants. This finding is inconsistent with studies examining SoI in people with other chronic diseases, such as multiple sclerosis (MS) and Parkinson's disease (PD), which found that SoI increased with disease progression.[39,40] However, it is important to consider that MS and PD are typically diagnosed later in life; CF is typically diagnosed early in life, which may account for these differences. Potentially, managing a lifelong illness has improved coping skills, support utilization, and outlook on life.

Subjective isolation was significantly higher in those who were not married or with a partner, suggesting that support received from a romantic partner is an important aspect of living with CF. This corresponds with a qualitative study indicating social support is the most important perceived aspect of a romantic relationship.[41] Females had significantly higher objective SoI scores, indicating the presence of a larger support network. This is consistent with literature suggesting that females may receive social support to a greater extent compared to males.[42,43] Females may be more likely to reach out for emotional support and verbalize feelings than males.

While there was not a significant difference in subjective and objective SoI between those who were working and those who were not, those who were working had higher PROMIS SoI scores ($p = 0.56$); there is potential that an adequately powered sample size will find those who work have significantly less subjective SoI. Working potentially expands one's social network, which may explain previous studies finding improved social functioning and increased perceptions of social support among working participants.[10,44]

When exploring the effects of COVID-19, those who saw or heard from others less had significantly lower subjective and objective SoI scores compared to those receiving more support during the pandemic. The majority of participants reported minimal or no COVID-19-related change to socialization; those who experienced distress reported their socialization was greatly affected. Participants who did not report a change in socialization felt that COVID-19 restrictions were nothing new, as they were used to wearing masks and restricting activities. Interviews took place relatively soon after the beginning of the pandemic, and those reporting significant social distress were struggling with adapting to the 'new normal'. These findings further compliment the finding that support and socialization is vital in adults with CF.

Preliminary signals of potential relationships were found between CFQ-R scores and subjective and objective SoI. An increase subjective SoI was associated with lower physical, emotion, treatment, health, social, body, and role domains scores; increased LSNS-R scores were associated with higher emotion domain scores. Those with lower physical and health domain scores likely experience more symptoms or perceive poor health. Increased physical symptoms and health problems likely prevent socialization and

the ability to attend social functions. For the emotion domain, it is possible that either emotional dysfunction decreases the desire to socialize or the lack of socialization results in emotional distress. These findings are consistent with CF literature demonstrating relationships between lower social functioning domain scores and poorer physical and psychological health.[45] This relationship should be explored further to identify how emotion and SoI correlate with each other.

Increased treatment burden likely causes SoI from a limited ability to socialize due to complex and time-consuming therapeutic regimens. Planning around multiple therapies, such as aerosol medications, intravenous therapy, and airway clearance, may be taxing on a person with CF, reducing the ability or desire to socialize. CF literature indicates that lower treatment burden domain scores are related to increased social support,[45] which may be related to increases in socialization.

Social functioning measures a component of socialization related to the ability to go out with friends, comfort with discussing CF with others, and how one feels others view their CF;[46] therefore, it is not surprising that a potential relationship exists. Participants who scored lower in the social functioning domain likely face social distress and experience higher levels of SoI due to the physical and psychological health challenges that may accompany CF. This correlates with CF literature suggesting poor social functioning scores leads to decreased physical and mental HRQOL.[45]

A potential explanation for lower body domain scores and higher subjective SoI scores may be those with poor body image or a negative self-image are less likely to socialize or participate in events. It also can suggest that those with poorer body domain scores experience more severe illness, potentially leading to body image disturbances,

such as not maintaining weight, having procedural or surgical scars, or feeling self-conscious about CF-related symptoms.

The potential relationship between subjective SoI and the role domain is likely complex. An adult with CF may be trying to manage various aspects of life, such as parenthood, marriage, and a career simultaneously while managing a chronic illness. There may be role confusion related to the spouse being the only care taker of the home or providing income. During times of acute illness, an adult with CF may feel conflicted between caring for themselves and their family, leaving them confused about their role within their family.

Implications

Practice

Given the correlations between objective and subjective SoI, assessing one's social network and support system may help to identify those at higher risk for SoI. This can lead to referrals to support groups, potential outlets to connect with others that have CF, and emphasizing the importance of socializing where appropriate. Almost all participants, with the exception of two, referred positively to using CF-based social network and the support the found from others. This indicates the importance of assessing access to these sites or providing resources with the potential different support groups. While we do not know much about SoI yet in this population, it is apparent that social support and socialization is an important part of living with CF. People with CF that are at high risk for SoI can receive beneficial support from a psychologist specializing in chronic disease processes to guide the patient in developing positive coping mechanisms and ways to improve socialization.

Research

There is a paucity of literature on SoI in adults with CF. To our knowledge, this is the first study to explore this construct in this population. Recent studies investigating SoI in other chronic illnesses, such as MS and PD, suggest that this is a new and emerging topic of interest among those with chronic illness.

Because adults with CF are living longer, there is a shifting focus on improving QOL from a holistic point of view, expanding upon psychological, emotional, and social health. While this study provides limited information, SoI needs to be investigated in a larger population and in a more clinically diverse population; it can be hypothesized that those with more severe illness experience more SoI as with other people with chronic illness.[39,40] Longer recruitment times and more face-to-face encounters with potential participants can possibly help recruit a more diverse population.

We need to explore how SoI affects those with varying severities of CF to understand which groups are at higher risk in order to prioritize interventions centered on decreasing perceptions of SoI. Longitudinal studies can allow us to monitor SoI over time to identify its effects on physical and mental HRQOL using the CFQ-R. By understanding how SoI presents in those with CF we can begin to design interventional studies centered around technology-based support, psychosocial support groups, and asynchronous peer support groups, as these have been found to significantly decrease feelings of SoI.[38]

Limitations

A major limitation of this study is the small sample size. While a focus of the study was feasibility of the methodology, data was elicited to provide a glimpse into how

people with CF experience SoI. Having a large and adequately powered study may provide further evidence related to the preliminary signals gained from this study. Additionally, this study does not provide a generalizable representation of the CF population. In 2019, 51.8% of people with CF were male, whereas our sample was predominately female (73.5%). Sample diversity related to race and ethnicity is unclear, as 94.1% described themselves as White but 5.9% selected 'prefer not to answer'. Given that 4.7% of the CF population is Black or African-American and 3.8% includes other racial groups,[3] it is possible that the participants who did not answer this question were fearful of being identified due to the small percentage of patients with CF who are not White. Future studies will explore various ways to ask about race and ethnicity in order to understand how different cultures experience SoI.

The LSNS-R has not been validated in younger populations, potentially creating another limitation, but it has demonstrated the ability to assess objective SoI in older populations. This instrument was chosen to assess objective SoI because of its assessment of the social network, allowing us to explore how one's social circle relates to subjective SoI. While the PROMIS SoI scale assesses subjective SoI, we need to further explore its capability to adequately measure this concept in those with chronic and progressive illnesses.

Lastly, the timing of this study compared to the beginning of the COVID-19 pandemic possibly altering perceptions of SoI. Data collection began in June of 2020, only three months after the beginning of the pandemic. This timing potentially changes how participants answered many of the questions related to subjective and objective SoI, as well as questions on the CFQ-R. While COVID-19 did not seem to pose a significant

burden on participants who were interviewed, it cannot be assumed this applies to those who were not interviewed.

Conclusion

This study provides our first glimpse into how the adult CF population experiences SoI. While we did not find high levels of SoI in this group of participants, socialization was identified as critical to individuals with CF. It will be important to explore this concept in those with more severe illness and with larger sample sizes. This MMR approach is feasible for future studies; however, longer recruitment periods, distributing surveys in different waves, and adding the recommendations from the participants will create a more robust study. Given the detrimental effects of SoI, it is worthwhile to develop a deeper understanding of how it presents in this population in order to develop interventions that can circumvent SoI to improve QOL.

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Appendix A

Pre-interview Script

The Experience of Social Isolation in Adults with Cystic Fibrosis
Interview Guide
Pre-interview Script

Before the interview, participants will be provided with the following script:

This interview is part of a research study exploring how adults with cystic fibrosis socialize and interact with those they care about and will last approximately 30-45 minutes. The goal of this study is to understand how having CF affects adult patients' ability to engage in social experiences with family, friends and other people that are important to them. This interview will be audio recorded and transcribed. Your responses will remain confidential. The only foreseeable risks are the potential loss of confidentiality and that some of the questions may cause emotional discomfort. Your participation in this interview is strictly voluntary and you can skip questions and end the interview at any time. Your participation in this interview implies your consent. Do you have any questions? (Allow time for questions) Do you wish to proceed to the interview?

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Appendix B

Qualitative Theme Codebook			
Themes	Subthemes	Definitions	Examples from Transcripts
Importance of socialization and social support	NA	Expression of: Positive life experiences, feelings, or influences as a result of socializing and/or social support; or Negative life experiences, feelings, or influences resulting from a lack of socialization and/or social support demonstrating its importance.	*"It* (socialization) *means a lot. It just kind of help life go by smoother."* *"Well, the interaction with others helps me mentally to feel positive, to feel like a part of the group and a part of the world and a part of humanity. CF can certainly make you feel like a non-human at times and having friends and getting together with people and doing things and doing quote-unquote typical, normal activity makes me feel good about myself and good about the things that I'm able to accomplish."*
CF's effects on socialization	NA	Interruption of socialization and social development (i.e. missing social functions, loss of friends from inability to socialize, etc.) as a result of CF and CF-related treatments. Examples include	*"The way my body reacts is it doesn't like to have infection in the long run so it is going to produce, you know, it's going to make me cough up this nasty stuff every day. That would be embarrassing in a social setting."*

		treatment burden, frequent illness, fatigue, and hospitalizations.	*"I didn't have the typical social interactions with girls and I had to learn that typical middle school social interaction in my 40s because if you don't learn it then, you get to learn it later in life, at least that's what I've found. And so, I was very delayed socially, but I made up for it in college."*
Feelings of isolation	Social isolation	Feeling isolated from others as a result of CF and the associated symptoms and treatments.	*"It was very, very isolating* (having CF). *I did not know a single person with CF growing up, and I still don't really personally know anybody with CF."* *"I would say that when I was a child, I felt extremely isolated. As an adult, I have not felt as isolated. As a married person, before I had a child, I felt very isolated. But having a child really didn't help me to bond with other people in my age and my stage of life, so there's times I have felt isolated […] But in general, I don't as much anymore."*

	Lack of understanding from others	Feeling a lack of understanding from family, peers, co-workers, or others they frequently interact with related to CF and its associated treatments and symptoms.	*"I felt nobody was paying attention to what I said, or willing to understand what I said."* *"Like none of them truly know what I'm going thru because none of them have CF."* *"But it is still hard sometimes knowing that they have their own things that they're going thru being part of my support system because I don't know what it is like to love or be married or anything to someone with CF because I'm the one with CF, so I don't know those feelings. And I know that they don't know my feelings of what it's like to wake up every day, and take a bunch of meds, and do a bunch of treatments, and go to three-hour appts and things like that."*
	Invisible illness	Sharing instances of others making direct comments, insinuations, or making one feel as if they are exaggerating symptoms, are actually healthy, etc.	*"Yeah, I feel like I have to have oxygen or wear a mask or not put myself together for people to realize like, this is how I feel."*

		because they do not outwardly appear sick or ill.	*"You know, sometimes there's things I can't do, and if you saw me, I do not look sick at all. I do not look like anything anybody would look like that's sick and that's hard for people to comprehend, but at the same time, I can do other things, but I can't do that, and that's also hard for people to understand. It's like, "Well, how come you can sit outside at the pool and go in and out and stuff like that, but you can't be on a cruise in the middle of the Caribbean in the middle of the summer?" I mean, people just don't understand."*
Importance of CF-specific support	NA	Sharing instances of receiving positive support and socialization from others with CF, including the use of social media, chat rooms, having family members with CF, developing close bonds with a friend or other person that has CF, etc.	*"It was very, very isolating. I did not know a single person with CF growing up, and I still don't really personally know anybody with CF."* *"I have one of my good friends, who has the same exact mutation as I do. He's pretty good to talk to about things. I feel we inspire*

			each other in different ways." *"Since I've had CF there have been times when my lung function was going down and the doctors couldn't figure out why. I have found myself thinking it would be nice* (having people to with CF to reach out to)*."*
COVID-19-related socialization and support	NA	Actual or perceived positive or negative changes in support and/or socialization related to the COVID-19 pandemic.	*"I'm lucky that we're locked in and doing virtual things, because the expectation of physically going in can be difficult, with stairs and all, and worrying about being around other people that might get me sick somehow. So, it's just a lot more convenient to do everything virtually right now."* *"It feels a lot better to not have to worry about if somebody outside is going to randomly flip out a cigarette or doing something to make me feel uncomfortable."* *"Post-COVID it's been kind of depressing, because*

			we have all been trying to stay away from each other, just because my sister and I do have CF."

Appendix C

Mann-Whitney U Comparison Tables

Mann-Whitney U Comparisons for PROMIS SoI scores (n = 34)				
	Median	Mean Rank	U	p-value
Sex[1]			69.5	.204
Male	48.9	20.8		
Female	43.1	15.8		
Marital Status			72.5	.022
Not married or not with a partner	50.0	22.4		
Married or with a partner	43.1	14.5		
Work Status			146.0	.056
Not working full or part time	50.0	17.3		
Working full or part time	39.1	17.7		
Insurance Status			118.5	.956
Medicaid/Medicare	49.5	17.7		
Private/Employer Insurance	43.1	17.4		
Geographic Area			85.5	.133
Metropolitan	44.4	16.05		
Non-metropolitan	59.7	23.88		
Oxygen Use			30.5	.121
No	43.8	16.6		
Yes	66.3	31.5		
Lung Transplant			36.5	.564
No	44.4	17.8		
Yes	41.4	14.2		
Providing social support during COVID-19			90.5	.591
Someone I live with	47.9	19.2		
No	43.8	17		
Yes			96	.381
Relative, friend, or neighbor who comes to my place	45.7	18.5		
No	42.9	15.1		
Yes			113.5	.420
Relative, friend, or neighbor who I talk with on the phone	45.7	19.3		
No	43.1	16.4		
Yes				

1. Missing sex for one participant

Mann-Whitney U Comparisons for LSNS scores (n = 34)				
	Median	Mean Rank	U	p-value
Sex[1]			167.5	.003
Male	28	8.6		
Female	43	19.7		
Marital Status			72.5	.232
Not married or not with a partner	35.0	22.4		
Married or with a partner	39.0	14.5		
Work Status			146.0	.918
Not working full or part time	38.0	17.3		
Working full or part time	38.0	17.7		
Insurance Status			118.5	.956
Medicaid/Medicare	39.9	17.7		
Private/Employer Insurance	37.5	17.4		
Geographic area			32.5	.166
Metropolitan	38	17.88		
Non-metropolitan	28.5	10.62		
Oxygen use			2.0	.182
Yes	18	3.0		
No	38.5	17.44		
Lung Transplant			54.5	.645
No	38.0	17.2		
Yes	47.0	20.2		
Who is providing you with social support during COVID-19				
Someone I live with			120.5	.510
No	39.5	15.4		
Yes	38	18.1		
Relative, friend, or neighbor who comes to my place			191	.006
No	35	14.5		
Yes	46.5	24.6		
Relative, friend, or neighbor who I talk with on the phone			201	.022
No	36	12.5		
Yes	46	20.6		

1. Missing sex for one participant

Appendix D

Kruskal-Wallis H Comparison Tables

Kruskal-Wallis for PROMIS SoI Scores (n = 34)				
	Median	Mean Rank	H	p-value
Education			6.3	.096
High school/GED or less	48.9	20.2		
Some college	47.9	23.3		
College degree	45.7	17.0		
Professional/graduate degree	36.5	12.1		
FEV_1 Range			2.0	.738
Greater than 90%	43.1	13.2		
70-90%	44.4	16.6		
40-69%	33.9	15.2		
Less than 40%	48.9	21.8		
Do not know	42.0	14.2		
CFTR Use			1.3	.530
No	45.7	18.4		
Yes	44.4	17.8		
Do not know	37.7	10.0		
Hospitalizations Over Past Year			3.9	.561
0	43.1	15.1		
1-3	46.7	19.8		
4-6	53.1	26.5		
7-9	39.1	12.5		
10 or more	48.9	22.5		
Do not know	547	24.0		
Since COVID-19 – the number of relatives, friends, or neighbors see/hear from at least once a month			9.0	.062
None				
1	71.6	33.3		
2	NA	NA		
3-4	33.9	6.0		
5-8	45.1	18.6		
9 or more	45.1	17.3		
	33.9	11.0		
Since COVID-19 – How often do you see/hear from those whom you have had the most contact[1]			10.3	.036
Less than monthly	71.6	32.2		
Monthly	59.6	30.0		
Weekly	45.7	17.4		
Few times a week	33.9	10.6		
Daily	43.8	16.8		
Footnote: Post-hoc Pairwise Comparisons	H		p-value	
1. Few times a week – less than monthly	21.7		.043	

Kruskal-Wallis for LSNS Scores (n = 34)				
	Median	Mean Rank	H	P-value
Education			4.7	.196
High school/GED or less	43.0	14.5		
Some college	32.5	14.5		
College degree	35.0	15.9		
Professional/graduate degree	45.5	23.2		
FEV_1 Range			.651	.957
Greater than 90%	44.0	15.7		
70-90%	39.0	17.1		
40-69%	37.0	14.4		
Less than 40%	47.0	17.8		
Do not know	39.0	14.5		
CFTR Use			2.9	.234
No	36.0	13.6		
Yes	38.0	17.8		
Do not know	47.5	27.0		
Hospitalizations Over Past Year			5.4	.365
0	39.0	18.9		
1-3	43.0	19.2		
4-6	31.0	9.0		
7-9	38.0	17.0		
10 or more	16.0	2.0		
Do not know	31.0	8.5		
Since COVID-19 – Number of relatives, friends, or neighbors you see or hear from at least once a month[2]			10.5	.033
None	13	2.0		
1	NA	NA		
2	36	14		
3-4	32.5	14.2		
5-8	44.5	22		
9 or more	47	24		
Since COVID-19 – How often do you see/hear from those whom you have had the most contact[3]			12.0	.017
Less than monthly	13	2.0		
Monthly	30	6.0		
Weekly	34	12.7		
Few times a week	51	23.4		
Daily	43.5	19.5		
Footnote: Post-hoc Pairwise Comparisons	H		*p*-Value	
2. None – 5-8	-19.7		.009	
None – 9 or more	-21.5		.010	
3. No significant pairwise comparisons found during post-hoc testing				

Appendix E

Triangulation of Quantitative and Qualitative Findings		
Variable	**Quantitative Instrument Scores Overall Population**	**Qualitative Narratives**
Subjective SoI ***(as measured by the PROMIS SoI Score)***	*M*(SD): 45.4(11.2) Median: 44.4	*"I have two sisters and they don't have CF. I think it's hard to get them to understand when I don't have energy or the time that I do have energy just how much that time means to me to actually hang out and socialize."* 29-year-old female with CF [PROMIS SoI 66.3, LSNS 28] *"It's very lonely anyway. Especially if you're the only person in the family that has it."* 32-year-old male with CF [PROMIS SoI 55.3, LSNS 25] *"Definitely* [when asked about feelings of SoI], *because sometimes I feel that people don't understand how they're being inconsiderate to me in a lot of aspects (…) just a misunderstanding of why I can't go to things sometimes (…) but the loneliness is pretty hard to escape."* 24-year-old female with CF [PROMIS SoI 59.6, LSNS 30] *"Sometimes, I guess it's a little hard (…) I feel like sometimes they just don't get it at the same time, because they don't have to experience it* [having CF]. *And I guess sometimes it's hard for me to explain what's going on."* 28-year-old female with CF [PROMIS SoI 44.4, LSNS 39] *"Socialization is a big part of having CF, because, if you don't have a support system, then you don't really have (…) there's not really more of a reason to take care of yourself and make sure that you're healthy. Because sometimes you feel like, "Well, what's the point?"* 28-year-old

		female with CF [PROMIS SoI 44.4, LSNS 39] *"Really through my entire childhood, I was really confidential about it* (having CF) *(…) I didn't want people to view me as being weak or sick (…) I think I had been very deeply affected by something that happened when I was a kid (…) A girl who I was in school with (…) her family knew I had CF and her dad said something to her (…) about being cautious about not becoming too close friends with me because I was likely to die and he didn't want her to have to cope with the loss of a friend (…) so it has been a journey for me (…) to try and figure out how to talk about it more comfortably."* Female of unknown age with CF [PROMIS SoI 39.1, LSNS 51] *"I'm pretty social. I get together with friends. We go out to dinners…and those that don't feel comfortable* [due to COVID], *we actually have a Zoom meeting (…) I usually have a lot of people over (…) I'd say I'm pretty social in that way."* 54-year-old female with CF [PROMIS SoI 33.9, LSNS 47] *"Times like that* [having exacerbations or concerning symptoms] *I'm like it would be nice to talk to somebody, who (…) is kind of is going through that."* 32-year-old female with CF [PROMIS SoI 33.9, LSNS 55] *"I don't look sick; therefore, I must have the same energy level as they do. And I don't think they understand…with this whole mask thing* [COVID recommendations] *(…) they don't understand the importance of wearing a mask."* 54-year-old female with CF [PROMIS SoI 33.9, LSNS 47]

		"I love my support system (…) but it is sometimes hard to know that (…) like none of them truly know what I'm going through because none of them have CF." 24-year-old female with CF [PROMIS SoI 33.9, LSNS 51]
Objective SoI ***(as measured by the LSNS Score)***	*M*(SD): 38.2(11.2) Median: 38 (Participants as a whole do not demonstrate a significant risk for SoI)	*"I recently joined a support group on Facebook. And that's been kind of helpful. It was, it let me see that finally, that other people did understand what it's like."* 32-year-old male with CF [PROMIS SoI 55.3, LSNS 25] *"I've gone through a lot of friends just because just being in the hospital all the time takes away from forming any sort of friend groups (…) I maybe have one friend (…) that so far has been really supportive and completely understands that my CF, she doesn't judge if I need to talk to her about things. I feel like she's one person that I can actually confide in."* 29-year-old female with CF [PROMIS SoI 66.3, LSNS 28] *"I have a few friends that I call and we're pretty good at staying in touch and all, that definitely helps to have at least four people I can really call or text. Because otherwise I do get pretty lonely."* 24-year-old female with CF [PROMIS SoI 59.6, LSNS 30] *"That's* [socialization] *very important. I have lots of friends, lots of family. We try to get together. Obviously, with COVID, not a much right now. But I'm very active socially. I try to do as much as I can."* 41-year-old female with CF [PROMIS SoI 33.9, LSNS 38] *"Having friends and getting together with people and doing things and doing quote-unquote typical, normal activity makes me feel good about myself and good about the things that I'm able to accomplish (…)*

		when I was a child I felt extremely isolated [...] but in general I don't anymore (...) I finally have a really good support system" 50-year-old female with CF [PROMIS SoI 53.1, LSNS 39] *"The more I socialize, the better."* 32-year-old female with CF [PROMIS SoI 44.4, LSNS 46] *"Not that I like getting sick, but it's nice that when you are sick or need prayers there's just tons, thousands even, that are praying for you and checking in on you (...) that just really makes me feel very loved and people caring for me."* 54-year-old female with CF [PROMIS SoI 33.9, LSNS 47] *"It* [socialization] *means everything. I think it helps to have people that support you, that you can cry to, talk with and family means a lot to me. I'm very close to my family (...) I'm satisfied, I have a good support system. I have a good family, lots of people I can call on if I need any help or advice or anything like that."* 46-year-old female with CF [PROMIS SoI 50, LSNS 49] *"I'm not really on any online support groups. I kind of sought that out when I was initially diagnosed and received good support that time, but it's just not necessarily something I need at this point (...) I just felt like I wasn't facing the same needs as a lot of those people."* 45-year-old female with CF [PROMIS SoI 33.9, LSNS 50] *"I just think it* [socialization] *is important for everybody no matter who they are to have good friends (...) if you have people who really care about you and who are kind and respectful and who help you, just someone that you know is always going to*

		be there for you, that greatly adds to your joy in life .I'm thankful I that I know the importance of socialization." 32-year-old female with CF [PROMIS SoI 33.9, LSNS 55]

SUMMARY

Overview of Each Manuscript's Contributions to Answering the Overarching Research Question

The first manuscript, *Social Support and Social Isolation in Adults with Cystic Fibrosis: An Integrative Review*, served as a critical starting point for this dissertation. This review exposed the dearth of literature exploring SoI not only in adults with CF, but among other chronic illness populations.[1] Considering this population experiences progressive physiologic symptoms and are at increased risk for psychological illness, there is a clear need to understand how challenges faced by adults with CF contribute to SoI.[2-4] While there is a lack of empirical evidence describing this concept among adults with CF, information regarding social spheres was elicited from this review. Poorer physical and mental health were primary key factors related to poorer social functioning,[1] which supports the need to explore this area further.

The conceptual idea for the second manuscript, *Coping in Adolescents and Adults with Cystic Fibrosis: An Integrative Review*, was developed during the interview process of the dissertation study.[5] While coping was not a main theme found during these interviews, there was preliminary evidence indicating that coping may play a significant role in how adults with CF perceive and respond to SoI. Because of the wide age range of dissertation study participants, adolescents were chosen to be included in this review to explore connections of coping styles developed during adolescence and transition to adult care. Evidence suggests differences of coping styles between these age groups but the pattern deserves further exploration.[6] The results of this review indicate that while some coping strategies have positive outcomes, such as positive reappraisal, each is dependent on the individual and situation.[5] The results of this review will help inform future large-

scale MMR studies exploring SoI, as coping strategies may be an integral part of socialization and the social network.

The dissertation manuscript, *The Experience of Social Isolation in Adults with Cystic Fibrosis: Results of a Mixed-Methods Feasibility Study*, provided a preliminary look into how adults with CF experience subjective and objective SoI, as well as provide feasibility data to guide future studies.[7] Main findings indicate that similar studies on a large scale are feasible with revisions to recruitment and survey/interview questions, subjective SoI scores are likely correlated with objective SoI scores, participants in this study did not experience high levels of SoI, socialization and social support are an important aspect in their lives, and that CF-centered support potentially decreases feelings of SoI. However, patients with moderate or severe CF may be more likely to experience increased SoI, which was not captured from this healthier participant sample. A more diverse sample may shed some light on how clinical status affects SoI during future studies.

There were preliminary signals that identified potential predictors to SoI, including sex, marital status, work status, social network size, physical symptoms, emotional status, treatment burden, health perception, social functioning, body image, and role. Future studies should further explore these possible predictors of SoI.

Limitations of Dissertation and Lessons Learned

One of the biggest limitations of this dissertation was the multiple influences of the COVID-19 pandemic. This affected the investigator's ability to be on-site at the CF clinic to actively participate in the recruitment process. This would have been a great opportunity to not only experience this process in-depth but also to connect with potential

participants and answer any questions. Not only did COVID-19 change recruitment, it more importantly may have changed participant's perceptions of SoI. While the majority of participants did not feel COVID-19 greatly affected them, the pandemic was only starting to impact the areas where the majority of the participants were living at the time of the study. Interview questions consisted of pre-COVID-19 and post-COVID-19 questions, but it may have been difficult for participants to recall pre-COVID-19 answers. A huge lesson was learned about clearly distinguishing which time frame was being referred in both the survey and interview questions.

Another limitation is the concept of SoI itself. This abstract concept is rather intangible and open to one's own interpretation. It was important, yet difficult, to operationalize this concept at the beginning of dissertation due to the considerable variations in terminology and definitions. Multiple sources and frameworks were considered to help the investigator find the best fit to answer the research question. While this was a challenging process, the importance of having a concrete concept operationalized was emphasized.

As mentioned in the dissertation manuscript, there are limitations concerning generalizability of the results given the relatively healthy nature of the participants. Additionally, males were not heavily represented and it is unknown if there were participants answering the survey who were not White. Having a sample size diverse in clinical status, percentages of sex, race, and ethnicity similar to the general CF population, and a sample from a more varied geographic distribution can allow us to gain a robust and generalizable picture of SoI among adults with CF.

Many other lessons were learned throughout this process. The importance of collaboration and team science were critical to completing not only my dissertation study, but also my compendium. As a novice researcher, this allowed me to gain skills necessary to communicate, request and receive feedback, and watch and learn from expert researchers. The importance of flexibility cannot be overlooked as the investigator's initial proposal and recruitment plan were heavily revised due to COVID-19; the dissertation committee demonstrated the importance of going back to the drawing board with an open mind and flexibility.

Importance of Model to Guide Overall Findings

Multiple frameworks and conceptual models were explored for their approach of SoI as both an objective and subjective concept. Because of the variability in how SoI is operationalized, it was important that the conceptual model outline differences between subjective and objective isolation to best delineate between these two interrelated concepts. Cornwell and Waite's model of SoI was ultimately selected because it approaches SoI from both subjective and objective points of view.[8] This model was identified as the strongest candidate to help corroborate or refute the hypothesis that adults with CF experience objective and subjective SoI as a result of symptoms and treatments. By exploring one's social network for objective SoI and perceptions and feelings of isolation and loneliness for subjective SoI, the investigators were able to obtain a preliminary description of the prevalence of SoI in adults with CF. Using Cornwell and Waite's conceptual model of SoI aligned with research question and study aims, making it a perfect fit for the purposes of the study.

Research Trajectory

Ongoing research into how adults with CF are impacted by SoI is justified to understand the prevalence of the problem, physiological and psychological effects of SoI, and ways to mitigate these effects can improve care, outcomes, and QOL. A larger study with a more diverse sample may be beneficial to explore preliminary results of this study further, provide insights and data not elicited from this sample, and provide knowledge that can inform interventions aimed at improving social support and decreasing SoI. This data can be used to design longitudinal studies that explore effects of SoI over time on clinical indicators, outcomes, and CFQ-R domains.

Considering infection control guidelines recommend people with CF segregate from others with CF, technology-based and virtual support interventions are prospective sources of support.[9,10] Technology and support-based interventions have shown to significantly reduce SoI in younger adults, providing a potential starting point.[10] While increased social media is was correlated with increased SoI in young adults in the general population, literature suggests it may improve care in those with chronic illness.[11-13] After first gaining a robust picture of SoI in adults with CF, exploring feelings related to social media use can elicit more data to inform future interventional studies aimed at social support and decreasing SoI. While it was not used in the dissertation study, preliminary data was obtained on how social media use and satisfaction relates to SoI during the study survey. This data will be used as part of the investigator's next steps regarding her research trajectory.

Contribution of Research to Health, Nursing, or Interprofessional Sciences and Clinical Care

SoI is emerging in the literature, even more so due to COVID-19 social distancing guidelines. However, there remains a scarcity of the exploration of SoI among people

with CF. Research investigating social support's effect on CF is of recent interest demonstrated by emerging literature, indicating that social spheres in people with CF is gaining traction.[14,15] As this dissertation indicates, objective SoI, which is closely related to social support, is likely correlated with subjective SoI.[7] Those with smaller social networks experienced higher levels of perceived isolation, indicating there is a vital link between these concepts that may play an important role in QOL.

While there are many limitations to this study, its methodology is feasible to approach future large-scale work that can confirm and explore these findings more in-depth, along with extracting new data, ideas, and predictors of SoI to help identify those at high risk. This study is the first of its kind attempting to describe SoI in adults with CF and determine its prevalence. While this sample indicates that SoI is not problematic in this population, an adequately powered study may find contradicting evidence that it is a wide-spread concern among those with more severe illness. By using this work as a stepping stone for future studies, we can begin to explore interventions aimed at improving QOL by decreasing feelings of SoI.

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APPENDICES

Appendix A

IRB Approval Letter for the Study Reported in Manuscript 3

Institutional Review Board for Human Research (IRB)
Office of Research Integrity (ORI)
Medical University of South Carolina

Palmetto Place Office Park
1 South Park Circle, Bldg. 1, Suite 401
Charleston, SC. 29407
Federal Wide Assurance # 1888

APPROVAL:
This is to certify that the research proposal **Pro00100962** entitled:
The Experience of Social Isolation in Adults with Cystic Fibrosis

submitted by: **Amy Gulledge**
Department: **NURSING GROUP - MUSC**
Sponsor: **Sigma Theta Tau International Society of Nursing Omicron Delta Chapter scholarship**

for consideration has been reviewed by **IRB-I - Medical University of South Carolina** and approved. The Institutional Review Board for Human Research (IRB) also recommends approval of the investigator's request for a HIPAA Waiver of Authorization, as it appears that the criteria of the Privacy Rule have been satisfied. The HIPAA Waiver of Authorization was reviewed under exempt review procedures.

In accordance with 45 CFR 46.101(b), the referenced study is exempt from Human Research Subject Regulations. No further action or IRB oversight is required, as long as the project remains the same. However, you must inform this office of any changes in procedures involving human subjects. Changes to the current research protocol could result in a reclassification of the study and further review by the IRB.

Because this project was determined to be exempt from further IRB oversight, consent document(s), if applicable, are not stamped with an expiration date.

Approval Date: **6/19/2020**

Type: **Exempt**

Administrator, **IRB-I - Medical University of South Carolina**
Kristin Zaks∗

∗***Electronic Signature****: This document has been electronically signed by the IRB Chairman through the HSSC eIRB Submission System authorizing IRB approval for this study as described in this letter.*

Important Note: Approval by the Institutional Review Board does not, in and of itself, constitute approval for the implementation of this research. Other MUSC clearances and approvals or other external agency or collaborating institutional approvals may be required before study activities are initiated. Research undertaken in conjunction with outside entities, such as drug or device companies, are typically contractual in nature and require an agreement between the University and the entity.

Appendix B

Permission to use CFQ-R Instrument in Dissertation Study

CYSTIC FIBROSIS QUESTIONNAIRES - REVISED

Copyright Agreement for the Cystic Fibrosis Questionnaires – Revised

Alexandra L. Quittner, Ph.D.

The undersigned agrees:

1. to administer and score the CFQ-R for research or clinical purposes only,
2. not to alter the items or scoring of the CFQ-R in any way,
3. to acknowledge the authors of the CFQ-R in any publications that include the use of the CFQ-R,
4. not to distribute the CFQ-R to anyone without the explicit, written permission of the copyright holders,
5. not to administer or score, or in any way provide services related to the CFQ-R to a third party, for a fee without the explicit, written permission of the copyright holders,
6. that permission for the individual/organization named below to use the CFQ-R may be rescinded by the copyright holders at any time.

Amy Gulledge, MSN/Ed, RN, CNE
Medical University of South Carolina
PhD Student, College of Nursing
99 Jonathan Lucas Street MSC 160
Office 329
Charleston, SC 29425
gulledge@musc.edu

Name Company/Institution/University Address City e-mail address

Signature 

State Zip: SC, 29425

Date April 1, 2020

Please sign, scan and email to: Dr. Alexandra L. Quittner: aquittner0202@gmail.com (305) 992-2411

Re: CFQ-R Permission for use

You replied on Mon 4/27/20209:51 AM

AQ

Alexandra Quittner <aquittner0202@gmaii.com >

Mon 4/27/2020 9:16 AM

To: Gulledge, Amy

Cc: Alexandra Quittner <aquittner0202@gmail.com>

pdf All Versions English CFQ-R Fl...

151 KB

Hi Amy

Yes, you can use it in your research...here is the English Teen/Adult version. I am sending you **all** of the age versions.

Best of luck,

Alexandra

Dr. Alexandra Quittner
305 992-2411

Appendix C

Recruitment Letter Provided to Participants

June 22, 2020

Hello,

My name is Amy Gulledge and I am a PhD student at the Medical University of South Carolina (MUSC) in the College of Nursing. I have been a nurse for 20 years and have always been very interested in improving the quality of life in adults with cystic fibrosis (CF). The purpose of this letter is to notify you of a research opportunity for which you may be eligible. The goal of this new study is to understand how having CF affects adult patients' ability to engage in social experiences with family, friends and other people that are important to them. Data from this study will help us: 1) identify any challenges with socialization that people with CF may experience, 2) understand how being able to socialize with others affects the quality of life and health status of adults with CF, and 3) design future activities to improve opportunities to socialize for adult CF patients.

I am recruiting potential research participants from the MUSC Adult Cystic Fibrosis Clinic that are interested in answering some questions about their social experiences. To be eligible, you must be 18 years or older and have cystic fibrosis. The study will involve 2 parts: 1) completion of an online survey sent via email and 2) participating in an interview with me either over the phone or via video chat. You will receive a $5 Amazon gift card via email for completing the online survey. Participants that complete both the survey and interview portion of the study will receive an additional $5 Amazon gift card. Information about how to participate in an interview is provided at the beginning of the survey.

If you are interested in participating in this study, you can access the survey by clicking on the link provided in this email or click on the following: https://redcap.musc.edu/surveys/?s=RAXA8J7874. If this does not work, you can go to https://redcap.musc.edu/surveys/ and copy and paste the following code: JJLJ3M9PA. Additionally, you can begin the survey by scanning the QR code below with your mobile device.

If you have any questions about participating, please call me at (843) 792-9237 or email me at gulledge@musc.edu. Thank you in advance for helping us understand what we need to know about your ability to engage in social activities as an adult with CF and how it affects your life. This is an important opportunity to contribute to research that seeks to improve the quality of life for adult patients with CF.

Sincerely,

Amy Gulledge, MSN/Ed, RN, CNE
PhD Student – College of Nursing
Principal Investigator

QR Code

MUSC
Medical University of South Carolina
Changing What's Possible

IRB Number: Pro001000962
Date Approved 6/19/2020

Appendix D

PROMIS Item Bank v2.0 - Social Isolation – Short Form 8a

Social Isolation – Short Form 8a

		Never	Rarely	Sometimes	Usually	Always
UCLA11x2	I feel left out.....	□ 1	□ 2	□ 3	□ 4	□ 5
UCLA13x3	I feel that people barely know me.....	□ 1	□ 2	□ 3	□ 4	□ 5
UCLA14x2	I feel isolated from others	□ 1	□ 2	□ 3	□ 4	□ 5
UCLA18x2	I feel that people are around me but not with me	□ 1	□ 2	□ 3	□ 4	□ 5
Iso-CaPS1	I feel isolated even when I am not alone ..	□ 1	□ 2	□ 3	□ 4	□ 5
Iso-CaPS2	I feel that people avoid talking to me	□ 1	□ 2	□ 3	□ 4	□ 5
Iso-CaPS3	I feel detached from other people	□ 1	□ 2	□ 3	□ 4	□ 5
Iso-CaPS9	I feel like a stranger to those around me	□ 1	□ 2	□ 3	□ 4	□ 5

Please respond to each item by marking one box per row.

23 June 2016

Appendix E
PROMIS Social Isolation Short Form 8a Scoring Guide

SOCIAL ISOLATION

A brief guide to the PROMIS Social Isolation instruments:

ADULT
PROMIS Item Bank v2.0 – Social Isolation
PROMIS Short Form v2.0 – Social Isolation 4a
PROMIS Short Form v2.0 – Social Isolation 6a
PROMIS Short Form v2.0 – Social Isolation 8a

ABOUT SOCIAL ISOLATION

Quality of social support refers to functional aspects of supportive relationships, i.e., interpersonal relationships that serve particular functions. This includes the interactive process by which emotional, instrumental or informational support is obtained from one's social network. It also includes companionship, feeling cared for and valued as a person, communication with others, and feelings of belonging and trust. Measures of social support generally seek information about a person's perception of the availability or adequacy of resources provided by others.

The PROMIS Social Isolation item bank assesses perceptions of being avoided, excluded, detached, disconnected from, or unknown by, others. The item bank does not use a time frame (e.g. over the past seven days) when assessing social isolation.

Social Isolation instruments are available for adults (ages 18+).

(For complete definition see http://nihpromis.org/measures/domainframework3)

INTRODUCTION TO ASSESSMENT OPTIONS

There are two administration options for assessing Social Isolation: short forms and computerized adaptive test (CAT). When administering a short form, instruct participants to answer all of the items (i.e., questions or statements) presented. With CAT, participant responses guide the system's choice of subsequent items from the full item bank (14 items in total). Although items differ across respondents taking CAT, scores are comparable across participants. Some administrators may prefer to ask the same question of all respondents or of the same respondent over time, to enable a more direct comparability across people or time. In these cases, or when paper administration is preferred, a short form would be more desirable than CAT. This guide provides information on all Social Isolation short form and CAT instruments.

Whether one uses a short form or CAT, the score metric is Item Response Theory (IRT), a family of statistical models that link individual questions to a presumed underlying trait or concept of social isolation represented by all items in the item bank. When choosing between CAT and a short form, it is useful to consider the demands of computer-based assessment, and the psychological, physical, and cognitive burden placed on respondents as a result of the number of questions asked.

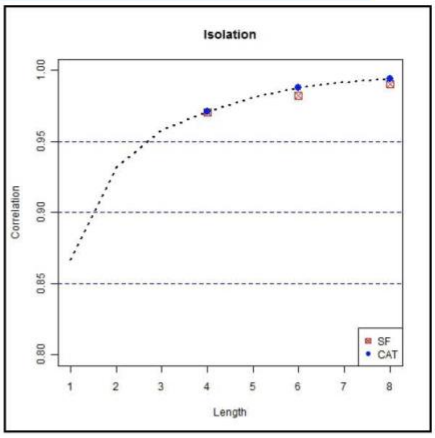

Figure 1

Figure 1 illustrates the correlations (strength of relationship) of the full bank with CAT and with short forms of varying length. The correlation of CAT scores with the full bank score is greater than a short form of any length. A longer CAT or longer short form offers greater correlation, as well as greater precision. When evaluating precision, not all questions are equally informative. The flexibility of CAT to choose more informative questions offers more precision.

SHORT FORM DIFFERENCES

The short forms (4a, 6a, 8a) were constructed by the domain team with a focus on representing the range of the trait and also representing the content of the item bank. Domain experts reviewed short forms to give input on the relevance of each item. Each domain group worked independently and the original short forms are 6-10 items long depending on the domain. Psychometric properties and clinical input were both used and likely varied in importance across domains.

Similar selection criteria guided the choice of items to include for each short form version. The longer version of the short form will provide a more precise score with less error than the shorter short form. However, this does increase the respondent burden.

In selecting between short forms, the difference is instrument length. The reliability and precision of the short forms within a domain is highly similar. If you are working with an adult sample in which you wanted the most precise measure, select the 8a short form. If you are working in an adult sample in which you expected huge variability in a domain area and wanted different subdomains covered, you should select the 8a short form. If you had little room for additional measures but really wanted to capture something as a secondary outcome, you should use one of the shorter instruments (4a, 6a).

SCORING THE INSTRUMENT

Short Forms: PROMIS instruments are scored using item-level calibrations. This means that the most accurate way to score a PROMIS instrument is to utilize scoring tools within Assessment Center or API that look at responses to each item for each participant. Data collected in either of these platforms will automatically score in this way. We refer to this as "response pattern scoring." Response pattern scoring can be used when data was collected on paper or in another software package through the Assessment Center Scoring Service. Because response pattern scoring is more accurate than the use of raw score/scale score look up tables, it is preferred. However, if you aren't able to use response pattern scoring, you can use the instructions below which rely on raw score/scale score look-up tables.

For adults, each question has five response options ranging in value from one to five. To find the total raw score for a short form with all questions answered, sum the values of the response to each question. For example, for the adult 6-item form, the lowest possible raw score is 6; the highest possible raw score is 30 (see all short form scoring tables in Appendix).

A score can be approximated if a participant skips a question. If items are missing, first check how many items were answered. For short forms with at least 5 items, confirm that 4 or 50% of items, whichever is greater,

were answered. For example, a 4-item short form can only be scored with complete data. A 5-item short form can be scored as long as 4 items were answered. A 10-item short form can be scored as long as the participant answered at least 5 items. After confirming that enough responses were provided, sum the response scores from the items that were answered (not including any screening question). Multiply this sum by the total number of items in the short form. Finally, divide by the number of items that were answered. For example, if a respondent answered 5 of 8 questions and answered all items with the second lowest response option (2), you would sum all responses (10), multiply by the number of items in the short form (8) and divide by the number of items that were answered (5). Here (10x8)/5=16. If the result is a fraction, round up to the nearest whole number. This is a pro-rated raw score. Again, the formula is:

$$\frac{\text{(Raw sum x number of items on the short form)}}{\text{Number of items that were actually answered}}$$

Locate the applicable score conversion table in the Appendix and use this table to translate the total raw score or pro-rated score into a T-score for each participant. The T-score rescales the raw score into a standardized score with a mean of 50 and a standard deviation (SD) of 10. Therefore a person with a T-score of 40 is one SD below the mean. It is important to note that Assessment Center will convert a participant's pattern of responses to a standardized T-score after they have finished a CAT. The standardized T-score is reported as the final score for each participant.

For the Social Isolation 8a short form, a raw score of 10 converts to a T-score of 41.4 with a standard error (SE) of 2.4 (see scoring table for the 8a short form in appendix). Thus, the 95% confidence interval around the observed score ranges from 37.0 to 45.8 (T-score $\pm$ (1.96*SE) or 41.4 $\pm$ (1.96*2.4).

For pro-rated scores, this calculation assumes that responses are missing at random. This isn't always true. Therefore, use caution when interpreting the final pro-rated T-score.

CAT: A minimum number of items must be answered in order to receive a score for Social Isolation CAT. The first item is selected because it provides the most information about the U.S. general population. The response to this item will guide the system's choice of the next item for the participant. The participant's response to this item will dictate the selection of the following question, and so on. As additional items are administered, the potential for error is reduced and confidence in the respondent's score increases. CAT will continue until either the standard error drops below a specified level, or the participant has answered the maximum number of questions (12), whichever occurs first.

For most PROMIS instruments, a score of 50 is the average for the United States general population with a standard deviation of 10 because calibration testing was performed on a large sample of the general population. However, social health instruments such as these short forms were not calibrated on a national sample and so a score of 50 represents the average of the calibration sample which was generally more enriched for chronic illness. As these instruments, a score of 50 likely represents somewhat sicker people than the general population. The T-score is provided with an error term (Standard Error or SE). The Standard Error is a statistical measure of variance and represents the "margin of error" for the T-score.

Important: *A higher PROMIS T-score represents more of the concept being measured.* For negatively-worded concepts like Social Isolation, a T-score of 60 is one SD worse than average. By comparison, a Social Isolation T-score of 40 is one SD better than average.

STATISTICAL CHARACTERISTICS

There are four key features of the score for Social Isolation:

- **Reliability**: The degree to which a measure is free of error. It can be estimated by the internal consistency of the responses to the measure, or by correlating total scores on the measure from two time points when there has been no true change in what is being measured (for z-scores, reliability = $1 - SE^2$).
- **Precision**: The consistency of the estimated score (reciprocal of error variance).
- **Information:** The precision of an item or multiple items at different levels of the underlying continuum (for z-scores, information = $1/SE^2$).
- **Standard Error (SE):** The possible range of the actual final score based upon the scaled T-score. For example, with a T-score of 52 and a SE of 2, the 95% confidence interval around the actual final score ranges from 48.1 to 55.9 (T-score $\pm$ (1.96*SE) = 52 $\pm$ 3.9 = 48.1 to 55.9).

Scaling Model Used For Calibration	Graded Response Model
Total Number of Items	14

Sample	N	Alpha Reliability
PROMIS Supplement Full-Bank	801	0.96

Score Distributions									
	Mean	SD	P5	P10	P25	P50	P75	P90	P95
Raw	28.09	11.85	14.00	14.00	18.00	26.00	36.00	44.00	51.00
Scale	47.87	9.53	31.71	31.71	41.23	48.07	54.24	59.59	63.98

									Min	Max
Scale Score	10.0	20.0	30.0	40.0	50.0	60.0	70.0	80.0	90.0	31.7	80.2
SE	8.26	2.68	.78	.22	.16	.16	.16	.43	1.31		
Reliability	.00	.00	.39	.95	.98	.97	.97	.81	.00		

Figure 2

The final score is represented by the T-score, a standardized score with a mean of 50 and a standard deviation (SD) of 10.

Figure 2 is a sample of the statistical information available in Assessment Center for the Social Isolation CAT. More information is available online via Assessment Center (assessmentcenter.net).

PREVIEW OF SAMPLE ITEM

Figure 3 shows a Social Isolation item from the full item bank as it would appear to a study participant during data collection in Assessment Center. Several formats for presenting the items are available for computer-based administration through Assessment Center (see FAQ section).

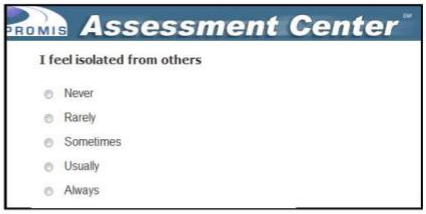

Figure 3

Figure 4 is an excerpt from the paper version of the eight-item short form. This is the paper version format used for all Social Isolation instruments. It is important to note, CAT is not available for paper administration.

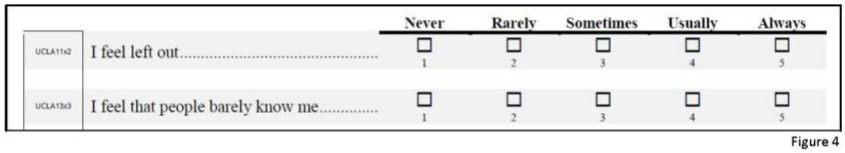

Figure 4

FREQUENTLY ASKED QUESTIONS (FAQ)

Q: *I am interested in learning more. Where can I do that?*

All instruments are available on the PROMIS website through Assessment Center, which houses all PROMIS instruments for each domain.

Assessment Center is a free online research management tool. It enables researchers to create study-specific websites for capturing participant data securely. Studies can include measures within the Assessment Center library, as well as custom instruments created or entered by the researcher. PROMIS instruments (short forms, CATs, profiles) are a central feature of the instrument library within Assessment Center. Any PROMIS measure can be included in an online study or downloaded for administration on paper.

Detailed statistical information and development history about PROMIS items and instruments are available for review at nihpromis.org or assessmentcenter.net. To learn more, contact help@assessmentcenter.net.

Q: *Do I need to register with PROMIS to use these instruments?*

Yes, to get a copy of these instruments, we ask that you register with Assessment Center and endorse the PROMIS terms and conditions of use, so that we are better able to track who has accessed instruments for research. Assessment Center is available at assessmentcenter.net.

Q: *Are these instruments available in other languages?*

Yes, these instruments are currently available in Spanish in Assessment Center. The PROMIS group is also working to translate this form into other languages. Information on available translations is updated periodically at http://nihpromis.org/measures/translations.

Q: Can I make my own short form?

Yes, custom Social Isolation short forms can be made by selecting any items from the item bank. Instructions for creating a custom short form in Assessment Center can be found in the Assessment Center User Manual https://www.assessmentcenter.net/UserManuals.aspx.

Q: How do I handle multiple responses when administering a short form on paper?

Guidelines on how to deal with multiple responses have been established. Resolution depends on the responses noted by the research participant.

- If two or more responses are marked by the respondent, and they are next to one another, then a data entry specialist will be responsible for randomly selecting one of them to be entered and will write down on the form which answer was selected. *Note: To randomly select one of two responses, the data entry specialist will flip a coin (heads - higher number will be entered; tails – lower number will be entered).To randomly select one of three (or more) responses, a table of random numbers should be used with a statistician's assistance.*
- If two or more responses are marked, and they are NOT all next to one another, the response will be considered missing.

Q: *What is the minimum change on a PROMIS instrument that represents a clinically meaningful difference?*

This question is related to an area of active research in the PROMIS network, namely the determination of the "minimally important difference" or "MID" for a PROMIS instrument. A manuscript in the *Journal of Clinical Epidemiology* outlines the process for MIDs for adult PROMIS measures and estimates the MIDs for six PROMIS-Cancer scales: Yost, K. J., Eton, D. T., Garcia, S. F., & Cella, D. (2011). Minimally important differences were

estimated for six PROMIS-Cancer scales in advanced-stage cancer patients. *Journal of Clinical Epidemiology, 64(5)*, 507-16.

As described in that manuscript, the MID is a tool to enhance the interpretability of patient-reported outcomes and is often defined as the "the smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient's management" (Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. *Controlled Clinical Trials* 1989; 10(4):407-415).

APPENDIX-SCORING TABLES

Social Isolation 4a
Short Form Conversion Table

Raw Score	Scale Score	SE*
4	34.8	5.1
5	40.4	3.2
6	43.3	2.8
7	45.7	2.7
8	47.8	2.6
9	49.8	2.6
10	51.8	2.6
11	53.9	2.6
12	56.1	2.6
13	58.1	2.7
14	60.1	2.6
15	62.0	2.6
16	63.8	2.5
17	65.5	2.6
18	67.5	2.7
19	69.9	2.9
20	74.2	4.2

*SE = Standard Error on T-score metric
Adult version

Social Isolation 6a
Short Form Conversion Table

Raw Score	Scale Score	SE*
6	34.4	5.0
7	39.7	3.1
8	42.2	2.6
9	44.2	2.3
10	45.8	2.2
11	47.3	2.2
12	48.7	2.2
13	50.1	2.2
14	51.5	2.2
15	53.0	2.2
16	54.4	2.2
17	55.9	2.2
18	57.3	2.3
19	58.8	2.3
20	60.2	2.2
21	61.5	2.2
22	62.8	2.2
23	64.0	2.2
24	65.2	2.1
25	66.5	2.2
26	67.7	2.2
27	69.1	2.3
28	70.8	2.6
29	72.6	2.8
30	76.2	4.0

*SE = Standard Error on T-score metric

Social Isolation 8a
Short Form Conversion Table

Raw Score	Scale Score	SE*
8	33.9	4.9
9	39.1	3.0
10	41.4	2.4
11	43.1	2.1
12	44.4	2.0
13	45.7	1.9
14	46.8	1.9
15	47.9	1.9
16	48.9	1.9
17	50.0	1.8
18	51.0	1.8
19	52.0	1.9
20	53.1	1.9
21	54.2	1.9
22	55.3	1.9
23	56.4	1.9
24	57.5	1.9
25	58.6	1.9
26	59.6	1.9
27	60.7	1.9
28	61.7	1.9
29	62.6	1.8
30	63.6	1.8
31	64.5	1.8
32	65.4	1.8
33	66.3	1.8
34	67.2	1.8
35	68.2	1.9
36	69.2	2.0
37	70.4	2.1
38	71.8	2.4
39	73.4	2.6
40	76.9	3.9

*SE = Standard Error on T-score metric
Adult version

Appendix F

Lubben Social Network Scale – Revised

FAMILY: *Considering the people to whom you are related by birth, marriage, adoption, etc…*

1. How many relatives do you see or hear from at least once a month?
   0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

2. How often do you see or hear from the relative with whom you have the most contact?
   0 = *less than monthly* 1 = *monthly* 2 = *few times a month* 3 = *weekly* 4 = *few times a week*
   5 = *daily*

3. How many relatives do you feel at ease with that you can talk about private matters?
   0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

4. How many relatives do you feel close to such that you could call on them for help?
   0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

5. When one of your relatives has an important decision to make, how often do they talk to you about it? 0 = *never* 1 = *seldom* 2 = *sometimes* 3 = *often* 4 = *very often* 5 = *always*

6. How often is one of your relatives available for you to talk to when you have an important decision to make? 0 = *never* 1 = *seldom* 2 = *sometimes* 3 = *often* 4 = *very often* 5 = *always*

FRIENDSHIPS: *Considering all of your friends including those who live in your neighborhood…*

7. How many of your friends do you see or hear from at least once a month?
   0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

8. How often do you see or hear from the friend with whom you have the most contact?
   0 = *less than monthly* 1 = *monthly* 2 = *few times a month* 3 = *weekly* 4 = *few times a week*
   5 = *daily*

9. How many friends do you feel at ease with that you can talk about private matters?

0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

10. How many friends do you feel close to such that you could call on them for help? 0 = *none* 1 = *one* 2 = *two* 3 = *three or four* 4 = *five thru eight* 5 = *nine or more*

11. When one of your friends has an important decision to make, how often do they talk to you about it? 0 = *never* 1 = *seldom* 2 = *sometimes* 3 = *often* 4 = *very often* 5 = *always*

12. How often is one of your friends available for you to talk to when you have an important decision to make? 0 = *never* 1 = *seldom* 2 = *sometimes* 3 = *often* 4 = *very often* 5 = *always*

LSNS-R total score is an equally weighted sum of these twelve items. Scores range from 0 to 60.

Appendix G
Cystic Fibrosis Questionnaire - Revised

CFQ-R **Adolescents and Adults (Patients 14 Years Old and Older)**

CYSTIC FIBROSIS QUESTIONNAIRE - REVISED

Understanding the impact of your illness and treatments on your everyday life can help your healthcare team keep track of your health and adjust your treatments. For this reason, this questionnaire was specifically developed for people who have cystic fibrosis. Thank you for your willingness to complete this form.

Instructions: The following questions are about the current state of your health, as you perceive it. This information will allow us to better understand how you feel in your everyday life.

Please answer all the questions. There are **no** right or wrong answers! If you are not sure how to answer, choose the response that seems closest to your situation.

Section I. Demographics

Please fill-in the information or check the box indicating your answer.

A. What is your date of birth?

Date ☐☐ ☐☐ ☐☐☐☐
Mo Day Year

B. What is your gender?

☐ Male ☐ Female

C. During the **past two weeks**, have you been on vacation or out of school or work for reasons **NOT** related to your health?

☐ Yes ☐ No

D. What is your current marital status?

☐ Single/never married
☐ Married
☐ Widowed
☐ Divorced
☐ Separated
☐ Remarried
☐ With a partner

E. Which of the following best describes your racial background?

☐ Caucasian
☐ African American
☐ Hispanic
☐ Asian/Oriental or Pacific Islander
☐ Native American or Native Alaskan
☐ Other (please describe) _____
☐ Prefer not to answer this question

F. What is the highest grade of school you have completed?

☐ Some high school or less
☐ High school diploma/GED
☐ Vocational school
☐ Some college
☐ College degree
☐ Professional or graduate degree

G. Which of the following best describes your current work or school status?

☐ Attending school outside the home
☐ Taking educational courses at home
☐ Seeking work
☐ Working full or part time (either outside the home or at a home-based business)
☐ Full time homemaker
☐ Not attending school or working due to my health
☐ Not working for other reasons

Section II. Quality of Life

Please check the box indicating your answer.

*During the past **two weeks**, to what extent have you had difficulty:*	**A lot of difficulty**	**Some difficulty**	**A little difficulty**	**No difficulty**
1. Performing vigorous activities such as running or playing sports	☐	☐	☐	☐
2. Walking as fast as others	☐	☐	☐	☐
3. Carrying or lifting heavy things such as books, groceries, or school bags	☐	☐	☐	☐
4. Climbing one flight of stairs	☐	☐	☐	☐
5. Climbing stairs as fast as others	☐	☐	☐	☐

***During the past two weeks**, indicate how often:*	**Always**	**Often**	**Sometimes**	**Never**
6. You felt well	☐	☐	☐	☐
7. You felt worried	☐	☐	☐	☐
8. You felt useless	☐	☐	☐	☐
9. You felt tired	☐	☐	☐	☐
10. You felt energetic	☐	☐	☐	☐
11. You felt exhausted	☐	☐	☐	☐
12. You felt sad	☐	☐	☐	☐

Please circle the number indicating your answer. Please choose only one answer for each question.

*Thinking about the state of your health over the last **two weeks**:*

13. To what extent do you have difficulty walking?
1. You can walk a long time without getting tired
2. You can walk a long time but you get tired
3. You cannot walk a long time because you get tired quickly
4. You avoid walking whenever possible because it's too tiring for you

14. How do you feel about eating?
1. Just thinking about food makes you feel sick
2. You never enjoy eating
3. You are sometimes able to enjoy eating
4. You are always able to enjoy eating

15. To what extent do your treatments make your daily life more difficult?
1. Not at all
2. A little
3. Moderately
4. A lot

16. How much time do you currently spend each day on your treatments?
1. A lot
2. Some
3. A little
4. Not very much

17. How difficult is it for you to do your treatments (including medications) each day?
1. Not at all
2. A little
3. Moderately
4. Very

18. How do you think your health is now?
1. Excellent
2. Good
3. Fair
4. Poor

Please select a box indicating your answer.

*Thinking about your health during the past **two weeks**, indicate the extent to which each sentence is true or false for you.*	Very true	Somewhat true	Somewhat false	Very false
19. I have trouble recovering after physical effort	☐	☐	☐	☐
20. I have to limit vigorous activities such as running or playing sports	☐	☐	☐	☐
21. I have to force myself to eat	☐	☐	☐	☐
22. I have to stay at home more than I want to	☐	☐	☐	☐
23. I feel comfortable discussing my illness with others	☐	☐	☐	☐
24. I think I am too thin	☐	☐	☐	☐
25. I think I look different from others my age	☐	☐	☐	☐
26. I feel bad about my physical appearance	☐	☐	☐	☐
27. People are afraid that I may be contagious	☐	☐	☐	☐
28. I get together with my friends a lot	☐	☐	☐	☐
29. I think my coughing bothers others	☐	☐	☐	☐
30. I feel comfortable going out at night	☐	☐	☐	☐
31. I often feel lonely	☐	☐	☐	☐
32. I feel healthy	☐	☐	☐	☐
33. It is difficult to make plans for the future (for example, going to college, getting married, advancing in a job, etc.)	☐	☐	☐	☐
34. I lead a normal life	☐	☐	☐	☐

Section III. School, Work, or Daily Activities

Questions 35 through 38 are about school, work, or other daily tasks.

35. To what extent did you have trouble keeping up with your schoolwork, professional work, or other daily activities during the past **two weeks**?

1. You have had no trouble keeping up
2. You have managed to keep up but it's been difficult
3. You have been behind
4. You have not been able to do these activities at all

36. How often were you absent from school, work, or unable to complete daily activities during the last two weeks because of your illness or treatments?

☐ Always ☐ Often ☐ Sometimes ☐ Never

37. How often does CF get in the way of meeting your school, work, or personal goals

☐ Always ☐ Often ☐ Sometimes ☐ Never

38. How often does CF interfere with getting out of the house to run errands such as shopping or going to the bank?

☐ Always ☐ Often ☐ Sometimes ☐ Never

Section IV. Symptom Difficulties

Please select a box indicating your answer.

*Indicate how you have been feeling during the past **two weeks**.*	**A great deal**	**Somewhat**	**A little**	**Not at all**
39. Have you had trouble gaining weight?	☐	☐	☐	☐
40. Have you been congested?	☐	☐	☐	☐
41. Have you been coughing during the day?	☐	☐	☐	☐
42. Have you had to cough up mucus?	☐	☐	☐	☐ Go to Question 44

43. Has your mucus been mostly: ☐ Clear ☐ Clear to yellow ☐ Yellowish-green ☐ Green with traces of blood ☐ Don't know

*How often during the past **two weeks**:*	**Always**	**Often**	**Sometimes**	**Never**
44. Have you been wheezing?	☐	☐	☐	☐
45. Have you had trouble breathing?	☐	☐	☐	☐
46. Have you woken up during the night because you were coughing?	☐	☐	☐	☐
47. Have you had problems with gas?	☐	☐	☐	☐
48. Have you had diarrhea?	☐	☐	☐	☐
49. Have you had abdominal pain?	☐	☐	☐	☐
50. Have you had eating problems?	☐	☐	☐	☐

Please be sure you have answered all the questions.

THANK YOU FOR YOUR COOPERATION!

Appendix H
Participant REDCap Survey

Confidential

Cystic Fibrosis Patient Survey

This survey is part of a research study that will provide information about how adults with cystic fibrosis experience social isolation. There are two parts to this study: 1) this survey (which will take approximately 15 minutes to complete) and 2) an interview that you have the option of participating in on the next screen. Your participation in this study is strictly voluntary. You may choose to withdrawal from this study at any time. There are minimal risks associated with this study, including a possible loss of confidentiality, and that some of the questions may be upsetting. We take every precaution to protect your confidentiality, information, and responses. Participants completing the survey portion of this study will be provided with an electronic $5 Amazon gift card via email. If you have questions about this research study, please contact Amy Gulledge by phone at (843) 792-9237 or email at gulledge@musc.edu.

Do you wish to continue to take the survey?

◯ Yes
◯ No

Are you 18 years or older?

◯ Yes
◯ No

Have you been diagnosed with cystic fibrosis?

◯ Yes
◯ No

About You

After completing this survey, you have the opportunity to participate in the interview portion of this study. During the interview, we will ask you questions about your experience with social isolation and social support. Interviews will take place either by phone or video chat and may last 30-45 minutes. Participants completing the interview portion of this study will receive an additional $5 electronic Amazon gift card (in addition to the gift card received for completing the survey). Your participation in this interview is voluntary and you may choose not to participate at any time. Are you interested in participating in an interview?

◯ Yes
◯ No

Your preferred name (this information will only be used to schedule an interview): _____

Please enter your preferred phone number or email for scheduling an interview.

_____

Are you interested in participating in future, similar studies exploring your experiences with socialization and interacting with others? (This information is only being collected for purposes of this current study)

◯ Yes
◯ No

How old are you?

(please select your age using the drop-down)

- ◯ 18
- ◯ 19
- ◯ 20
- ◯ 21
- ◯ 22
- ◯ 23
- ◯ 24
- ◯ 25
- ◯ 26
- ◯ 27
- ◯ 28
- ◯ 29
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◯ 105
◯ 106
◯ 107
◯ 108
◯ 109
◯ 110
◯ 111
◯ 112
◯ 113
◯ 114
◯ 115
◯ 116+
◯ Unknown
◯ Prefer not to say

What is your gender?

◯ Male
◯ Female
◯ Non-binary
◯ Prefer to self-describe_____(please specify)
◯ Prefer not to answer

What is your gender?

_____

What is your current marital status?

◯ Single/never married
◯ Married
◯ Widowed
◯ Divorced
◯ Separated
◯ Remarried
◯ With a partner

Which of the following best describes your racial background?

◯ American Indian or Alaskan Native
◯ Asian
◯ Black or African American
◯ Hispanic or Latino
◯ Native Hawaiian or Other Pacific Islander
◯ White
◯ Other_____(please specify)
◯ Prefer not to answer

If other, please describe:

_____

Which is the highest grade of school you have completed?

◯ Some high school or less
◯ High school diploma/GED
◯ Vocational school
◯ Some college
◯ College degree
◯ Professional or graduate degree

What is your current zip code?

_____

What type of health insurance do you have?

◯ No insurance
◯ Medicaid
◯ Medicare
◯ Private or employer insurance
◯ Other_____ (please specify)
◯ Do not know

If other type of insurance please tell us what it is.

_____

Do you know your most recent FEV1 (forced expiratory volume)?

◯ Yes
◯ No

What was your most recent FEV1? Enter the numerical value only (ex. 88):

_____

If you do not know your most recent FEV1, do you know which of the following ranges it falls under?

◯ Greater than 90%
◯ 70-90%
◯ 40-69%
◯ Less than 40%
◯ Do not know

Do you use oxygen?

◯ Yes
◯ No

How many liters of oxygen do you usually use?

◯ Less than 1 liter
◯ 1-3 liters
◯ 4-6 liters
◯ 7-9 liters
◯ 10 or more liters
◯ Do not know

When do you use your oxygen?

◯ Only when needed
◯ At night
◯ During activity
◯ All the time

Do you take a CFTR modulator medication, such as ivacaftor (Kalydeco), lumacaftor/ivacaftor (Orkambi), tezacaftor/ivacaftor (Symdeko), or elexacaftor/tezacaftor/ivacaftor (Trikafta)?

◯ Yes
◯ No
◯ Do not know

How many overnight hospitalizations related to cystic fibrosis have you had in the past year?

◯ 0
◯ 1-3
◯ 4-6
◯ 7-9
◯ 10 or more
◯ Do not know

Have you had a lung transplant?

◯ Yes
◯ No
◯ Do not know

Are you scheduled for a lung transplant or on the waiting list to receive one?

◯ Yes
◯ No

Social Media Use

Do you use either internet-based social media or online support groups?

◯ I only use social media
◯ I only use online support groups
◯ I use both social media and online support groups
◯ I do not use social media or online support groups

On a typical day, which of the following best describes how often you use social media and/or online support groups?

◯ Multiple times a day
◯ 1-2 times a day
◯ A few times a week
◯ A few times a month
◯ It varies
◯ Do not know

Which of the following best describes your activity when you use social media or online support groups? Select all that apply to you.

☐ Scrolling and reading posts by other people
☐ Reading about news and current events
☐ Posting personal stories, pictures, updates, etc.
☐ Keeping in contact with friends and family
☐ Participating in online discussions
☐ Asking for recommendations or guidance
☐ Support from others with cystic fibrosis
☐ Other_____ (please specify)

If you participate in another type of social media/online support group activity not listed, please include here.

_____

How satisfied are you with the support you receive from social media and/or online support groups?

◯ Very satisfied
◯ Satisfied
◯ Dissatisfied
◯ Very dissatisfied

Cystic FIbrosis Questionnaire-Revised

Instructions: The following questions are about the current state of your health, as you perceive it. This information will allow us to better understand how you feel in your everyday life. Please answer all the questions. There are no right or wrong answers! If you are not sure how to answer, choose the response that seems closest to your situation.

During the past 2 weeks, have you been on vacation or out of school or work for reasons NOT related to your health?

◯ Yes
◯ No

Which of the following best describes your current work or school status?

◯ Attending school outside the home
◯ Taking educational courses at home
◯ Seeking work
◯ Working full or part time (either outside the home or at a home-based business)
◯ Full time homemaker
◯ Not attending school or working due to my health
◯ Not working for other reasons

During the past two weeks, to what extent have you had difficulty:				
	A lot of difficulty	Some difficulty	A little difficulty	No difficulty
Performing vigorous activities, such as running or playing sports	○	○	○	○
Walking as fast as others	○	○	○	○
Carrying or lifting heavy things such as books, groceries, or school bags	○	○	○	○
Climbing one flight of stairs	○	○	○	○
Climbing stairs as fast as others	○	○	○	○

During the past two weeks, indicate how often:				
	Always	Often	Sometimes	Never
You felt well	○	○	○	○
You felt worried	○	○	○	○
You felt useless	○	○	○	○
You felt tired	○	○	○	○
You felt energetic	○	○	○	○
You felt exhausted	○	○	○	○
You felt sad	○	○	○	○

Thinking about the state of your health over the last two weeks:

To what extent do you have difficulty walking?

◯ You can walk a long time without getting tired
◯ You can walk a long time but you get tired
◯ You cannot walk a long time because you get tired quickly
◯ You avoid walking whenever possible because it's too tiring for you

How do you feel about eating?

◯ Just thinking about food makes you feel sick
◯ You never enjoy eating
◯ You are sometimes able to enjoy eating
◯ You are always able to enjoy eating

To what extent do your treatments make your daily life more difficult?

◯ Not at all
◯ A little
◯ Moderately
◯ A lot

How much time do you currently spend each day on your treatments?

◯ A lot
◯ Some
◯ A little
◯ Not very much

How difficult is it for you to do your treatments (including medications) each day?

◯ Not at all
◯ A little
◯ Moderately
◯ Very

How do you think your health is now?

◯ Excellent
◯ Good
◯ Fair
◯ Poor

Thinking about your health during the past two weeks, indicate the extent to which each sentence is true or false for you.

	Very true	Somewhat true	Somewhat false	Very false
I have trouble recovering after physical effort	○	○	○	○
I have to limit vigorous activities such as running or playing sports	○	○	○	○
I have to force myself to eat	○	○	○	○
I have to stay at home more than I want to	○	○	○	○
I feel comfortable discussing my illness with others	○	○	○	○
I think I am too thin	○	○	○	○
I think I look different from others my age	○	○	○	○
I feel bad about my physical appearance	○	○	○	○
People are afraid that I may be contagious	○	○	○	○
I get together with my friends a lot	○	○	○	○
I think my coughing bothers others	○	○	○	○
I feel comfortable going out at night	○	○	○	○
I often feel lonely	○	○	○	○
I feel healthy	○	○	○	○
It is difficult to make plans for the future (for example, going to college, getting married, advancing in a job, etc.)	○	○	○	○
I lead a normal life	○	○	○	○

To what extent did you have trouble keeping up with your schoolwork, professional work, or other daily activities during the past two weeks?

☐ You have had no trouble keeping up
☐ You have managed to keep up but it's been difficult
☐ You have been behind
☐ You have not been able to do these activities at all

	Always	Often	Sometimes	Never

How often were you absent from school, work, or unable to complete daily activities during the last two weeks because of your illness or treatments?	○	○	○	○
How often does CF get in the way of meeting your school, work, or personal goals?	○	○	○	○
How often does CF interfere with getting out of the house to run errands such as shopping or going to the bank?	○	○	○	○

Indicate how you have been feeling during the past two weeks				
	A great deal	Somewhat	A little	Not at all
Have you had trouble gaining weight?	◯	◯	◯	◯
Have you been congested?	◯	◯	◯	◯
Have you been coughing during the day?	◯	◯	◯	◯
Have you had to cough up mucus?	◯	◯	◯	◯

Has your mucus been mostly:

◯ Clear
◯ Clear to yellow
◯ Yellowish-green
◯ Green with traces of blood
◯ Don't know

How often during the past two weeks:				
	Always	Often	Sometimes	Never
Have you been wheezing?	○	○	○	○
Have you had trouble breathing?	○	○	○	○
Have you woken up during the night because you were coughing?	○	○	○	○
Have you had problems with gas?	○	○	○	○
Have you had diarrhea?	○	○	○	○
Have you had abdominal pain?	○	○	○	○
Have you had eating problems?	○	○	○	○

Lubben Social Network Scale (Revised Version) FAMILY

Considering the people to whom who are related by birth, marriage, adoption, etc.

How many relatives do you see or hear from at least once a month?

- ◯ None
- ◯ 1
- ◯ 2
- ◯ 3 or 4
- ◯ 5-8
- ◯ 9 or more

How often do you see or hear from the relative with whom you have the most contact?

- ◯ Less than monthly
- ◯ Montly
- ◯ Few times a month
- ◯ Weekly
- ◯ Few times a week
- ◯ Daily

How many relatives do you feel at ease with that you can talk about private matters?

- ◯ None
- ◯ 1
- ◯ 2
- ◯ 3 or 4
- ◯ 5-8
- ◯ 9 or more

How many relatives do you feel close to such that you could call on them for help?

- ◯ None
- ◯ 1
- ◯ 2
- ◯ 3-4
- ◯ 5-8
- ◯ 9 or more

When one of your relatives has an important decision to make, how often do they talk to you about it?

- ◯ Never
- ◯ Seldom
- ◯ Sometimes
- ◯ Often
- ◯ Very often
- ◯ Always

How often is one of your relatives available for you to talk to when you have an important decision to make?

- ◯ Never
- ◯ Seldom
- ◯ Sometimes
- ◯ Often
- ◯ Very often
- ◯ Always

Lubben Social Network Scale (Revised Version): FRIENDSHIPS

Considering all of your friends including those who live in your neighborhood...

How many of your friends do you see or hear from at least once a month?

- ◯ None
- ◯ 1
- ◯ 2
- ◯ 3-4
- ◯ 5-8
- ◯ 9 or more

How often do you see or hear from the friend with whom you have the most contact?

- ◯ Less than monthly
- ◯ Monthly
- ◯ Few times a month
- ◯ Weekly
- ◯ Few times a week
- ◯ Daily

How many friends do you feel at ease with that you can talk about private matters?

- ◯ None
- ◯ 1
- ◯ 2
- ◯ 3-4
- ◯ 5-8
- ◯ 9 or more

How many friends do you feel close to such that you could call on them for help?

- ◯ None
- ◯ 1
- ◯ 2
- ◯ 3-4
- ◯ 5-8
- ◯ 9 or more

When one of your friends has an important decision to make, how often do they talk to you about it?

- ◯ Never
- ◯ Seldom
- ◯ Sometimes
- ◯ Often
- ◯ Very often
- ◯ Always

How often is one of your friends available for you to talk to when you have an important decision to make?

- ◯ Never
- ◯ Seldom
- ◯ Sometimes
- ◯ Often
- ◯ Very often
- ◯ Always

PROMIS Social Isolation Scale

Please respond to each item by marking one box per row

	Never	Rarely	Sometimes	Usually	Always
I feel left out	○	○	○	○	○
I feel that people barely know me	○	○	○	○	○
I feel isolated from others	○	○	○	○	○
I feel that people are around me but not with me	○	○	○	○	○
I feel isolated even when I am not alone	○	○	○	○	○
I feel detached from other people	○	○	○	○	○
I feel like a stranger to those around me	○	○	○	○	○
I feel that people avoid talking to me	○	○	○	○	○

Impact of the coronavirus (COVID-19)

Please answer the following questions based on how you feel since the coronavirus (COVID-19) pandemic started.

Since the coronavirus (COVID-19) pandemic has begun, how many relatives, friends, or neighbors do you see or hear from at least once a month?

◯ None
◯ 1
◯ 2
◯ 3-4
◯ 5-8
◯ 9 or more

Since the coronavirus (COVID-19) pandemic has begun, how often do you see or hear from the relatives, friends, or neighbors with whom you have the most contact?

◯ Less than monthly
◯ Monthly
◯ Few times a month
◯ Weekly
◯ Few times a week
◯ Daily

Since the coronavirus (COVID-19) pandemic has begun, who is providing you with social support? (Mark all that apply)

☐ Someone I live with
☐ Relative, friend, or neighbor who comes by my place
☐ Relative, friend, or neighbor who I talk with on the phone (or video chat)
☐ Other _____ (please specify)

If other, please enter who else is providing you with social support:

_____

Has the coronavirus (COVID-19) pandemic had a significant impact on your ability to socialize or interact with others?

◯ Yes, a lot
◯ Yes, somewhat
◯ Not at all

Thank you for participating in this survey. Your participation and responses will remain confidential. To receive your electronic $5 Amazon gift card, please enter your preferred email address.

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