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UNIVERSITY OF MIAMI

PAIN AND HEALTH-RELATED QUALITY OF LIFE IN ADOLESCENTS WITH CYSTIC FIBROSIS

By

Laura Sheldon Blackwell

A DISSERTATION

Submitted to the Faculty
of the University of Miami
in partial fulfillment of the requirements for
the degree of Doctor of Philosophy

Coral Gables, Florida

August 2013

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Laura Sheldon Blackwell

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BLACKWELL, LAURA S. (Ph.D., Psychology)
Pain and Health-Related Quality of Life in Adolescents with Cystic Fibrosis (August 2013)

Abstract of a dissertation at the University of Miami.

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Objective: CF is a progressive, life-shortening disease treated primarily with palliative medications. Among the consequences of the disease's progression and daily treatments are discomfort and pain. Previous studies have suggested that pain is common in patients with CF; however, little is known about the factors associated with this pain or its impact on clinical outcomes. The relationships between pain and health outcomes over time, such as adherence and health-related quality of life (HRQOL), are largely unknown in this population. The purpose of this study was to systematically assess pain in adolescents with CF and evaluate its associations with adherence, social support, and HRQOL over a six-month period.

Methods: The current study is part of a multi-center NIH SBIR Phase II randomized, controlled trial. The sample consisted of 95 participants, with a mean age of 15.69. Participants completed a battery of measures during three consecutive clinic visits, approximately 3 months apart. Participants also completed an online pain diary for the 6 days following each clinic visit. Diaries assessed pain intensity, location, duration, affective rating, and coping responses.

Results: Overall, 73% of participants completed one or more of the online pain diaries across these time points, with 44% of the sample completing all six diaries. Pain was reported by 74.5% of participants. Of those who experienced pain, intensity was

generally mild. Daily pain ratings, as assessed by online diaries, were highly variable within participants. Path analyses indicated that worse treatment adherence and poor social functioning were directly related higher pain and ultimately related to worse HRQOL.

Conclusions: These results indicated that pain is common in adolescents with CF and that it interferes significantly with HRQOL. Treatment adherence appears to be particularly predictive of pain in this population. Regular assessment of pain and HRQOL is recommended.

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Chapter 1: Introduction

Cystic Fibrosis (CF) is a life-shortening, genetic disease affecting all racial and ethnic populations, with a higher prevalence among Caucasians. An estimated 30,000 individuals in the United States have CF, with slightly more than half (52%) under the age of 18 years (Cystic Fibrosis Foundation, 2011). CF is a progressive disease caused by a recessive gene, and affects multiple organs including the lungs, pancreas and digestive systems. Although life span has increased dramatically in the last 20 years, modal age of death is still in the mid-20's, patients with CF inevitably experience more frequent pulmonary exacerbations, requiring intravenous antibiotics and hospitalizations, and a decline in lung function leading to earlier mortality (Cystic Fibrosis Foundation, 2011).

Treatment of CF is primarily palliative and requires multiple medications and treatments, which can take between two and four hours per day (Quittner, Alpern, & Blackwell, 2012). Considerable progress has been made in developing effective medications to treat the critical pulmonary and digestive symptoms associated with CF, including airway clearance, inhaled antibiotics, oral medications, and increased calorie intake. These treatments are invasive and uncomfortable and further the process of chronic inflammation and infection can lead to frequent and lengthy hospitalizations. Pain and discomfort are among the consequences of the disease's progression and treatments.

Previous studies in CF have shown that pain is frequent in both adults (Bilton, Landy, Gunn & Saunders, 2001; Festini, Ballarin, Codamo, Doro, & Loganes, 2004; Hayes, Yasrer, Haythornthwaite, Riekert, McMillan, White, et al., 2012) and children

(Koh, Harrison, Palermo, Turner, & McGraw, 2005; Ravilly, Robinson, Suresh, Wohl, & Berde, 1996; Sermet-Gaudelus, De Villartay, de Dreuzy, Clairicia, Vrielynck, Canoui, et al., 2009). However, detailed information about the severity, intensity and location of pain are not well known and few studies have examined its long-term consequences on patient-reported outcomes, such as health-related quality of life (HRQOL). Thus, the current study measured the frequency and intensity of pain in adolescents with CF and systematically measured its longitudinal relationship with HRQOL.

Pain in Cystic Fibrosis

CF affects the functioning of several organ systems, which can result in significant discomfort and pain. Due to a defective gene, individuals with CF lack a protein (cystic fibrosis transmembrane regulator; CFTR) needed to regulate the exchange of salt and water across the cell membrane. This leads to thick, sticky mucus secretions in the respiratory, digestive, pancreatic, and reproductive systems. Over time, thick mucus clogs the bronchi that carry air in and out of the lungs, causing persistent coughing, wheezing, mucus production, inflammation and recurrent infections. Additionally, mucus blocks tubes within the digestive track that carry enzymes from the pancreas to the small intestine. Thus, nutrients are not efficiently absorbed from food, resulting in poor weight gain and growth, abnormal stools, constipation, and intestinal blockage (Quittner, Barker, Marciel, & Grimley, 2009; Wilmott, Boat, Bush, Chernick, Deterding, & Ratjen, 2012). Females with CF may have difficulty getting pregnant due to thick vaginal secretions and 99% of males with CF are sterile due to blocking of the vas deferens in utero. Pain may result directly from these chronic symptoms of chest infections and poor digestion (e.g. abdominal cramping) or from physiological changes in

affected organs (e.g. headaches from sinusitis and musculoskeletal pain).

Over time, the lungs are further damaged by chronic inflammation and infections (i.e. due to colonization with *Pseudomonas aeruginosa* or other bacteria) from the accumulation of mucus. This process leads to a variety of symptoms, including persistent cough, congestion, and mucus production. Structural changes to the lungs and increased scarring and tissue damage lead to increased respiratory symptoms and a decline in lung function Irreversible damage occurs in the pancreas and liver (Davies, Alton, & Bush, 2007), leading to a greater risk for development of CF-related diabetes (CFRD) in adolescence and adulthood, as well as liver disease.

Medical advances have led to the development of new treatments to manage these symptoms, including the development of new inhaled antibiotics (Retsch-Bogart, Quittner, Gibson, Oermann, McCoy, Montgomery, et al., 2009) and mucolytics (Donaldson, Bennett, Zeman, Knowles, Tarran, & Boucher, 2006). Treatments, such as airway clearance, break up the thick, sticky mucus secretions that build up in the lungs and are effective in reducing respiratory symptoms (Agnew & McIlwaine, 2012). Additionally, inhaled and IV antibiotics are used to treat pulmonary infections which occur with increasing frequency (Wilmott, et. al., 2012). Many of these treatments, including airway clearance, inhaled antibiotics and use of hypertonic saline can cause coughing and irritation in the lungs. Airway clearance, which can be performed using a vest that delivers high frequency chest wall vibrations, can cause discomfort and pressure on the chest due to intense chest compressions. Finally, these patients have frequent blood draws, IV antibiotics, and insertions of peripherally inserted central catheters (PICC) lines.

Although pain is known to occur in this population, its prevalence has received little attention. One of the first studies to measure pain in CF found that 84% of sicker, younger patients reported experiencing pain. Additionally, they found that pain was most commonly experienced in the chest and head (Ravilly, et al., 1996). Although this was the first study of pain in CF, it was limited by the use of retrospective chart review and a small sample of patients. Thus, it captured only serious episodes of pain.

In a larger study of adults with CF, 94% of patients reported that they had had episodes of pain in the previous two months (Festini, et al., 2004). Of these patients, over 32% reported that these pain experiences were intense and severe, with headache, gastric pain, and backache reported as most common. Interestingly, only 43% of those with pain asked a CF Center physician for help. Authors speculated that CF clinics may have difficulty effectively addressing and treating pain and therefore, patients are not motivated to ask for help. This study had a considerably larger sample size, with over 200 patients; however it was limited in its measurement of pain, neglecting to include procedural pain.

Significant pain has also been reported in children and adolescents with CF. Koh and colleagues (2005) found that those with mild disease, as indicated by body mass index (BMI) and lung function (FEV_1%), commonly experienced low-intensity but frequent pain, particularly in the abdomen, chest and neck. Furthermore, they reported experiencing pain during common CF-related medical procedures, such as blood draws, PICC line placement, and pulmonary function tests (PFTs). Common pain locations included abdominal/pelvic region, chest, and head/neck, respectively. The majority of children stated that they managed their pain through rest, medication, relaxation, and

support from family and friends. Although this was one of the first studies to assess pain more comprehensively in children and adolescents, its methodology was limited by reliance on retrospective reports of pain (one month prior).

A more recent study specifically examined general and procedural pain in both children and adults with CF (Sermet-Gaudelus et al., 2009). Results indicated that a considerable number of children (59%) reported at least one episode of general pain in the prior month. Chronic pain was reported in children as young as three years and pain increased in prevalence significantly after the age of eight. This suggested that assessment of the progression of pain in older children and adolescents warrants attention. Further, 85% of children reported at least one episode of procedural pain in the previous month, and these episodes became significantly more frequent in those with severe disease. Pain during chest physiotherapy was reported by 28% of children, almost 60% of children reported pain during regular blood draws, and nearly 80% during capillary blood sampling. Results from this study suggested it is important to distinguish between general and procedural pain, and to measure pain episodes in older children and adolescents because of the progression of their disease. Although this study provided important descriptive information, it was cross-sectional and retrospective in its design. In contrast, the current study measured pain longitudinally through repeated sampling of pain in real time in an adolescent population.

Pain and HRQOL

Untreated acute, recurrent, or chronic pain has been found to have lifelong physiological and psychological consequences, leading to poor quality of life, particularly in children and adolescents (Frank, Kleinman, Rentz, Ciesla, Kim, & Zacker, 2002;

Skevington, 1998). Despite the documentation of these consequences in pediatric populations, studies of pain and its relationship to HRQOL in individuals with CF is scarce. Understanding this relationship is a critical step toward developing effective interventions to treat pain and potentially improve HRQOL.

HRQOL is a multidimensional construct with four core domains including: 1) disease state and physical symptoms, 2) functional status, 3) psychological and emotional functioning, and 4) social functioning (Quittner, Cruz, Modi, & Marciel, 2009). HRQOL measures have been used to quantify the effects of chronic illness and its impact on patients' daily functioning. Reliable, valid, disease-specific measures of HRQOL for CF have been recently developed. The Cystic Fibrosis Questionnaire-Revised (CFQ-R; Quittner, Buu, Messer, Modi, & Watrous, 2005; Quittner, Sawicki, McMullen, Rasouliyan, Pasta, Yegin, et al., 2012) is currently the most widely-used HRQOL instrument for CF and was rated "well-established" in a recent review (Palermo, Long, Lewandowski, Drotar, Quittner & Waller, 2008). The CFQ-R has not only been translated into 34 languages, with validation studies in the US, Europe and Australia, but has demonstrated responsivity in several clinical trials of medications with different mechanisms of action (e.g., antibiotics, mucus hydrators, gene potentiators) (Donaldson, et al., 2006; Elkins, Robinson, Rose, Harbour, Moriarty, Marks, et al., 2006; Ramsey, Davies, McElvaney, Tullis, Bell, Dřevínek, et al., 2011; Retsch-Bogart et al., 2009).

In adults with CF, Hayes and colleagues (2011) found that pain interfered with general activities, internalizing symptoms, and work functioning. Symptoms of depression and anxiety, as well as lower HRQOL scores on the CFQ-R, were associated with greater pain intensity. Further, pulmonary exacerbations and the risk of death were

greater in patients with higher pain intensity scores. This study yielded important information about the clinical significance of pain in adults with CF.

Palermo and colleagues (2006) also measured pain and HRQOL in children with CF. In a small sample of children and adolescents (N = 46), pain symptoms were associated with significant decrements in HRQOL. Specifically, those children with more frequent pain had worse scores on the Physical and Social functioning scales of the CFQ-R, worse Respiratory Symptoms and worse overall Health Perceptions, compared to children with no or infrequent pain. Furthermore, frequent pain had a stronger effect on HRQOL than disease severity, as measured by pulmonary function tests. Although this study was the first to systematically measure pain in relation to HRQOL in children, it was limited by a small sample size and retrospective reports of pain. Additionally, the cross-sectional design limited any conclusions about causal relationships. In contrast, the current study sought to expand our understanding of the effects of pain on adolescents with CF by recruiting a larger sample, using real-time pain diaries, and measuring trajectories of pain over time.

Factors Influencing Pain

It is widely recognized that when children have a chronic illness, such as CF, its course is jointly influenced by physical, psychological, and social factors (Beale, 2006). Biopsychosocial models of pain have long recognized the importance of psychological and environmental factors, such as social support and internalizing symptoms, as moderators of pain outcomes in children and adolescents. Although biomedical factors, such as acute infection or adherence to airway clearance, often activate initial reports of pain, psychosocial factors, such as social support, often play a role in both the

perceptions and course of pain episodes (Turk & Melzack, 2001). Thus, psychosocial factors that influence pain should be identified to better address both acute pain episodes and their impact on HRQOL.

Treatment adherence-related pain. Adherence to medical regimens in adolescents with CF is a significant challenge, directly affecting their HRQOL (Quittner, 1998). Due to the complex and demanding regimen they must perform, rates of adherence are quite low (Briesacher, Quittner, Saiman, Sacco, Fouayzi, & Quittell, 2011; Modi, Cassedy, Quittner, Accurso, Sontag, Koenig, et al., 2010; Modi & Quittner, 2006), leading to a variety of negative consequences, such as increased hospitalizations, school absences, increased health-care costs and potentially, increased pain. Rates of adherence for children and adolescents with CF are estimated to be between 40–47% for chest physical therapy, (Passero, Remor, & Solomon, 1981; Quittner, Espelage, Ievers-Landis, & Drotar, 2000; Smith, Modi, Quittner, & Wood, 2010), whereas adherence to dietary recommendations is even lower, ranging from 11 to 34% (Stark & Powers, 2005).

A number of barriers have been documented in relation to poor adherence, including knowledge of disease management, patient-provider communication, side-effects, and regimen characteristics (Modi & Quittner, 2006). Although no studies have specifically measured pain or uncomfortable side effects in relation to adherence in adolescents with CF, one possibility is that those who are less adherent to medications, may report more intense and/or frequent pain. The current study was the first to examine this relationship between adherence and pain in a CF population.

Social support. Laboratory and clinic-based studies have shown a strong relationship between social support and pain in adolescents (Brown, Sheffield, Leary, &

Robison, 2003; Holtzman, Newth, & Delongis, 2004), with poor social support associated with more frequent and intense pain. However, adolescents with CF have less opportunity to receive social support due to frequent hospitalizations and current infection control guidelines that require segregation of patients with CF from one another, to limit the spread of multi-resistant organisms (Saiman & Siegel, 2003). Given that previous research has demonstrated that social support can reduce experiences of pain, infection control policies and frequent school absences for hospitalizations may limit social support as a means of reducing pain. Web-based social networks may facilitate social connections among these teens. Thus, one aim of the current study was to examine a social networking website in relation to perceived support and pain in adolescents with CF.

Measurement of Pain

Pain diaries are considered the "gold standard" for measuring pain in children and adolescents (Cohen, Lemanek, Blount, Dahlquist, Lim, Palermo, et al., 2008; Palermo, Valenzuela, & Stork, 2004). Studies have consistently shown that prospective pain diaries yield better accuracy and less recall bias than retrospective measures and thus, have greater validity (Gil, Shand, Fuggle, Dugan, & Davies, 1997; Modi & Quittner, 2006). In addition, patients tend to overestimate their "remembered" pain due to the biasing influence of psychosocial stressors and the severity of their pain. Therefore, pain diaries are the preferred approach to measuring pain frequency, intensity, duration, and activity limitations than single, retrospective assessments (Palermo & Valenzuela, 2003; van den Brink, Bandell-Hoekstra & Abu-Saad, 2001).

Paper diaries have been used extensively to measure pain in various populations, including cancer, sickle cell and chronic pain. The Pain Diary (Hunfeld, van der Wouden, den Deurwaarder, van Suijlekom-Smit, & Hazebroek-Kampschreur, 1997), a paper-based diary, was initially developed to assess the intensity, frequency, and duration of general pain in children. Ratings of pain are conducted at specified times throughout the day and focus primarily on recurrent pain. This measure, however, is limited to ages 12 through 18, with a parent proxy form for children younger than 12 years. The Pain Diary was assigned a rating of "approaching well-established" according to the Chambless criteria (Cohen, at al., 2008).

A disease-specific pain diary, the Daily Pain Diary (Gil, 1994), was developed specifically to measure daily pain occurrences in children with sickle cell disease. This diary was one of the first to measure the pain experience more specifically, rather than using global ratings of pain. However, these paper-based pain diaries have several limitations, including a higher likelihood of incomplete and missing information, and poor adherence to the protocol because it is completed at home. In a study conducted by Palermo and colleagues (2004), paper diaries resulted in more missing data, contained more errors and omissions, and had fewer completed entries than an electronic version of the same diary. This study suggested that electronic diaries are more feasible with children and adolescents, in terms of both adherence to the assessment protocol and the accuracy of their pain ratings.

In contrast, electronic versions of diaries have recently been developed to measure treatment adherence (Modi & Quittner, 2006), anxiety (Henker, Whalen, & Jamner, 2002), and risk behaviors in adolescents (Whalen, Jamner, Henker, & Delfino, 2001).

However, few studies have utilized an electronic diary to measure pain in children and adolescents, and limited information is available regarding the development, feasibility and validity of these approaches. McClellan and colleagues (2009) utilized a smartphone device with a pain diary application in patients with sickle cell disease. Participants completed a daily pain intensity rating in addition to reporting the location of their pain for an eight week period. Results revealed better participation, increased diary completion, and higher consumer satisfaction with this smartphone diary application.

An electronic diary, using a Personal Digital Assistant (PDA) device, was also developed specifically for adolescents with arthritis (Stinson, Stevens, Feldman, Streiner, McGrath, Dupuis, et al., 2008). Results of this study indicated that overall compliance with the pain diaries was 78% and that participants found the device quick and easy to use. However, both of these electronic pain diaries used devices that were purchased for the study. These devices are not only expensive, but require the patient to have the device with them when making an entry. They are also susceptible to breakage and malfunction. In contrast, web-based diary methods may provide a more user-friendly, less expensive, and more accessible method of measuring pain. Thus, the current study measured pain in a comprehensive way using a diary sent to participants on an accessible website.

The Current Study

To obtain a comprehensive understanding of pain in adolescents with CF, it must be measured systematically and monitored over time in relation to associated variables, such as disease severity, treatment adherence, social support, and HRQOL. Based on previous literature, all of these variables may influence the frequency and severity of

pain. To date, however, few studies have examined pain in this population and no studies have examined its long-term consequences on disease management or health outcomes. The following objectives and hypotheses were evaluated.

Study Aims and Hypotheses.

1. The first aim was to systematically measure the prevalence, intensity, and location of pain and how patients coped with these pain episodes.
    a. Hypothesis 1: Adolescents with CF were expected to report more general and procedure-related pain and greater pain intensity, than the general population, using normative data collected by Perquin and colleagues (2000).
    b. Hypothesis 2: The most frequent pain locations were expected to be in the head, chest, and stomach.
2. The second aim was to assess the cross-sectional relationships between treatment adherence, social support, pain and HRQOL at Baseline using a path analysis in structural equation modeling (SEM).
    a. Hypothesis 3: Poor social support was expected to predict worse overall pain and worse HRQOL.
    b. Hypothesis 4: Adherence was expected to be associated with worse overall pain and worse HRQOL.
    c. Hypothesis 5: Pain was expected to mediate the relationship between social support and HRQOL, as well as treatment adherence and HRQOL.

3. The third aim was to measure the relationship between pain and HRQOL over time, by modeling the trajectory of its occurrence across a six-month period using a Latent Difference Score Analysis (LDS).
    a. Hypothesis 6: Pain intensity was expected to be negatively associated with three domains of functioning on the CFQ-R: Social Functioning, Treatment Burden and Respiratory Symptoms, administered over three time points, after controlling for adherence.
    b. Hypothesis 7: Those randomized to the CFfone™ intervention (Treatment condition) were expected to report decreases in pain and increases in HRQOL over time, compared to those in the Comparison condition (i.e., educational website); the Comparison group was expected to remain stable over time.

Chapter 2: Methods

Procedure

This study was part of a larger investigation funded by the National Institutes of Health (R44 SBIR Phase 2 to PI Kevin Dawkins; Co-PI Alexandra L. Quittner, PhD). The protocol and consent forms were approved by the appropriate Institutional Review Boards/Human Research Ethics Committee. Eligibility criteria included: 1) a diagnosis of CF confirmed by a sweat test, 2) age at enrollment of 11 to 20 years, 3) no developmental disability that could affect responses to the survey questions, 4) no sibling currently in the study, and 5) regular access to an internet-connected computer without firewall restrictions.

Participants in the target age range were initially mailed letters describing the study. The letter provided parents and adolescents with a brief overview of the study, potential benefits of the study, and information regarding compensation. Potential participants were also identified from the schedule of upcoming, routine clinic visits at each CF center. Interested participants were first consented for the primary study and then asked if they would complete a supplemental, online pain diary study for additional compensation.

Those who agreed to participate and met the inclusion criteria were randomly assigned to one of two intervention conditions: 1) a web-enabled cell phone combined with a social networking site (i.e. Intervention condition), or 2) an educational website (i.e. Comparison condition). Randomization took place during their clinic visit, with stratification based on age and disease severity. Age was divided into two categories: 1) younger adolescents, 11 to 14 years and 2) older adolescents, 15 to 18 years. Disease

severity, as measured by FEV_1% predicted (i.e. forced expiratory volume in 1 second), was also divided into two categories: 1) normal to mild lung disease (≥ 70%), or 2) moderate to severe disease (< 70%).

The Intervention condition included a broadband-capable, cellular telephone that provided access to CFfone™, a secure, interactive website specifically designed for children, adolescents, and adults with CF. The website provided engaging online learning activities, resources specific to individuals with CF, and an online forum and support group. Cellphone technology was chosen because it provided a high degree of mobility and access, and avoided the risk of direct patient contact, which is prohibited. The Comparison condition consists of access to an already-established website, www.cysticfibrosis.com. This website was designed specifically for individuals with CF and their caregivers, and offered tools, information, and discussion boards.

The larger study consisted of four clinic visits, scheduled approximately every 3 months. For the current study, only the first three clinic visits were used in the analyses due to length of the study and because three time points are sufficient to complete the proposed analyses. Following each visit, participants completed an online pain daily for the subsequent six days. An email reminder was sent at the end of each day for six days directing them to the online diary. Participants were given $15 for completion of each of the six online diaries.

Participants

Overall, 160 patients were approached in CF clinics (see Figure 1). Of those, 11 were excluded based on a sibling already enrolled in the study or no internet access in the home. 48 patients' declined to participate due to various reasons including the length of

the study, uninterested, parent restrictions on social networking, and living too far away from the clinic. In total, 101 participants were recruited from seven CF centers in the eastern and southeastern United States. Of those recruited, 6 declined to complete the supplemental online pain diary, leaving 95 participants in the final sample (see Table 1). Sixty-two percent of the sample was female and the mean age of participants was 15.8 years. The sample was racially and ethnically diverse, with a majority being Caucasian (69%), 19% Hispanic, 10% African American and 1% Asian (see Table 1). Mean FEV_1% predicted at Baseline was 80.6% (SD = 25.6), indicating mild severity. On average, 4.36 pain diaries were completed at the Baseline visit (73%), with approximately 49.5% of participants completing all six diaries.

Measures

Demographic and medical characteristics. Parents and young adults completed a Background Information Form at the initial visit which included date of birth, gender, parent's age, racial/ethnic background, income, occupation, and composition of the family. Information about the patient's medical status (FEV_1%), was also collected from PortCF, an electronic medical database of all patients run by the CF Foundation, at the Baseline visit.

Pharmacy Refill History. To measure adherence, data on patients' medications and refill histories were collected from pharmacies covering prescriptions from the Baseline visit and the prior 12 months. Assessment of adherence began nine months prior to the participants' Baseline visit and was conducted for each pulmonary medication prescribed. Adherence was measured using medication possession ratio (MPR), defined as cumulative days' supply of pulmonary medications received divided by the total

number of days during the refill history period (approximately 275 days less any days spent in the hospital). Values were truncated to 100%. For each patient, drug-specific MPRs were calculated separately for every unique pulmonary medication, and were then averaged to obtain his/her annual composite MPR (Quittner et al. 2009). Prescription refill history of enzymes was not included in the adherence composite due to considerable missing data across participants.

Daily Pain Assessment Questionnaire for Cystic Fibrosis (DPAQ-CF). The DPAQ-CF measured the occurrence of pain, including its frequency, duration, intensity, location, and coping response. The DPAQ-CF consists of seven pain-related questions, designed specifically for this study, because no comprehensive measure has been validated for this population. The reliability and validity of each component of the DPAQ-CF has been established in a series of previous studies, with one question developed specifically for this population (see Appendix A).

Number of pain episodes was measured on a 5-point likert rating scale including "0," "1-2," "2-3", "4-5," "6 or more" (Palermo et al., 2006). Pain duration was measured on a 4-point likert scale including “less than 1 hour”, “a few hours”, “half of the day”, and “all day” (Koh, et al., 2005). Type of pain was evaluated by asking adolescents whether or not the pain was related to their treatments (procedure-related pain). For those endorsing procedure-related pain, they indicated which CF-specific medications or procedures caused their pain (e.g. chest physiotherapy, IV antibiotics). The list of CF-specific treatments were developed based on previous research and in consultation with CF experts (Festini, et al., 2004; Koh, et al., 2005). Sensory, affective, evaluative and temporal dimensions of pain were assessed through a qualitative word list containing 12

previously identified words (e.g. “throbbing,” “aching,” “stiff;” Crandall & Savedra, 2005). Pain location was measured using a well-validated body outline displaying anterior and posterior views (Savedra et al., 1989). Coding of the body location was conducted using nine standardized body regions including the face, head, shoulders, chest, arms and hands, pelvic region, spine, lower back, and legs and feet (Lester, Lefebvre, & Keefe, 1996). Pain intensity for the “worst pain” during the day was measured using a well-established 10cm Visual Analogue Scale (VAS; McGrath, 1987). Participant’s ratings ranged from 0 (“no pain”) to 10 (“worst pain possible”), with corresponding faces anchoring the scale (Faces Pain Scale; Bieri, Reeve, Champion, Addicoat, & Siegler, 1990). Pain management was assessed through a list of coping responses commonly used to relieve pain (e.g. rest, medication, heat/ice, etc.; Koh, et al., 2005).

Daily Pain Assessment Questionnaire for Cystic Fibrosis (DPAQ-CF) – Online Diary Version. The diary version of the DPAQ-CF was administered on a secure website using Filemaker. Patients entered their email address into the website and answered seven questions identical to the paper version described above.

Cystic Fibrosis Questionnaire-Revised (CFQ-R; Quittner, et al., 2005). Patients completed age-appropriate versions of the CFQ-R, a disease-specific health-related quality of life measure, designed to assess the physical, emotional, and social impact of CF on patients. Two of the three versions were utilized: a child version for ages 6 to 13 and a teen/adult version for ages 14 through adulthood. The child version of the CFQ-R consists of 35 items with 8 generic and disease-specific scales (see Appendix B and C). The teen/adult version of the CFQ-R consists of 50 items with 12 generic and disease-

specific scales (see Appendix D). For the current study, only three domains were used: Treatment Burden, Respiratory Symptoms, and Social Functioning. Quality of life dimensions were assessed using likert scales and scores were standardized from 0 to 100, with higher scores indicating better HRQOL. Currently, the CFQ-R is the only disease specific measure of HRQOL available for children with CF and has been shown to have good reliability and validity in several national validation studies (Modi & Quittner, 2003; Quittner et al., 2005; Quittner, et al., 2009; Quittner et al., 2012). Internal consistency ranged from 0.51 to 0.73 for the Child version and from 0.57 to 0.94 for the Teen/Adult version for the domains assessed in this study. Test–retest reliability has ranged from 0.45 to 0.90 for the Teen/Adult version (Quittner et al., 2005; Quittner, et al., 2012). Significant associations have been found between the CFQ-R domain scores and pulmonary functioning, indicating good discriminate validity (Quittner et al., 2005; Quittner, et al., 2012). Additionally, Palermo and colleagues (2008) deemed it "well-established" using the Chambless (1998) criteria. For the current study, alpha levels ranged from .38 to .80 for the child version and .36 to .79 or the teen/adult version.

Perceived Adolescent Social Support: Cystic Fibrosis (PASS-CF). The PASS-CF was used to measure CF-specific support provision from family, friends, and healthcare providers (see Appendix E). This newly developed scale measured the frequency of supportive and non-supportive behaviors from family, friends and healthcare providers, as well as adolescents' perception of their importance over the past two weeks. Supportive behaviors were measured on a likert-type scale, ranging from 1 ("very supportive") to 5 ("very unsupportive"). The frequency of social support was also measured on a likert-type scale, ranging from 1 ("never") to 4 ("always"). Items included "asked me if I did my

treatment," and "encouraged me to eat more." The composite social support scale was created through multiplying the mean of the 14 items measuring strength of social support strength from family and friends without CF, and the mean of the frequency of social support on the same items. The total values ranged from 5.36 to 20.0. The alpha for the current sample was .82 for frequency of social support and .92 for the strength of social support.

Chapter 3: Results

Statistical Procedure

Missing data were addressed individually for each analysis. Given that the pain data were completed online, some missing data was expected (Palermo, 2004). To ensure maximum completion of pain diaries, Filemaker was programmed to produce error messages between screens/pages whenever participants left an item blank. Participants were required to either return to the previous page and complete the item, or acknowledge leaving the item(s) blank. Overall, 57.9% of participants completed a minimum of one online pain diary across each time point.

Missing longitudinal data was handled using a full information maximum likelihood (FIML) estimator with Mplus software for the second and third aims of the study (Muthen & Muthen, 2008). This procedure estimates the model parameters using all available information, rather than deleting cases with incomplete data (Enders, 2001). Thus, participants who did not complete all of the diaries could still be utilized in the analyses.

Aim1. The first aim was to systematically measure the prevalence, intensity, and location of pain and how patients coped with these pain episodes. Descriptive statistics and initial comparisons between treatment groups were computed using the SPSS (Green, Salkind, & Akey, 2000) statistical software.

Aim 2. The second aim was to assess the cross-sectional relationships between treatment adherence, social support, pain and HRQOL at Baseline using a path analysis. SEM was conducted using MPlus software (Muthen & Muthen, 2006) to evaluate the unique contributions of the independent variable on pain ratings and HRQOL. Specifically, the independent variables were social support and adherence, while the dependent variable was

quality of life. SEM was considered superior to other analytic techniques, such as multiple regression, because it tests more complex models with both latent and single-indicator variable, to reduce measurement error and include cases with missing data in the model (Nelson, Aylward, & Steele, 2008).

Aim 3. The third aim was to measure the relationship between pain and HRQOL over time, by modeling the trajectory of its occurrence across a six-month. LDS (McArdle, 2009; McArdle, 2001) was used to explore the longitudinal dynamics of pain and HRQOL across time. LDS is a statistical technique that integrates features of latent growth curves and cross-lagged regression models (Hamagami, & McArdle, 2000; Hawley, Ho, Zuroff, & Blatt, 2007). Specifically, LDS considers dynamic longitudinal growth within a time series, while still permitting examination of multivariate relationships. Univariate LDS also examines the types of linear and nonlinear changes that occur throughout the trajectory (e.g. no change, constant change, or proportional change), in addition to the basic characteristics (i.e. slope and intercept) provided by the latent growth curve model (McArdle & Epstein, 1987). In order to represent the average pain rating at each time point, pain intensity scores on the diary were averaged. Separate models were used for each of the three HRQOL scales: Social Functioning, Treatment Burden, and Respiratory Symptoms.

Supplementary analyses were conducted using the PROC MIXED procedure in SAS (Littell, Milliken, Stroup, & Wolfinger, 1996) to analyze multilevel models. PROC MIXED uses a random regression model to derive parameter estimates both within and between individuals (Singer, 1998). This strategy is preferable to ordinary regression analyses because the latter ignores the nesting of diaries within persons. Another advantage of mixed models is

that time does not have to be consistent; therefore participants can have different amounts of time between assessments.

Descriptive Statistics

Demographic characteristics: Treatment versus Comparison group. Comparisons were made to assess differences in demographic characteristics between the Treatment and Comparison groups at Baseline. No statistically significant differences were found between the groups. T-tests for continuous variables and chi square tests for categorical variables were conducted to evaluate these differences (see Table 2).

Analyses were also conducted to assess the effectiveness of the social networking intervention on the measured variables. A repeated measures ANOVA indicated that pain intensity did not differ over time between the Treatment and Comparison groups, $F(1.79, 108.9) = .46$, $p = .60$. Further, there were no differences in HRQOL over time between the groups: Social Functioning $F(2,120) = .50$, $p = .60$; Treatment Burden $F(1.84,106.5) = .1.9$, $p = .16$; and Respiratory Symptoms $F(2,120) = .82$, $p = .44$. Based on these null findings, the Treatment and Comparison groups were collapsed for all subsequent analyses to increase sample size and power. Means and standardizations at each time point for these measured variables are provided in Table 3. Compared to the normative sample on the CFQ-R, the current sample has overall worse HRQOL on respiratory symptoms, treatment burden and social functioning in both age groups (child and teen/adult) and across genders.

Online pain diary characteristics. A total of 897 diaries were completed by 95 participants, with an average of 3.61 observations per participant for each set of diaries. At the baseline assessment, 15.8% of the sample did not complete any online pain diaries,

11.6% completed between 1 to 3 online diaries, 28.4% completed 4 to 5 diaries, and 44.2% completed all 6 diaries. Comparisons were made between those who completed all of the diaries (i.e., "completers") versus those who completed a portion of the diaries (i.e., less than six diaries, range 0- <6= "non-completers"). Chi-square tests were used for categorical variables (i.e., demographics) and t-tests were used for continuous variables (i.e., mean item responses). No significant differences were found between completers and non-completers on any demographic variables (i.e., disease severity, age, gender, income). However, a significant difference was found for completers vs. non-completers for average pain intensity ratings ($t(92) = 2.9$, $p = <.01$). Completers had less intense pain ($M = 1.0$, $SD = 1.2$) than non-completers ($M = 2.1$, $SD = 2.1$). Completers were also more adherent to their treatments ($M = 69.76$, $SD = 31.4$) than non-completers ($M = 50.32$, $SD = 22.3$), ($t(51) = -2.6$, $p = <.05$). No other significant differences were found between groups on variables of interest.

Pain intensity ratings: Online diary versus clinic visit. Pain at the first clinic visit was not significantly different than an average of the pain ratings across the six diaries ($t(94) = -.98$, $p=.33$). However, examination of individual trajectories of pain over the course of the diary showed that they were highly variable (see Figure 2). The intraclass correlation for daily pain ($\rho = .36$) indicated that a considerable portion of total variance was accounted for by within-person variance (Singer, 1998).

Prevalence of Pain Characteristics at Baseline

The first aim was to measure the prevalence of pain in adolescents with CF. These patients were expected to report more general and procedural pain episodes and greater pain intensity than the general population of adolescents. The most frequent locations of pain were expected to be in the stomach, head, and chest. Average ratings of pain

intensity, frequency, duration, location and coping responses were measured at Baseline. At the Baseline assessment, one or more pain episodes were reported by 74.5% of participants across the 6 diary days. Of those who experienced pain, mean intensity was 2.12 (out of 10 points).

When compared to the general adolescent population (Perquin et al., 2000), adolescents with CF experienced more pain episodes (74.5% vs. 53.67%), z =-4.01, p = <.01; however, average pain intensity ratings were significantly lower (2.2 vs. 4.1). Adolescents with CF also reported more incidences of pain than adolescents with other chronic conditions: HIV (74.5% vs. 25%), sickle cell (74.5% vs. 65%), and cancer (74.5% vs. 48%), (Gaughan, Hughes, Seage, Selwyn, Carey, Gortmaker, et al., 2002; Gil, Porter, Ready, Workman, Sedway, & Anthony, 2000; Miser, Dothage, Wesley & Miser, 1987). Significant differences were observed between all other groups and CF, except for the sickle cell group (p = .14). Note that average intensity of pain for adolescents with CF was generally lower than that reported by other disease groups. This suggests that despite having more frequent pain episodes, intensity of these episodes were relatively mild.

The most frequent location of pain was the stomach (49.3%), followed by head/neck (42.3%), and chest (36.6%). More than one pain location was reported by 53.5% of participants. Emotional descriptions of pain were variable, with “sore” being the most frequently reported (49.3%), followed by “aching” (43.2%), “pounding” (36.6%), “cramping” (35.3%), and “stiff” (21.1%). The most frequently used coping mechanisms were: resting (63.4%), relaxing (59.2%) and taking medication (49.3%). Interestingly, 63.3% of participants reported doing nothing to relieve their pain. Treatment-related pain was also common (30%). Airway clearance was most frequently

reported treatment and associated with pain (N=11), but was also significantly related to *better* lung function compared to other treatments (t (17) = -2.97, p < .01). Treatment-related pain at Baseline was significantly different from general pain in its intensity (t (68) = -2.45, p = .02), with treatment-related pain rated as more intense. All participants with treatment-related pain had significantly worse CFQ-R Treatment Burden score (M=51.32 vs. M=59.64), t (93) = 2.27, p = .03, and worse CFQ-R Respiratory Symptoms (M=51.19 vs. M=66.10), t (93)= 3.49, p <.01. In contrast, no significant difference was found in treatment-related versus non treatment-related pain on the CFQ-R Social Functioning scale.

Structural Model of Pain: Treatment Adherence, Social Support and HRQOL

The second aim of the study was to identify associations between pain and several health outcome variables. Simple correlations were performed and are presented in Table 4. Significant relationships were found between pain and Treatment Burden (r = -.322), Respiratory Symptoms (r = -.445), and treatment adherence (r = -.317). No significant relationships were found between pain and social support, social functioning, and FEV_1%. Of note, the social support variable from the PASS-CF was not significantly correlated with other variables of interest. As a result, the Social Functioning variable, from the CFQ-R, was used as a substitute in all subsequent models. Although not a direct measure of perceived social support, this domain of the CFQ-R includes items addressing the impact of CF on a patient's ability to interact with peers (e.g., "you felt left out", "you stayed home more than you wanted to").

In order to control for variables such as age, gender, and disease severity, as well as use multiple indicators of HRQOL, two SEM models were examined to test

relationships between pain and health outcomes. Two models were chosen over one complete model because of the current studies smaller sample size. The final models tested the relationships among the observed and latent variables, with rectangles indicating observed variables and ovals indicating latent variables. The latent variables included pain, with the following indicators: pain intensity, pain duration, and pain episodes, and HRQOL, with the following indicators: Social Functioning, Treatment Burden, and Respiratory Symptoms. It was hypothesized that greater pain (number of episodes, higher intensity, longer duration) would be associated with worse adherence, less social support, and worse HRQOL. Estimated parameters of primary interest were the path coefficients which assessed the direct effects.

The first model (see Figure 3) assessed the relationship between social functioning, pain, and HRQOL. The social functioning variable was taken out of the latent HRQOL because it was used as a predictor, substituting for the social support variable on the PASS-CF. The final model fit was acceptable, χ^2 (18) = 30.74, p = .06 (RMSEA = .08, SRMR = .05, CFI = .96). The direct effect from social functioning to pain was significant, β = -.23, p =.03, as was the direct effect from social functioning to HRQOL, β = .49, p <.01 and the direct effect from pain to HRQOL β = -.58, p =<.01. Overall, worse social functioning led to more pain and worse HRQOL.

The second model (see Figure 4) assessed the relationships among treatment adherence, pain, and HRQOL (using the same HRQOL indicators as the first model). The final model fit was acceptable, χ^2 (18) = 23.93, p = .16 (RMSEA = .08, SRMR = .07, CFI = .96). The direct effect from adherence to pain was tested and was significant, β = -.31, p =.02 as well as the direct effect from pain to HRQOL, β = -.62, p =<.01. However, the

direct effect from adherence to HRQOL was not significant, β = -.07, p = .70. Overall, worse treatment adherence led to more pain and worse HRQOL.

Finally, it was also hypothesized that pain would mediate the relationship between the direct paths from social functioning and HRQOL in addition to treatment adherence and HRQOL. In the first model, the indirect effect from social support to HRQOL via pain was statistically significant, β = .13, p =.04. Results from a Sobel test of mediation (Baron & Kenny, 1986) indicated complete mediation (z = 2.12, p = .02). In the second model, the indirect effect from treatment adherence to HRQOL via pain approached significance, β = .19, p =.07. The Sobel test results were not significant, but suggests partial mediation (z = 1.85, p = .07).

Post hoc analyses were conducted to further assess the relationship between social functioning and pain. It was originally hypothesized that pain mediated the effects between social functioning and HRQOL; however, another possibility is that social functioning mediates the relationship between pain and HRQOL. The model in question, which included social functioning as the mediator, was not significant, χ^2 (21) = 39.83, p = .01 (RMSEA = .09, SRMR = .07, CFI = .93). In sum, our results were consistent with proposed hypotheses indicating that pain mediates the relationship between social functioning and treatment adherence, such that poor social functioning and worse treatment adherence led to more pain which in turn lead to worse HRQOL.

Predictors of Pain Intensity over Time

Given that pain intensity was measured as a continuous variable, it was chosen for the analyses of the trajectories of pain over the 6-month period.

Univariate LDS models. It was hypothesized that the trajectory (i.e. slope) of pain and HRQOL would differ between treatment groups, with the CFfone™ group exhibiting a dual change score model, in which pain decreased and HRQOL increased over time, after controlling for adherence. In contrast, for the Comparison group, a proportional change score model was expected between pain and HRQOL over time, indicating a generally flat linear trend with small changes over time, after controlling for adherence. This hypothesis was not supported; no changes were found in pain or HRQOL over time for either the Treatment or Comparison group. Therefore, univariate LDS models were tested with all participants.

Four univariate LDS longitudinal models of pain and each of the HRQOL variables were evaluated: 1) the no change model, 2) the additive constant change model, 3) the proportional change model, and 4) the combined dual change model. Table 5 presents summary results for each of the univariate models, indicating parameter estimates and goodness-of-fit indices. Examination of these results indicated that changes in pain and HRQOL were best represented by the no change LDS models: pain intensity (χ^2=4.93, CFI= .91, SRMR= .11, RMSEA= .13); Social Functioning (χ^2=4.52, CFI= .99, SRMR= .14, RMSEA= .04), Treatment Burden (χ^2=9.11, CFI= 93, SRMR= .07, RMSEA= .12), and Respiratory Symptoms (χ^2=5.79, CFI= .98, SRMR= .09, RMSEA= .07). This indicated that little change was observed across the three time points, lending no support to the change models.

Bivariate latent difference models. The bivariate models of pain and each of the HRQOL variables could not be tested because of an inadequate sample size. Furthermore, previous results indicated significant within-person variability across the diaries and this

individual level data could not be captured using an LDS model. As a result, supplemental analyses were conducted to test these hypotheses using a different methodology.

Multilevel modeling. The pain data are hierarchical in nature, consisting of up to 21 observations (i.e., number of diaries and clinic visits) nested within 95 participants. This data structure was more appropriately suited for MLM (Littell, et al., 1996; Singer, 1998). Multilevel regression equations tested associations between pain and HRQOL over time. In these analyses, Level 1 measures represented daily measurements of pain and Level 2 measures included control variables, such as adherence and HRQOL variables (i.e., Social Functioning, Treatment Burden and Respiratory Symptoms). Each Level 2 variable was sample-centered (Singer, 1998). The model fit the data well, $\chi^2 < .01$. With the inclusion of adherence in the model, Treatment Burden was the only significant predictor of the initial pain mean (i.e., intercept), $\beta = -.02$, SE = .01, $p = .05$). However, Respiratory Symptoms ($\beta = -.02$, SE = .01, $p = .12$) and Social Functioning ($\beta = -.01$, SE = .01, $p = .80$) did not significantly predict pain. Further, adherence contributed a great deal of variance to the intercept of the model (59%). There were no significant interactions between the HRQOL variables and the slope of pain over time (see Table 6). Overall, this model indicated that across the six months and three pain diaries, pain was variable within each person. Both adherence and treatment burden significantly predicted initial levels of pain intensity. However, there was no evidence that any of the variables tested were related to individual trajectories of pain.

Chapter 4: Discussion and Conclusions

To our knowledge, this was the first study to examine the prevalence of pain longitudinally in adolescents with CF using an online diary. Although life span has increased dramatically in the last 20 years, patients with CF inevitably experience a decline in lung function, leading to more frequent pulmonary exacerbations, increased structural lung damage, and more invasive surgeries. These sequalae can lead to increased pain. This study provided detailed descriptive information on pain in adolescents with CF and evaluated how pain was related to other important variables, such as adherence and HRQOL. Another aim was to evaluate pain using real-time assessments over a six-month period to examine its trajectory and relationship to other health outcome variables.

Results of the first aim indicated that pain is common among these adolescents, but its intensity is relatively mild. In addition, the pain diary revealed that pain intensity, frequency, and duration varied greatly within individuals. In support of our hypotheses, and consistent with previous literature, the most frequent location of pain was in the stomach, followed by the head and chest. Given that CF is characterized by malabsorption of fat, it is likely that patients experience a great deal of gastrointestinal distress from early in life, despite taking enzymes with each meal and snack. Patients often report that they have frequent abdominal pain, cramps and difficulty digesting food. Titration of enzymes is difficult and adherence to enzymes has been estimated at or below 50%. It would have been valuable to measure adherence to enzymes, which directly affects abdominal symptoms, however this was not possible due to the high rates of missing and inconsistent enzyme refill data. The high prevalence of abdominal pain in

this study indicated that there is a need to develop effective tools to assess this type of pain in order to treat it more effectively. A recent study by Munck and colleagues (2012) also documented recurrent abdominal pain in patients with CF and was the first to develop a behavioral intervention to treat these symptoms. Results were promising and indicated a need for more extensive evaluations of behavioral treatments for pain in this population. Pain assessment should also become an integral part of care in CF centers.

Comparisons of pain in teens with CF versus those with other chronic conditions and the general population indicated that pain was more prevalent in CF, but was, on average, less intense. It is possible that patients with CF have experienced chronic pain for most of their lives and thus, have habituated to its occurrence. Over half of the participants reported doing nothing to cope with their pain, suggesting that they may have "given up" and have learned to live with frequent pain. Based on these results, it may be important to treat symptoms of pain in CF earlier and more aggressively, with ongoing monitoring of pain intensity. Previous research on chronic pain suggests that long-term consequences may include a higher risk for continuing pain, greater use of health care resources, medication, use of non-drug methods of pain control, and greater functional disability (including school/work absence) (Martin, McGrath, Brown & Katz, 2007; Mulvaney, Lambert, Garber, & Walker, 2006). Therefore, alleviation of pain early in a chronic condition may be important for long-term HRQOL.

A unique contribution of this study was the use of online daily diaries, which provided rich and meaningful information about pain in this population. Interestingly, significant variability was found in pain ratings within individuals on the diary. This was true of pain intensity, frequency and duration measures. The diary highlighted this

variability, which would not have been detected in measures that average pain ratings. It was also useful for identifying significant peaks and valleys in patients' pain across several days. However, this variability also made it difficult to identify specific predictors of pain over time. Despite this variability, average pain intensity (i.e., clinic visit rating in addition to the six online diaries) was significantly related to dimensions of HRQOL and adherence. This is consistent with our results showing a direct relationship between average pain intensity across the six diaries and pain intensity measured at the initial clinic visit. Our findings suggested that there are other factors that explain daily pain; however, unfortunately this study was not focused on identifying these triggers. Future research should consider using a diary measure that captures both pain ratings and triggers.

Another interesting finding was the difference between participants who completed the diary versus those who did not. Diary completion rates were consistent with previous studies, with approximately half of the sample completing all six diaries at Baseline. Completers were found to have less overall pain, but were more adherent to their treatment regimen than non-completers. Thus, it appeared that their inability to adhere to their treatment regimen may have generalized to other domains of functioning, such as completing their pain diary. These participants are likely to have poor executive functioning skills, which may relate to poor disease management and ability to set goals and organize tasks. Measuring executive functioning in the care of patients with CF may be helpful in understanding protective factors associated with better disease management and adherence.

Contrary to our predictions, demographic and medical variables, such as age, gender, and disease severity, were not significantly related to overall pain. There are several possible explanations for these results. First, although many previous studies in the general population and other chronic conditions have found these associations (Kojima et al., 2009; Perquin et al., 2000), recent studies in CF have not (Koh et al., 2005; Munck, Pesle, Cunin-Roy, Gerardin, Ignace, Delaisi, et al., 2012). Age and sex effects may be relevant for those reporting pain who are otherwise healthy, but may not be as strongly linked in a sample with a chronic illness. Further, the lack of association with disease severity is not surprising, given that most adolescents fell within the mild range of disease severity (Hayes et al., 2011). Post hoc analyses were conducted comparing patients with severe versus mild disease; however, no significant differences were found between these two groups on pain intensity. Because pain is typically a marker of disease severity, including increased inflammation, we expected it to be more common in sicker patients. Our null results suggested that pain may be common among patients at all stages of disease. Further, it may be that FEV_1% is not a reliable marker of disease severity and a more sensitive measure is needed, such as pulmonary exacerbations or a computed tomography scan.

Results from the second aim indicated a strong cross-sectional relationship between pain and health outcome variables, as noted by the significant correlations. The final models suggested that social functioning and adherence was significantly related to more pain (i.e., intensity, duration of pain, number of episodes), which ultimately led to worse HRQOL. These results are consistent with previous studies in both adult and pediatric CF populations (Hayes et al., 2011; Palermo, 2006). Further, pain was found to

mediate the relationship between these variables and HRQOL. Of note, the domain of HRQOL was not a complete composite of HRQOL variables and included only those involved with the disease and its treatments. Adherence was not related to the HRQOL measures of respiratory symptoms and treatment burden. If patients are not adhering to their medical regimen, it would make sense that they are not reporting significant burden. However, it is unclear why adherence was not related to respiratory symptoms, which is related to disease severity. In looking at the simple correlations, however, adherence was significantly related to FEV_1%.

Although these results indicated that worse adherence was related to more intense pain, the directionality remains unclear. We tested the notion that poor adherence leads to worsening disease and ultimately more pain. However, it is also possible that more frequent, intense pain prevents teens from completing their treatments. To test this causal association with greater rigor would require assessment of adherence in real-time paired with pain diaries. Measures, such as the Daily Phone Diary (Quittner, Modi, Lemanek, Ievers-Landis, & Rapoff, 2008), could be used as an unobtrusive measure of adherence to monitor both adherence behaviors and ratings of pain.

This study was also the first to evaluate associations between pain and rates of adherence to the daily treatment regimen. Although the collection of pharmacy refill histories was challenging, including having to call and fax each pharmacy to obtain individual records, it provided very useful data. Generally, we found that patients adhered to 60% of their daily treatments. In addition, medication possession ratios indicate the number of prescriptions filled, but not whether the medication was actually consumed. However, this method is best suited for multicenter studies, is more reliable than self-

reported rates of adherence, which are inflated, and correlates well with electronic monitoring systems.

Importantly, adherence contributed a great deal of variance to the final multilevel model, indicating that worse adherence to pulmonary medications led to more intense pain above and beyond other variables (HRQOL). This relationship has not been tested in prior studies, but may help explain the low rates of adherence found in this population. Those patients experiencing more pain will be less likely to complete their treatments, which in turn, exacerbates their symptoms. Pain has not been frequently discussed as a potential barrier to completing treatments and should be investigated in future studies.

In terms of the third aim, mixed results were found. First, the CFfone™ intervention did not improve participants' pain ratings or HRQOL over the six-month period. This may be partly explained by the adequacy of the "dose" of the intervention that was delivered. Participants had to be interested and engaged in the intervention and were able to choose how often they would access the CFfone™ website. Although we have data indicating how frequently participants "logged on" to the website, we do not know how long they were visiting and interacting with the site and other participants. Due to the website's formatting, participants did not typically "log off" after every use and so it was difficult to determine their precise usage. Further, the website was aimed at improving education, particularly disease-related knowledge, and was not designed to directly affect pain or HRQOL. Our results suggested that the indirect support provided by the website did not have a significant effect on these dimensions of functioning. Interventions aimed at reducing pain and improving HRQOL will have to focus more directly on these issues to demonstrate a positive effect.

Significant relationships between pain and HRQOL were found over the six-month period. Based on the multilevel regression analyses, adherence (aggregated from the nine months prior to the start of the study) and Treatment Burden significantly predicted initial levels of pain intensity. However, the slope of pain intensity across the six-months was not significant, indicating a relatively flat trend over time. This finding is consistent with the discussion above documenting the variability in pain ratings within individuals, and the need for concordant ratings of pain and health outcome variables over time.

Limitations

These results should be interpreted in light of several limitations. First, this study was limited by its measurement of social support and HRQOL only at each clinic visit and not in real-time via diaries. Although our results suggested that HRQOL was impacted by pain, the slope and variability of pain across the six days may have been driven by other issues. Previous research has indicated that mood and sleep may be important predictors of daily pain (Bromberg, Gil, & Schanberg, 2012). In this study, they measured daily mood, sleep and pain and found that poorer sleep quality was associated with higher pain ratings the next day, and mood moderated this relationship; as positive mood increased, the relationship between poor sleep quality and pain intensity weakened. This study highlighted the importance of measuring pain and predictor variables using a daily diary methodology to understand their temporal and causal associations.

Second, the sample size, although reasonable for this rare disease, was relatively small for the analyses that were conducted. Thus, this study was likely underpowered to

detect some of the predicted relationships. There was also a significant amount of missing data for the adherence variable. Obtaining pharmacy refill histories for each participant posed significant challenges and only 59% of the data was obtained. Thus, only a portion of the sample could be included in the second aim of the study. However, the relationship between adherence and pain was exceptionally strong and this association would likely hold true with more pharmacy refill data. Further, adherence to enzymes could not be computed due to missing and inconsistent data. Missing data was also noted for the pain diary, despite frequent, daily email reminders.

Finally, the social support variable, as measured by the PASS-CF, did not appear to be related to several key variables. The PASS-CF is a new measure that has not yet undergone rigorous reliability and validity testing and it is possible that a better established measure would have yielded different results. As an alternative, the Social Functioning variable, from the well-validated CFQ-R measure, was used to represent social support in the model. Although not ideal, this domain is composed of items that assess the ways in which patients' disease interferes with their ability to have positive social relationships. Further, the HRQOL latent variable was only composed of three indicators, which does not fully encompass HRQOL and is a measure of overall disease functioning.

Future Directions

This study highlighted several possible future directions related to pain in CF. Based on the findings from the current study, pain is a major barrier to completing treatments in teens with CF. Given that rates of adherence are particularly poor in adolescents, identifying potential barriers is important for improving disease

management. To our knowledge, pain has not been identified as a barrier to adherence in prior studies and is a potentially meaningful variable to include in the future.

There is also a need to identify methods to reduce pain and improve HRQOL in children and adolescents with CF. Results indicated that patients are using a variety of methods to relieve their pain, however a majority of patients are doing nothing and pain is not being monitored by the CF team. Effective pain management would likely include a combination of pharmacologic and psychological interventions. To our knowledge, few studies have looked at psychological interventions for pain in this population. In a recent study, a small sample of children with CF with abdominal pain (N=8) participated in a behavioral intervention. Results showed improvements in pain and ultimately, a positive impact on anxiety and quality of life. However, this study only included patients with severe abdominal pain who met clinical criteria for recurrent abdominal pain.

Utilization of pain ratings, such as the DPAQ-CF, could be used to evaluate interventions addressing pain. This would require identification of the minimal important difference (MID) scores for pain intensity ratings. MID provides an estimate of the smallest improvement patients can detect. In pain studies, a key global measure of improvement is the degree of pain relief reported by the patient. To determine the meaning of a change in pain intensity, patients would need to report simultaneously on changes in the pain scores and the degree of pain relief (Cepeda, Africano, Poloa, Alcalaa, & Carr, 2003). In children, a 1-1.3 unit decrement in VAS pain ratings has been reported to be the threshold for clinical significance, or “minimal improvement” on pain ratings (Cepeda et al., 2003; Powell, Kelly, & Williams, 2001). However, it may be that this threshold is different for patients with CF, particularly given their pain intensity

ratings are lower than other chronic illness groups. Future studies are needed to identify MIDs for pain ratings in CF.

It is also important for future studies to examine the specific triggers associated with pain episodes in teens with CF. Utilizing a diary approach, such as the DPAQ-CF, and including additional questions that aim at identifying antecedent events to pain is vital to understanding the causes of pain. This information would facilitate development of appropriate interventions for different types of pain, including treatment-related pain or more general pain.

Conclusion

This study provided additional evidence documenting a high prevalence of pain in adolescents with CF. Pain is a significant, but highly variable, symptom that interferes with patients overall functioning and is a barrier to completing daily treatments. The cause of daily pain in this population is still unknown, but it is likely affected by a number of factors. Additional research is needed to understand the triggers associated with daily pain to inform development of appropriate interventions. As patients with CF live longer, the problem of managing pain is likely to become a more serious issue that should be systematically measured and treated. The assessment of pain should become a routine procedure in CF clinics and examination and attention to pain-related problems should become an integral part of routine care.

References

Agnew, J. & McIlwaine, M. (October, 2012). Canadian National Airway Clearance Therapy Study: Positive Expiratory Pressure Mask Versus. Presentation at the 26th annual North American Cystic Fibrosis Conference, Orlando, FL.

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. Journal of Personality and Social Psychology, 51, 1173-1182.

Beale, I.L. (2006). Scholarly literature review: Efficacy of psychological interventions for pediatric chronic illnesses. *Journal of Pediatric Psychology, 31*(5), 1-15.

Bieri, D., Reeve, R.A., Champion, G.D., Addicoat, L., &Siegler, J.B. (1990). The Faces Pain Scale for the self-assessment of the severity of pain experienced in children: Development, initial validation, and preliminary investigation for ratio scale properties. *Pain, 41*, 139–50.

Bilton, D., Landy, A., Gunn, E., Saunders, M. (2001). Is pain and discomfort common in CF adults? *Journal of Cystic Fibrosis*, 320.

Briesacher, B.A., Quittner, A.L., Saiman, L., Sacco, P., Fouayzi, H., & Quittell, L.M. (2011). Adherence with tobramycin inhaled solution and health care utilization. *Pulmonary Medicine, 11*(5), 1-6.

Bromberg, M.H., Gil, K.M., & Schanberg, L.E. (2012). Daily sleep quality and mood as predictors of pain in children with juvenile polyarticular arthritis. *Health Psychology, 31*(2), 202-209.

Brown, J.L., Sheffield, D., Leary, M.R., & Robison, M.E. (2003). Social support and experimental pain. *Psychosomatic Medicine, 65*, 276-283.

Bush, J.P., Huchital, J.R., & Simonian, S.J. (2001). An introduction to program and research initiatives of the STARBRIGHT foundation. *Children's Health Care, 31*(1), 1-10.

Cepeda, M.S., Africano, J.M., Polo, R., Alcala, R., & Carr, D.B. (2003). What decline in pain intensity is meaningful to patients with acute pain? *Pain, 105,* 151–157.

Chambless, D.L., Baker, M.J., Baucom, D.H., Beutler, L.E., Calhoun, K.S., Crits-Christoph, P., et al. (1998). Update on empirically validated therapies, II. *The Clinical Psychologist, 51*(1), 3-16.

Cohen, L.L., Lemanek, K., Blount, R.L., Dahlquist, L.M., Lim, C.S., Palermo, T.M., McKenna, K.D., & Weiss, K.E. (2008). Evidence-based assessment of pediatric pain. *Journal of Pediatric Psychology, 33*(9), 939-955.

Crandall, M. & Savedra, M. (2005). Multidimensional assessment using the Adolescent Pediatric Pain Tool: A case report. *Journal of Specialist in Pediatric Nursing, 10*(3), 115-123.

Davies, J.C., Alton, E., & Bush, A. (2007). Cystic Fibrosis. *British Medical Journal, 335*, 1255-1259.

Davis, M.A., Quittner, A.L., Stack, C.M., & Yang, M.C.K. (2004). Controlled evaluation of the STARBRIGHT CD-ROM program for children and adolescents with cystic fibrosis. *Journal of Pediatric Psychology, 29*(4), 259-267.

Donaldson, S. H., Bennett, W. D., Zeman, K. L., Knowles, M. R., Tarran, R., & Boucher, R. C. (2006). Mucus clearance and lung function in cystic fibrosis with hypertonic saline. *New England Journal of Medicine, 354*, 241–250.

Elkins, M. R., Robinson, M., Rose, B. R., Harbour, C., Moriarty, C. P., Marks, G. B., et al. (2006). A controlled trial of long-term inhaled hypertonic saline in patients with cystic fibrosis. *New England Journal of Medicine, 354*, 229–240.

Festini, F., Ballarin, S., Codamo, T., Doro, R., &Loganes, C. (2004). Prevalence of pain in adults with cystic fibrosis. *Journal of Cystic Fibrosis, 3*, 51-57.

Foundation CF. Patient Registry 2011 Annual Report. Bethesda: Cystic Fibrosis Foundation; 2011.

Frank, L., Kleinman, L., Rentz, A., Ciesla, G., Kim, J.J., & Zacker, C. (2002). Health-related quality of life associated with irritable bowel syndrome: Comparison with other chronic diseases. *Clinical Therapeutics, 24*(4), 675-689.

Gaughan, D.M., Hughes, M.D., Seage, G.R., Selwyn, P.A., Carey, V.J., Gortmaker, S.L., Oleske, J.M. (2002). The prevalence of pain in pediatric human immunodeficiency virus/acquired immunodeficiency syndrome as reported by participants in the Pediatric Late Outcomes Study (PACTG 219). *Pediatrics, 109*(6):1144-1152.

Gil, K.M. (1994). Behavioral assessment of sick cell disease pain. *Journal of Health and Social Policy, 5*(3/4), 19-38.

Gil, K., Porter, E., Ready, J., Workman, E., Sedway, J., & Anthony, K.K (2000). Pain in children and adolescents with sickle cell disease: An analysis of daily pain diaries. Children's Health Care, 29(4) 225-241.

Gill, L.J., Shand, P.A.X., Fuggle, P., Dugan, B., & Davies, S.C. (1997). Pain assessment for children with sickle cell disease: Improved validity of diary keeping versus interview ratings. *British* Journal of Health Psychology, 2, 131–140.

Hamagami, F., & McArdle, J.J. (2000). Advanced studies of individual differences linear dynamic models for longitudinal data analysis. In G. Marcoulides & R. Schumacker (Eds.) *New Developments and Techniques in Structural Equations Modeling*, pp. 47-85. Mahwah, NJ: Erlham.

Hawley, L.L., Ho, M.R., Zuroff, D.C., & Blatt, S.J. (2006). The relationship of perfectionism, depression, and therapeutic alliance during treatment for depression: Latent difference score analysis. *Journal of Consulting and Clinical Psychology, 74*, 930-942.

Hayes, M., Yaster, M., Haythornthwaite, J.A., Riekert, K.A., McMillan, K.N., White, E., Mogayzel, P.J., Lechtzin, N. (2011). Pain Is a Common Problem Affecting Clinical Outcomes in Adults With Cystic Fibrosis. *Chest, 140* (6), 1598-603.

Henker, B., Whalen, C.K,. Jamner, L.D., & Delfino, R.J. (2002). Anxiety, Affect, and Activity in Teenagers: Monitoring Daily Life With Electronic Diaries Volume. *The Journal of the American Academy of Child and Adolescent Psychiatry*, *41*(6), 660-670.

Hunfeld, J. A., van der Wouden, J. C., den Deurwaarder, E. S., van Suijlekom-Smit, L. W., & Hazebroek-Kampschreur, A. A. (1997). Measuring chronic pain in children: An exploration. *Perceptual and Motor Skills, 84*, 1176–1178.

Holtzman, S., Newth, S., & Delongis. (2004). The role of social support in coping with daily pain among patients with rheumatoid arthritis. *Journal of Health Psychology, 9*(5), 677-697.

Koh, J.L., Harrison, D., Palermo, T., Turner, H., & McGraw T. (2005). Assessment of acute and chronic pain symptoms in children with cystic fibrosis. *Pediatric Pulmonology, 40*, 330-335.

Lester, N., Lefebvre, J.C., & Keefe, F.J. (1996). Pain in young adults—III: Relationships of three pain-coping measures to pain and activity interference. *Clinical Journal of Pain, 12*, 291–300.

Littell, R.C., Milliken, G.A., Stroup, W.W., Wolnger, R.D. (1996). *SAS System for Mixed Models.* SAS Institute, Carey, NC.

Martin, A.L., McGrath, P.A., Brown, S.C., & Katz, J. (2007). Children with chronic pain: Impact of sex and age on long-term outcomes. *Pain, 128*(1), 13-19.

McArdle, J. J. (2001). A latent difference score approach to longitudinal dynamic structural analysis. In Cudeck, R., du Toit, S. H. C., & Joreskog, K. G. (Eds), Structural equation modeling: Present and future (pp. 341-380). Lincolnwood, IL: Scientific Software.

McArdle, J.J. (2009). Latent variable modeling of differences and changes with longitudinal data. *Annual Review of Psychology, 60*, 577-605.

McArdle J.J., & Epstein D.B. (1987). Latent growth curves within developmental structural equation models. *Child Development, 29*, 110–33.

McClellan, C.B., Schatz, J.C., Puffer, E., Sanchez, C.E., Stancil, M.T., & Roberts, C.W. (2009). Use of handheld wireless technology for a home-based sickle cell pain management protocol. *Journal of Pediatric Psychology*, 34(5), 564-573.

McGrath, P.A. (1987). An assessment of children's pain: A review of behavioral, physiological and direct scaling techniques. *Pain, 31*, 147–171.

Miser, A.W., Dothage, J.A., Wesley, R.A., & Miser, J.S. (1987). The prevalence of pain in a pediatric and young adult cancer population. *Pain, 29*, 73-83.

Modi, A.C., Cassedy, A.E., Quittner, A.L., Accurso, F., Sontag, M., Koenig, J.M., & Ittenbach, R.F. (2010). Trajectories of adherence to airway clearance therapy for patients with cystic fibrosis. *Journal of Pediatric Psychology, 35*(9), 1028-1037.

Modi, A. C. & Quittner, A.L. (2003). Validation of a disease-specific measure of health-related quality of life for children with cystic fibrosis. *Journal of Pediatric Psychology, 28*, 535-546.

Modi, A.C., & Quittner, A.L. (2006). Utilizing computerized phone diary procedures to assess health behaviors in family and social contexts. *Children's Health Care, 35*(1), 29-45.

Modi, A. C., & Quittner, A. L. (2006a). Barriers to treatment adherence for children with cystic fibrosis and asthma: What gets in the way? *Journal of Pediatric Psychology, 31*(8), 846–858.

Mulvaney, S., Lambert, E.W., Garber, J., & Walker, L.S. (2006). Trajectories of Symptoms and impairment for pediatric patients with functional abdominal pain: A 5-year longitudinal study. *Journal of American Academics of Child and Adolescent Psychiatry, 45*(6): 737–744.

Munck, A., Pesle, A., Cunin-Roy, C., Gerardin, M., Ignace, I., Delaisi, B., & Wood, C. (2012). Recurrent abdominal pain in children with cystic fibrosis: A pilot prospective longitudinal evaluation of characteristics and management. *Journal of Cystic Fibrosis, 11,* 46–48.

Muthén, L. K., & Muthén, B. O. (2006). *Mplus User's guide*. Los Angeles: Muthén & Muthén.

Muthen B., & Asparouhov, T. (2008). Growth mixture modeling: Analysis with non-Gaussian random effects. In G. Fitzmaurice, M. Davidian, G. Verbeke and G. Molenberghs (Eds.) *Longitudinal Data Analysis*, pp. 143–165. Chapman, all/CRC Press : Boca Raton.

Nelson, T.D., Aylward, B.S., & Steele, R.G. (2008). Structural equation modeling in pediatric psychology: overview and review of applications. *Journal of Pediatric Psychology, 33*(7), 679-687.

Palermo, T.M., Harrison, D., & Koh, J.L. (2006). Effect of disease-related pain on the health-related quality of life of children and adolescents with cystic fibrosis. *Clinical Journal of Pain, 22*(6), 532-537.

Palermo, T.M., Long, A.C., Lewandowski, A.S., Drotar, D., Quittner, A.L., & Walker, L.S. (2008). Evidence-based assessment of health-related quality of life and functional impairment in pediatric psychology. *Journal of Pediatric Psychology, 33*(9), 983-996.

Palermo, T.M., & Valenzuela, D. (2003). Use of pain diaries to assess recurrent and chronic pain in children. *The Suffering Child, 3*, 1–14.

Palermo, T.M,. Valenzuela, D., & Stork, P.P. (2004). A randomized trial of electronic versus paper pain diaries in children: Impact on compliance, accuracy, and acceptability. *Pain, 107*, 213-219.

Palermo, T.M., Zebracki, K., Cox. S., Newman, A.J., & Singer, N.G.. (2004). Juvenile idiopathic arthritis: parent–child discrepancy on reports of pain and disability. *Journal of Rheumatology, 31*, 1840–1846.

Passero, M. A., Remor, B., & Solomon, J. (1981). Patient-reported compliance with cystic fibrosis therapy. *Clinical Pediatrics, 20*, 264–268.

Perquin, C.W., Hazebroek-Kampschreur, A., Hunfeld, J.A.M., Bohnen, A.M., van Suijlekom-Smit, L.W.A. Passchier, J., & van der Wouden, J.C. (2000). Pain in children and adolescents: A common experience. *Pain, 87*, 51-58.

Powell, C.V., Kelly, A.M., Williams, A. (2001). Determining the minimum clinically significant difference in visual analog pain score for children. *Annals of Emergency Medicine, 37*, 28–31.

Quittner, A.L (1998). Measurement of quality of life in cystic fibrosis. *Current Opinion in Pulmonary Medicine, 4*, 326-331.

Quittner, A.L., Alpern, A.N., & Blackwell, L.S. (In Press). Treatment Adherence in Adolescents with Cystic Fibrosis. In C. Castellani, S. Elborn, & H. Heijerman (Eds.), *Health care issues and challenges in the adolescent with cystic fibrosis*.

Quittner, A.L., Barker, D.H., Marceil, K.K., & Grimley, M.E. (2009). Cystic fibrosis: A Model for drug discovery and patient care. In M.C. Roberts & R.C. Steele (Eds.). *Handbook of Pediatric Psychology*. (pp. 271-286). New York, NY: Guilford.

Quittner, A.L., Buu, A., Messer, M.A., Modi A.C., & Watrous, M. (2005). Development and Validation of the Cystic Fibrosis Questionnaire (CFQ) in the United States: A health-related quality of life measure for cystic fibrosis. *Chest, 128*, 2347-2354.

Quittner, A.L., Cruz, I., Modi, A.C., & Marciel, K.K. (2009). Health-related quality of life instruments for adolescents with chronic diseases. In W. O'Donohue, & L. Tolle (Eds). (pp. 311-328) *Behavioral Approaches to Chronic Disease in Adolescence.* Springer.

Quittner, A.L., Drotar, D., Ievers-Landis, C., Seidner, D., Slocum, N., & Jacobsen, J. (2000). Adherence to medical treatments in adolescents with cystic fibrosis: The development and evaluation of family based interventions. In D. Drotar (Ed.) (pp. 383-407), *Promoting adherence to medical treatment in childhood chronic illness: Concepts, Methods, and Interventions*. Mahwah N.J.: Lawrence Erlbaum Associates.

Quittner, A. L., Espelage, D. L., Ievers-Landis, C., & Drotar, D. (2000). Measuring adherence to medical treatments in childhood chronic illness: Considering multiple methods and sources of information. *Journal of Clinical and Psychology in Medical Settings, 7*, 41–54.

Quittner, A.L., Modi, A.C., Lemanek, K.L., Ievers-Landis, C.E., & Rapoff, M.A. (2008). Evidence-based Assessment of Adherence to Medical Treatments in Pediatric Psychology. *Journal of Pediatric Psychology, 33*(9), 916–936.

Quittner, A.L., Riekert, K., Swensin, A. iCARE: I Change Adherence and Raise Expectations. *Protocol* 2009.

Quittner, A.L., Sawicki, G.S., McMullen, A., Rasouliyan, L., Pasta D.J., Yegin, A., & Konstan, M.W. (2012) Erratum to: Psychometric evaluation of the Cystic Fibrosis Questionnaire-Revised in a national, US sample. Quality of Life Research Journal, 21, 1279–1290.

Ramsey, B.W., Davies, J., McElvaney, N.G., Tullis, E., Bell, S.C., Dřevínek, P., Griese, M., McKone, E.F., Wainwright, C.E., Konstan, M.W., Moss, R., Ratjen, F., Sermet-Gaudelus, I., Rowe, S.M., Dong, Q., Rodriguez, S., Yen, K., Ordoñez, C., Elborn, J.S. (2011). A CFTR potentiator in patients with cystic fibrosis and the G551D mutation. *New England Journal of Medicine, 365*(18), 1663-7162.

Ravilly, S., Robinson, W., Suresh, S., Who, M.E., & Berde, C.B. (1996). Chronic pain in cystic fibrosis. *Pediatrics, 98*, 741–747.

Retsch-Bogart, G.Z., Quittner, A.L., Gibson, R.L., Oermann, C.M., McCoy, K.S., Montgomery, A.B., & Cooper, P.J. (2009). Efficacy and safety of inhaled aztreonam lysine for airway pseudomonas in cystic fibrosis. *Chest, 135*(5), 1223-1232.

Saiman, L., & Siegel, J. (2003). Infection control recommendations for patients with cystic fibrosis: Microbiology, important pathogens, and infection control practices to prevent patient-to-patient transmission. *Infect Control Hospital Epidemiology, 24*(5 Suppl), S6-52.

Savedra, M.C., Tesler, M.D., Holzemer, W.L., Wilkie, D.J., & Ward, J.A. (1989). Pain location: Validity and reliability of body outline markings by hospitalized children and adolescents. *Research in Nursing Health, 12*, 307–314.

Sermet-Gaudelus, I., De Villartay, P., de Dreuzy, P., Clairicia, M., Vrielynck, S., & Canoui, P., et al. (2009). Pain in Children and Adults with Cystic Fibrosis: A Comparative Study. *Journal of Pain and Symptom Management*, 281-290.

Singer, J. D. (1998). Using SAS proc mixed to fit multilevel models, hierarchical models, and individual growth models. *Journal of Educational and Behavioral Statistics, 24*, 323-355.

Skevington, S.M. (1998). Investigating the relationship between pain and discomfort and quality of life, using the WHOQOL. *Pain*, 76, 395-406.

Smith, B.A., Modi, A.C., Quittner, A.L., & Wood, B.L. (2010). Depressive symptoms in children with cystic fibrosis and parents and its effects on adherence to airway clearance. *Pediatric Pulmonology*, 45, 756-763.

Stark, L.J., Powers, S.W. (2005). Behavioral aspects of nutrition in children with cystic fibrosis. *Current Opinion in Pulmonary Medicine*, 11(6),539-542.

Stinson, J.N., Stevens, B.J., Feldman, B.M., Streiner, D., McGrath, P.J., Dupuis, A., Gil, N., & Petroz, G.C. (2008). Construct validity of a multidimensional electronic diary for adolescents with arthritis. *Pain, 136*, 281-292.

Turk, D. C., & Melzack, R. (2001). The measurement of pain and the assessment of people experiencing pain. In D. C. Turk & R. Melzack (Eds.), *Handbook of pain assessment* (2nd edn, pp. 3–11). New York: The Guilford Press.

van den Brink, M., Bandell-Hoekstra, E.N., & Abu-Saad, H.H. (2001). The occurrence of recall bias in pediatric headache: a comparison of questionnaire and diary data. *Headache, 41*, 11–20.

Whalen, C.K., Jamner, L.D., Henker, B., & Delfino, R.J. (2001). Smoking and moods in adolescents with depressive and aggressive dispositions; Evidence from surveys and electronic diaries. *Health Psychology, 20,* 99-111.

Wilmott, R.W., Boat, T.F., Bush, A., Chernick, V., Deterding, R.R., & Ratjen, F. (2012). *Kendig and Chernick's Disorders of the Respiratory Tract in Children,* (8th Edition). Philadelphia, PA: Elsevier Saunders.

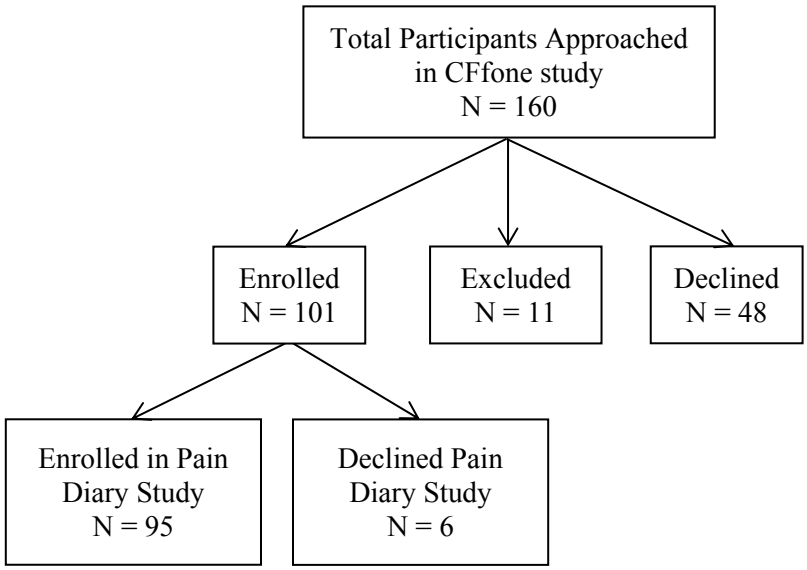


Figure 1. Flow diagram of the sample population in the CFfone study

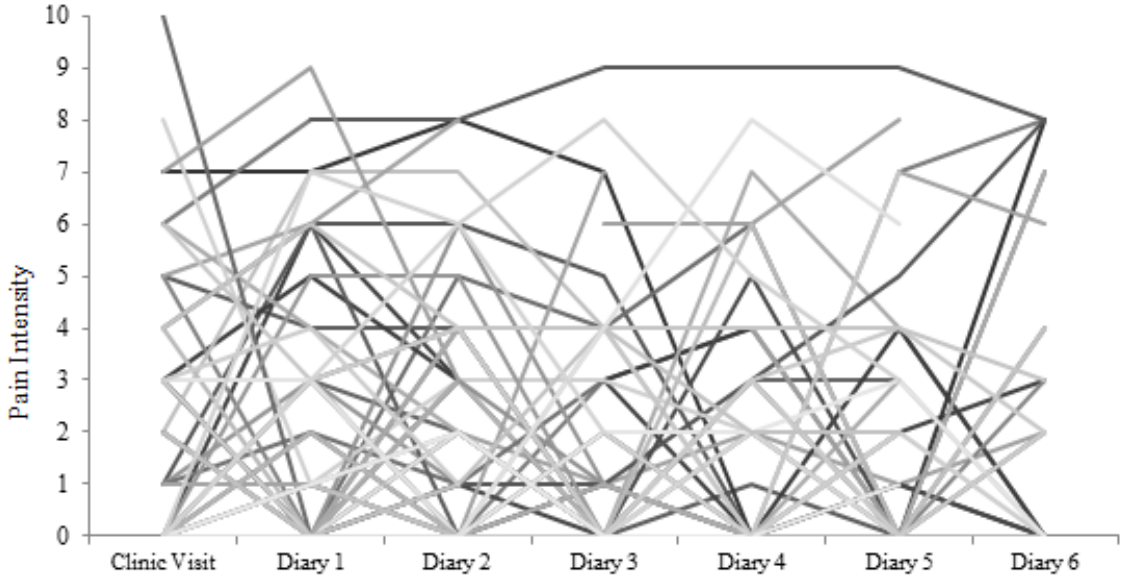


Figure 2. Variability of pain on each diary day at the Baseline assessment.

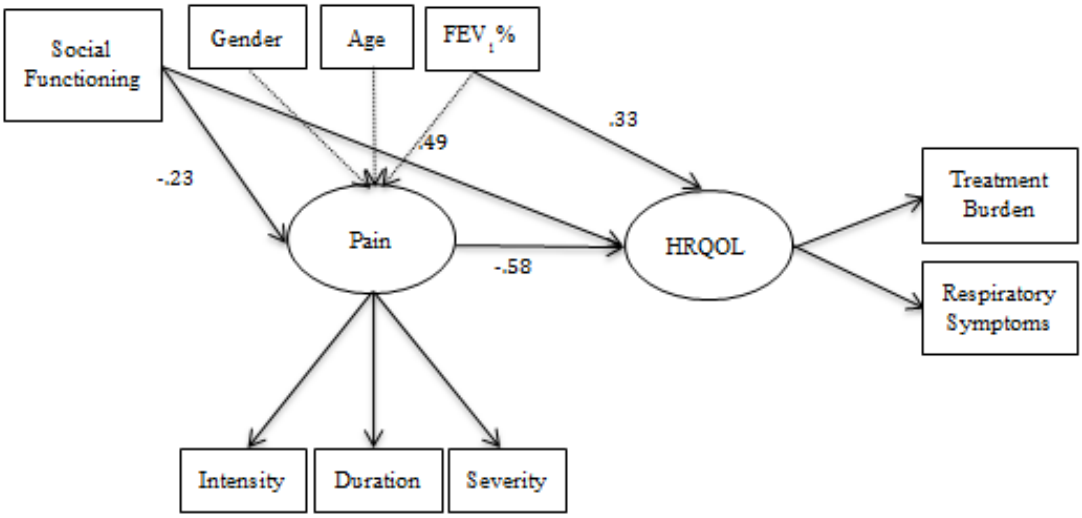


Figure 3. Structural model of the relationships among pain, social functioning and HRQOL at Baseline.

NOTE: Dashed lines indicate insignificant paths

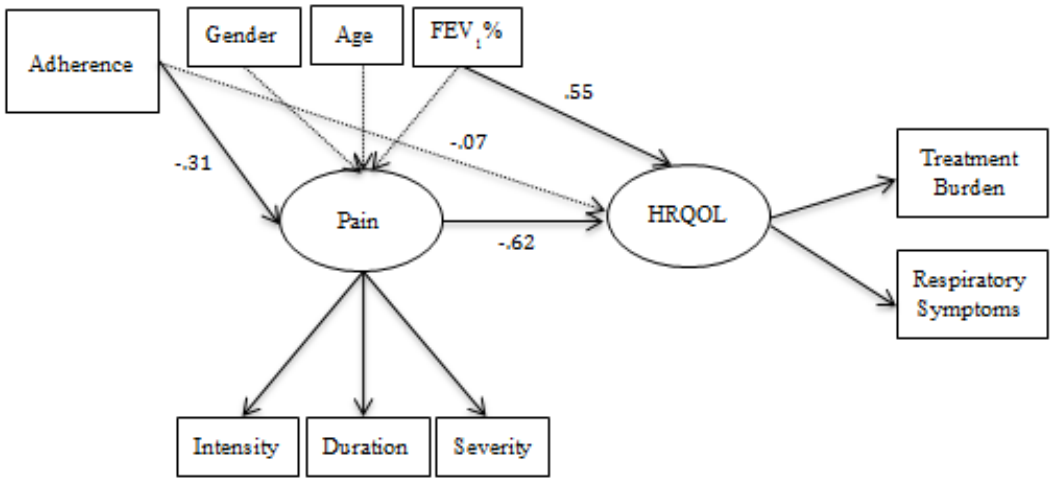


Figure 4. Structural model of the relationships among pain, treatment adherence, and HRQOL at Baseline.

NOTE: Dashed lines indicate insignificant pat

Table 1.

Participant Demographic Characteristics

Characteristic	**N (95)**	**M**	**%**
Age at enrollment (years)		15.8 (2.9)	
Gender			
Male	36		37.9
Female	59		62.1
Race/Ethnicity			
Caucasian	63		66.3
Hispanic	18		18.9
African American	9		9.5
Asian	1		1.1
Prefer not to answer	4		4.2
Parents' Income			
Under $19,999	20		21.0
$20,000 to $49,999	20		21.0
Above $50,000	50		52.6
Prefer not to answer	5		7.4

Table 2.

Demographic Comparisons of Participants in the Treatment and Comparison Conditions

Characteristic	**Treatment (N = 47)**	**Comparison (N = 48)**	**T or χ^2 (*p*-value)**
Age at enrollment (years)			-.84 (.40)
Mean age (SD)	15.5 (2.9)	15.9 (2.9)	
Gender			-.25 (.62)
Male	33%	32%	
Female	67%	68%	
Race/Ethnicity			
White	59%	71%	2.13 (.55)
African-American	13%	7%	
Hispanic	21%	19%	
Other	7%	3%	
Parents' Income			9.9 (.19)
< $5,000	5%	7%	
$5 – 9,999	13%	7%	
$10 – 19,999	13%	2%	
$20 – 29,999	10%	5%	
$30 – 39,999	8%	11%	
$40 - 49,999	8%	2%	
$50 – 59,999	8%	16%	
$60 – 69,999	30%	43%	
Decline	5%	7%	
FEV1% Predicted at enrollment	76.1 (28.6)	83.5 (25.4)	-1.3 (.19)
Average Pain (Baseline)	1.58 (1.8)	1.83 (1.9)	.19 (.40)

Table 3.

Pain Intensity, Treatment Adherence, Social Support and HRQOL by Treatment Group Over Time.

	Baseline Visit (Time 1) N =95			Interim Visit (Time 2) N = 76			Post Visit (Time 3) N = 72		
	Treatment *Mean (SD)*	Comparison *Mean (SD)*	All *Mean (SD)*	Treatment *Mean (SD)*	Comparison *Mean (SD)*	All *Mean (SD)*	Treatment *Mean (SD)*	Comparison *Mean (SD)*	All *Mean (SD)*
Pain Intensity	1.65 (2.0)	1.59 (1.6)	1.62 (1.8)	1.73 (2.2)	1.49 (2.1)	1.62 (2.1)	1.97 (2.4)	1.29 (1.9)	1.64 (2.2)
Social Functioning	63.51 (20.1)	68.70 (15.1)	66.13 (17.9)	68.76 (16.7)	70.27 (16.7)	69.47 (16.6)	69.44 (17.3)	70.32 (14.4)	69.86 (15.9)
Respiratory Symptoms	62.29 (21.9)	66.90 (20.4)	64.62 (21.2)	67.71 (22.3)	65.51 (23.5)	66.67 (27.8)	61.61 (24.5)	72.71 (18.7)	66.90 (22.5)
Treatment Burden	60.52 (18.5)	58.33 (19.4)	59.42 (18.9)	61.53 (21.5)	60.80 (14.4)	61.18 (18.4)	60.06 (19.9)	64.14 (15.8)	61.98 (18.0)
Social Support	12.77 (4.1)	13.28 (3.7)	13.03 (3.8)	13.84 (3.8)	13.43 (3.9)	13.64 (3.8)	14.14 (3.6)	13.72 (3.8)	13.94 (3.7)
Treatment Adherence	63.86 (33.3)	56.01 (23.4)	59.86 (28.7)	-	-	-	-	-	-

Table 4

Bivariate Correlations among Variables at the Baseline Assessment

Variable	1	2	3	4	5	6	7
1. Average Pain	-	-.02	-.18	-.32**	-.45**	-.01	-.32*
2. FEV_1%		-	.24*	.19	.34**	-.21	-.28*
3. Social Functioning			-	.34**	.46**	.18	-.13
4. Treatment Burden				-	.34**	-.04	.07
5. Respiratory Symptoms					-	-.11	-.12
6. Social Support						-	-.04
7. Treatment Adherence							-

Table 5.

Univariate Models of Pain and HRQOL

	No Change				**Constant Change**				**Proportional Change**				**Dual Change**			
Parameters and fit indices	Pain	Treatment Burden	Social Fx	Respiratory Sys	Pain	Treatment Burden	Social Fx	Respiratory Sys	Pain	Treatment Burden	Social Fx	Respiratory Sys	Pain	Treatment Burden	Social Fx	Respiratory Sys
M Slope (σ)	0(=)	0(=)	0(=)	0(=)	.001	1.16	2.02	0.71	0(=)	0(=)	0(=)	0(=)	-.26	-15.92	0(=)	-5.15
M Int (σ)	0(=)	0(=)	0(=)	0(=)	1.63	59.59	66.51	65.00	1.60	59.51	66.65	64.41	1.63	59.63	30.09	64.54
Proportional coefficients																
β1	0(=)	0(=)	0(=)	0(=)	0(=)	0(=)	0(=)	0(=)	.03	.01	.02	.02	.16	.27	-0.43	.10
β2	0(=)	0(=)	0(=)	0(=)	0(=)	0(=)	0(=)	0(=)	.03	.01	.02	.02	.16	.27	-0.43	.10
Goodness – of-fit indices																
Degrees of freedom	2	4	4	4	6	6	6	6	4	5	4	4	3	3	2	3
X2	4.93	9.11	4.52	5.79	32.33	72.82	123.11	77.56	13.92	8.44	4.79	4.11	13.53	6.59	25.95	3.93
SRMR	.11	.07	.14	.09	.26	.34	.43	.35	.14	.08	.10	.09	.12	.11	.32	.07
CFI	.91	.93	.99	.98	.21	.05	.02	.04	.70	.94	.99	.99	.68	.95	.81	.99
RMSEA	.13	.12	.04	.07	.22	.34	.45	.35	.16	.11	.05	.02	.19	.12	.28	.06

Table 6.

Multilevel Regression Analyses Predicting Daily Pain

Random Effects

Covariance Parameter Estimates	**Subject**	**β**	***SE*β**	**Z**	***p***
UN (1,1)	ID	1.07**	0.40	2.64	<0.01
UN (2,1)	ID	-0.04	0.04	-0.96	0.34
UN (2,2)	ID	0.01*	0.01	1.76	0.04
Residual	.	3.45**	0.20	17.30	<0.01

Fixed Effects

Predictor Variables	**β**	***SE* β**	***df***	***t***	***p***
Level 1					
Intercept	1.50**	0.20	52	7.75	<0.01
Δ Daily Pain	-0.01	0.02	633	-0.52	0.60
Level 2					
Treatment Adherence	-0.01	0.01	52	-2.89	<0.01
Social Functioning	-0.03	0.01	633	-0.25	0.80
Treatment Burden	-0.02*	0.01	633	-1.96	0.05
Respiratory Symptoms	-0.02	0.01	633	-1.54	0.12
Level 1 X Level 2					
Δ Daily Pain X Social Functioning	<0.01	<0.01	633	0.55	0.58
Δ Daily Pain X Treatment Burden	0.01	<0.01	633	1.61	0.11
Δ Daily Pain X Respiratory Symptoms	<0.01	<0.01	633	0.01	0.98

Notes: UN refers to unstructured model specification.
**p<.01.
*p<.05.

Appendix A: Daily Pain Assessment Questionnaire for Cystic Fibrosis

DPAQ-CF

DAILY PAIN ASSESSMENT QUESTIONNAIRE FOR CYSTIC FIBROSIS

1. How many different pain episodes did you have today?
   a. 1
   b. 2-3
   c. 4-5
   d. 6 or more

2. How long did the pain last?
   a. Less than 1 hour
   b. A few hours
   c. Half of the day
   d. All day

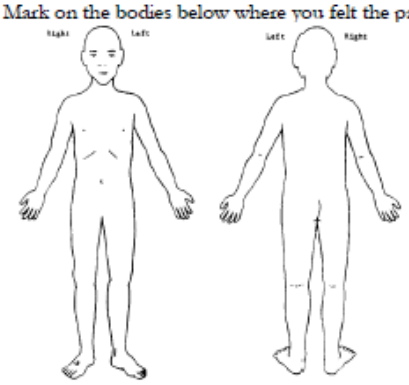
3. What was the pain related to?
   a. Treatment
   b. General Pain

   *** If b, go to question #5.**

Instructions: *Think about the* ***worst pain*** *that you experienced today and answer the following questions about that pain.*

4. During what treatment did the pain episode take place?
   a. Airway Clearance (Chest Physical Therapy (CPT), Flutter, Vest)
   b. Exercise
   c. Nebulized antibiotics
   d. Blood glucose checks
   e. IV
   f. Port accessed/cleaned
   g. Oral medications
   h. Other: _____

5. Mark on the bodies below where you felt the pain:



6. Mark on the scale how painful the episode was:

No pain Moderate pain Worst pain possible

7. What did the pain feel like?
   - ☐ Aching
   - ☐ Sore
   - ☐ Pounding
   - ☐ Stabbing
   - ☐ Cramping
   - ☐ Numb
   - ☐ Stiff
   - ☐ Pressure
   - ☐ Itching
   - ☐ Splitting
   - ☐ Swollen
   - ☐ Pinching/pricking

8. What method(s) did you use to relieve your pain?
   a. Resting
   b. Taking medications/pills
   c. Relaxing (sitting quietly)
   d. Heat/Ice
   e. Time with family or friends
   f. Distracting myself (playing a game, listening to music)
   g. Nothing
   h. Other:_____

Appendix B: Cystic Fibrosis Questionnaire- Revised Young Child Version

CFQ-R

Children Ages 6 to 11 (Interviewer Format)

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

ID: _____

Date: _____

This questionnaire is formatted for use by an interviewer. Please use this format for younger children. For older children who seem able to read and answer the questions on their own, such as 12 and 13 year olds, use this questionnaire in its self-report format.

There are directions for the interviewer for each section of the questionnaire. Directions that you should *read* to the child are indicated by quotation marks. Directions that you are to *follow* are underlined and set in italics.

Interviewer: *Please read the following to the child:*

"These questions are for children like you who have cystic fibrosis. Your answers will help us understand what this disease is like and how your treatments help you. So, answering these questions will help you and others like you in the future."

"For each question that I ask, choose one of the answers on the cards I'm about to show you."

Present the orange card to the child.

"Look at this card and read with me what it says: **very true, mostly true, somewhat true, not at all true**."

"Here's an example: If I asked you if it is **very true, mostly true, somewhat true, not at all true** that elephants can fly, which one of the four answers on the card would you choose?"

Present the blue card to the child.

"Now, look at this card and read with me what it says: **always / often / sometimes / never**."

"Here's another example: If I asked you if you go to the moon **always, often, sometimes, or never**, which answer on the card would you choose?"

Present the orange card to the child.

"Now, I will ask you some questions about your everyday life."

"Tell me if you find the statements I read to you to be **very true, mostly true, somewhat true, or not at all true**."

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CFQ-R **Children Ages 6 to 11 (Interviewer Format)**

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

Please check the box indicating the child's response.

Interviewer: *Present the blue card to the child.*

Please check the box indicating the child's response.

"And during these past two weeks, tell me how often":	Always	Often	Sometimes	Never
1. You had to stop fun activities to do your treatments	☐	☐	☐	☐

Interviewer: *Present the orange card to the child.*

"Now tell me if you find the statements I read to you to be **very true, mostly true, somewhat true,** or **not at all true**."

Please check the box indicating the child's response.

"During the past two weeks":	Very True	Mostly True	Somewhat True	Not at all True
2. You were able to do all of your treatments	☐	☐	☐	☐
3. You got together with friends a lot	☐	☐	☐	☐
4. You stayed at home more than you wanted to	☐	☐	☐	☐
5. You felt comfortable sleeping away from home (at a friend or family member's house or elsewhere)	☐	☐	☐	☐
6. You felt left out	☐	☐	☐	☐
7. You often invited friends to your house	☐	☐	☐	☐
8. You were teased by other children	☐	☐	☐	☐
9. You felt comfortable discussing your illness with others (friends, teachers	☐	☐	☐	☐
10. Doing your treatments bothered you	☐	☐	☐	☐

CFQ-R

Children Ages 6 to 11 (Interviewer Format)

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

Interviewer: *Present the blue card to the child again*

Please check the box indicating the child's response.

"Tell me how often in the past **two weeks**":	Always	Often	Sometimes	Never
11. You coughed during the day	☐	☐	☐	☐
12. You woke up during the night because you were coughing	☐	☐	☐	☐
13. You had to cough up mucus	☐	☐	☐	☐
14. You had trouble breathing	☐	☐	☐	☐

Please be sure all the questions have been answered.

THANK YOU FOR YOUR COOPERATION!

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Appendix C: Cystic Fibrosis Questionnaire- Revised Older Child Version

CFQ-R

Children Ages 12 and 13 (Self-report Format)

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

ID: _____

Date: _____

These questions are for children like you who have cystic fibrosis. Your answers will help us understand what this disease is like and how your treatments help you. So, answering these questions will help you and others like you in the future.

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.

Please check the box matching your response.

During these past **two weeks**, indicate how often:	Always	Often	Sometimes	Never
1. You had to stop fun activities to do your treatments	☐	☐	☐	☐

During the past **two weeks**:	Very True	Mostly True	Somewhat True	Not at all True
2. You were able to do all of your treatments	☐	☐	☐	☐
3. You got together with friends a lot	☐	☐	☐	☐
4. You stayed at home more than you wanted to	☐	☐	☐	☐
5. You felt comfortable sleeping away from home (at a friend or family member's house or elsewhere)	☐	☐	☐	☐
6. You felt left out	☐	☐	☐	☐
7. You often invited friends to your house	☐	☐	☐	☐
8. You were teased by other children	☐	☐	☐	☐
9. You felt comfortable discussing your illness with others (friends, teachers)	☐	☐	☐	☐
10. Doing your treatments bothered you	☐	☐	☐	☐

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CFQ-R

Children Ages 12 and 13 (Self-report Format)

CYSTIC FIBROSIS QUESTIONNAIRE-REVISED

Please check the box matching your response.

Let us know how often in the past **two weeks**:	Always	Often	Sometimes	Never
11. You coughed during the day	☐	☐	☐	☐
12. You woke up during the night because you were coughing	☐	☐	☐	☐
13. You had to cough up mucus	☐	☐	☐	☐
14. You had trouble breathing	☐	☐	☐	☐

Please be sure all the questions have been answered.

THANK YOU FOR YOUR COOPERATION!

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Appendix D: Cystic Fibrosis Questionnaire- Revised Teen/Adult Version

CFQ-R

Adolescents and Adults (Patients 14 Years Old and Older)

CYSTIC FIBROSIS QUESTIONNAIRE – REVISED (SELECTED SUBTESTS)

ID: _____

Date: _____

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

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:

1. To what extent do your treatments make your daily life more difficult?
   1. Not at all
   2. A little
   3. Moderately
   4. A lot
2. How much time do you currently spend each day on your treatments?
   1. A lot
   2. Some
   3. A little
   4. Not very much
3. 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

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
4. I have to stay at home more than I want to	☐	☐	☐	☐
5. I feel comfortable discussing my illness with others	☐	☐	☐	☐
6. People are afraid that I may be contagious	☐	☐	☐	☐
7. I get together with my friends a lot	☐	☐	☐	☐
8. I think my coughing bothers others	☐	☐	☐	☐
9. I feel comfortable going out at night	☐	☐	☐	☐

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CFQ-R

Adolescents and Adults (Patients 14 Years Old and Older)

CYSTIC FIBROSIS QUESTIONNAIRE – REVISED (SELECTED SUBTESTS)

Indicate how you have been feeling during the past two weeks.	A great deal	Somewhat	A little	Not at all
10. Have you been congested?	☐	☐	☐	☐
11. Have you been coughing during the day?	☐	☐	☐	☐
12. Have you had to cough up mucus?	☐	☐	☐	☐ Go to Question 13

13. 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
14. Have you been wheezing?	☐	☐	☐	☐
15. Have you had trouble breathing?	☐	☐	☐	☐
16. Have you woken up during the night because you were coughing?	☐	☐	☐	☐

Please be sure you have answered all the questions.

THANK YOU FOR YOUR COOPERATION!

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Appendix E: Perceived Adolescent Social Support Cystic Fibrosis

ID: ____________________

Date: ____________________

PASS-CF Perceived Adolescent Social Support Cystic Fibrosis

Instructions: The following questions are about what your family and friends do to help you manage your CF. There are no right or wrong answers. If you are not sure how to answer, choose the response that seems closest to your situation. *Please answer all of the questions.*

Please list your friends who do not have CF by their initials	Do they know about your CF?	How often do you talk to them?				How do you talk to them?			How close do you feel to this person?			
		Daily	Weekly	Monthly	Yearly	Email, IM, online	On the phone	In person	Not Close	Somewhat Close	Close	Very Close
	Yes No											
	Yes No											
	Yes No											
	Yes No											
	Yes No											
	Yes No											
	Yes No											
	Yes No											
	Yes No											

Please list your friends who do have CF by their initials ☐ No friends with CF	Do they know about your CF?	How often do you talk to them?				How do you talk to them?			How close do you feel to this person?			
		Daily	Weekly	Monthly	Yearly	Email, IM, online	On the phone	In person	Not Close	Somewhat Close	Close	Very Close
	Yes No											
	Yes No											
	Yes No											
	Yes No											
	Yes No											
	Yes No											
	Yes No											
	Yes No											
	Yes No											

PASS-CF: Health Care Team

At my last clinic visit, my healthcare team...	How often did this happen?				How supportive or unsupportive was this?				
	Never	Sometimes	Often	Always	Very Supportive	Supportive	Neither	Unsupportive	Very Unsupportive
1) Provided good care	N	S	O	A	☐	☐	☐	☐	☐
2) Helped me fit treatments into my daily schedule	N	S	O	A	☐	☐	☐	☐	☐
3) Made the clinic visit as short as possible	N	S	O	A	☐	☐	☐	☐	☐
4) Included me in decisions about my health	N	S	O	A	☐	☐	☐	☐	☐
5) Told me what to do	N	S	O	A	☐	☐	☐	☐	☐
6) Encouraged me to complete my treatments	N	S	O	A	☐	☐	☐	☐	☐
7) Helped me solve problems with doing my treatments	N	S	O	A	☐	☐	☐	☐	☐
8) Gave clear treatment instructions	N	S	O	A	☐	☐	☐	☐	☐
9) Listened to me when I was feeling down or sad	N	S	O	A	☐	☐	☐	☐	☐

PASS-CF: Friends without CF

During the past <u>two weeks</u>, my friends...	How often did this happen?				How supportive or unsupportive was this?				
	Never	Sometimes	Often	Always	Very Supportive	Supportive	Neither	Unsupportive	Very Unsupportive
1) Talked with me about my CF	N	S	O	A	☐	☐	☐	☐	☐
2) Asked me how I was feeling	N	S	O	A	☐	☐	☐	☐	☐
3) Kept me company while I was doing my treatments	N	S	O	A	☐	☐	☐	☐	☐
4) Changed their plans so I could do my treatments	N	S	O	A	☐	☐	☐	☐	☐
5) Reminded me to do my treatments	N	S	O	A	☐	☐	☐	☐	☐
6) Encouraged me to eat more	N	S	O	A	☐	☐	☐	☐	☐
7) Distracted me from doing my treatments	N	S	O	A	☐	☐	☐	☐	☐
8) Complained about my CF	N	S	O	A	☐	☐	☐	☐	☐
9) Did not judge me for having CF	N	S	O	A	☐	☐	☐	☐	☐
10) Showed me they care	N	S	O	A	☐	☐	☐	☐	☐
11) Called, texted, IM'd or emailed me	N	S	O	A	☐	☐	☐	☐	☐
The last time I was feeling down or sad, my friends...									
12) Helped me take my mind off of it	N	S	O	A	☐	☐	☐	☐	☐
13) Listened to me	N	S	O	A	☐	☐	☐	☐	☐
14) Tried to make me laugh	N	S	O	A	☐	☐	☐	☐	☐

PASS-CF: Friends with CF

During the past two weeks, my friends...	How often did this happen?				How supportive or unsupportive was this?				
	Never	Sometimes	Often	Always	Very Supportive	Supportive	Neither	Unsupportive	Very Unsupportive
1) Talked with me about my CF	N	S	O	A	☐	☐	☐	☐	☐
2) Asked me how I was feeling	N	S	O	A	☐	☐	☐	☐	☐
3) Kept me company while I was doing my treatments	N	S	O	A	☐	☐	☐	☐	☐
4) Changed their plans so I could do my treatments	N	S	O	A	☐	☐	☐	☐	☐
5) Reminded me to do my treatments	N	S	O	A	☐	☐	☐	☐	☐
6) Encouraged me to eat more	N	S	O	A	☐	☐	☐	☐	☐
7) Distracted me from doing my treatments	N	S	O	A	☐	☐	☐	☐	☐
8) Complained about my CF	N	S	O	A	☐	☐	☐	☐	☐
9) Did not judge me for having CF	N	S	O	A	☐	☐	☐	☐	☐
10) Showed me they care	N	S	O	A	☐	☐	☐	☐	☐
11) Called, texted, IM'd or emailed me	N	S	O	A	☐	☐	☐	☐	☐
The last time I was feeling down or sad, my friends...					☐	☐	☐	☐	☐
12) Helped me take my mind off of it	N	S	O	A	☐	☐	☐	☐	☐
13) Listened to me	N	S	O	A	☐	☐	☐	☐	☐
14) Tried to make me laugh	N	S	O	A	☐	☐	☐	☐	☐