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# Barriers to Treatment Adherence in Adolescents with Cystic Fibrosis: A Mixed-Methods Analysis

Katherine A. McLean

*University of Miami*, [katherine.ann.mclean@gmail.com](mailto:katherine.ann.mclean@gmail.com)

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UNIVERSITY OF MIAMI

BARRIERS TO TREATMENT ADHERENCE IN ADOLESCENTS WITH CYSTIC  
FIBROSIS: A MIXED-METHODS ANALYSIS

BY

Katherine Ann McLean

A DISSERTATION

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

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Katherine Ann McLean

Approved:

\_\_\_\_\_  
Alexandra L. Quittner, Ph.D.  
Professor of Psychology

\_\_\_\_\_  
Rebecca Shearer Ph.D.  
Associate Professor of  
Psychology

\_\_\_\_\_  
Brian Doss, Ph.D.  
Associate Professor of Psychology

\_\_\_\_\_  
Neena Malik, Ph.D.  
Scientist, Department of Pediatrics

\_\_\_\_\_  
Dean of the Graduate School

\_\_\_\_\_  
Matthias Salathe, M.D.  
Professor of Medicine

MCLEAN, KATHERINE ANN

(Ph.D., Psychology)

Barriers to Treatment Adherence in Adolescents  
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Poor treatment adherence is a significant challenge for patients, parents, and healthcare providers. Treatment adherence is a serious concern for adolescents with cystic fibrosis (CF), a life-limiting genetic disorder affecting multiple organ systems. Although some barriers to adherence have been documented in CF, little is known about how these barriers interact at an individual level. The purpose of this study was to conduct a mixed-methods analysis of barriers to adherence reported by adolescents and young adults with CF and their parents. This study utilized qualitative interviews and quantitative measures of adherence and psychosocial functioning to identify key barriers in relation to adherence behaviors. Interviews were conducted with 18 adolescents/young adults with CF and 17 of their caregivers (17 dyads). Participants were asked to rate the severity of the barriers they generated immediately after the interviews. Patients completed a 3-day phone diary to capture treatment adherence. Patients and parents completed quantitative measures of family conflict, depression, anxiety, and health-related quality of life. Interviews were analyzed utilizing grounded theory method; six major themes emerged during the analysis. There were important differences between the most frequently occurring barriers and the barriers identified as most severe. This study highlighted the range of barriers to adherence for adolescents/young adults with CF and the importance of capturing barrier frequency and severity separately.

This dissertation is dedicated to patients and families living with cystic fibrosis (CF) worldwide.

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## Chapter 1: Introduction

Rates of childhood chronic illness are increasing, with prevalence estimates ranging from 13% to 26% in children in the United States (Vanceleave, Gortmaker, & Perrin, 2010). Management of these conditions presents a significant challenge for patients, parents and healthcare providers. Many chronic conditions require long-term, complex treatment regimens, which are only effective when completed as prescribed. However, estimates of adherence indicate that patients complete approximately 50% or less of their treatments (Johnson & Carlson, 2004; Quittner et al., 2014; Rapoff 2010; Sabaté, 2003; Sackett & Snow, 1979). These low rates of adherence are associated with greater morbidity and earlier mortality (Balkrishnan, 2005; Briesacher et al. 2011a; DiMatteo et al., 2002; Eakin et al. 2011), as well as increased healthcare utilization and cost (Quittner et al., 2014). Recent estimates of the costs of poor adherence indicate that approximately 300 billion dollars are wasted annually (Bender & Rand, 2004; Osterberg & Blaschke, 2005). Although some variables that affect adherence have been identified, such as age, family functioning, and access to care, treatment barriers at an individual level are poorly understood (Logan et al., 2003). The purpose of the current study was to conduct a mixed-methods analysis of barriers to adherence reported by adolescents and young adults with cystic fibrosis (CF) and their caregivers.

### *Cystic fibrosis- A unique challenge*

CF has arguably the *most* complex treatment regimen of any pediatric chronic condition, with a median of 7 treatments required per day (Barry & Jones, 2015). Given

the low rates of adherence documented in a national CF sample, targeting improvements in disease management is critical (Quittner et al., 2014). This study identified the key barriers to adherence reported by adolescents, young adults and caregivers living with the disease. CF is a genetic, life-limiting disease most commonly found among Caucasian populations. It is caused by a genetic mutation of the CFTR protein (i.e., cystic fibrosis transmembrane regulator), resulting in the production of thick, sticky mucus in all mucus-secreting glands (Pittman & Ferkel, 2015). This process of inflammation and infection leads to repeated pulmonary exacerbations, ultimately resulting in lung damage and respiratory failure.

In a majority of patients, the pancreas is also blocked in utero, preventing release of pancreatic enzymes during digestion. This causes difficulties with weight gain and growth (CF Foundation, 2013; Pittman & Ferkol, 2015). Currently, the majority of treatments are palliative in nature and slow the progression of disease rather than addressing its underlying pathology. The exception to this are patients with the G551D and delta F508 mutations for whom new, disease modifying drugs have shown exceptional promise (ivacaftor; Ramsey et al., 2011; lumacaftor/ivacaftor; Boyle et al., 2014). However, the G551D mutation only occurs in 4% of the individuals with CF in the United States (Ledford, 2012). The homozygous delta F508 mutation is one of the most common in the world, representing almost 45% of patients with CF. However, lumacaftor/ivacaftor has demonstrated a less dramatic clinical improvement in these individuals than ivacaftor did in people with the G551D mutation (Wainwright et al., 2015).

Currently, mortality rates from CF are declining, and projected median life expectancy is approximately 37 years for men and 40 years for women (MacKenzie et al. 2014). However, according to the CF Foundation Patient Registry, modal age of death is in the mid-20's (Zemanick et al., 2010). The treatment regimen for CF is among the most complex and time-consuming, including airway clearance, aerosolized medications, oral antibiotics and vitamins, increased calorie intake of up to 210 % of the recommended daily allowance of calories and pancreatic enzymes with each meal and snack (Rowe & Clancy, 2006; Sawicki & Goss, 2015; Sawicki & Tiddens, 2012). As new drugs have been approved, they have been added to the list of prescribed treatments, however, no current treatments have been removed, leading to a daily regimen which can take 2-3 hours per day (Sawicki, Sellers, & Robinson, 2009; Sawicki & Goss, 2015).

Adherence is a significant challenge for individuals with CF and as they get older, rates of adherence decrease (Barker & Quittner, in press; Quittner et al., 2014). Studies of adherence have reported rates ranging from 27% to 82%, with overall adherence below 50% for the majority of treatments (Barker & Quittner, in press; Eakin et al. 2011; Modi & Quittner, 2006a; Quittner et al., 2014; Shakkottai et al., 2015, Zindani et al. 2006). Poor adherence in CF has been associated with increased morbidity (e.g., more hospitalizations; Briesacher et al., 2011a), higher health care costs (Briesacher et al., 2011b; Quittner et al., 2014), worse quality of life, and worse health outcomes (Eakin et al., 2011). Thus, improving adherence is critical to maximizing health outcomes. To date, however, few adherence interventions have been developed or tested, in part, because little is known about the specific barriers to adherence encountered by patients and families (Modi & Quittner, 2006a; George et al., 2010; Sawicki et al., 2015). This study

utilized a mixed methods approach, eliciting information directly from patients and parents, using qualitative interviews and quantitative measures of adherence and psychosocial functioning, to identify key barriers to adherence. Negative associations were expected between frequency and severity of barriers described by participants and their adherence, health related quality of life, and emotional functioning.

### *Barriers to adherence*

Treatment adherence has been defined as “the extent to which a patient’s behavior coincides with medical or health advice” (Sackett et al., 1979). Although this definition seems straightforward, achieving good adherence is a daily challenge for patients and is associated with a variety of individual, family and systems factors. Achieving good rates of adherence requires skillful self-management by patients and families. Modi and colleagues (2012) developed the Pediatric Self-Management Model to identify the complex factors that contribute to a patient’s ability to adhere to their treatment regimen. This model highlights the interaction of self-management behaviors with contextual variables across four domains, including: 1) individual, 2) family, 3) health care system, and 4) community influences. The modifiability of these factors plays an important role in how they interact with self-management behaviors; for example, many health-care factors (access to insurance) are not modifiable and thus, are a formidable challenge for patients and families.

More recently, a meta-analysis by Hanghøj & Boisen (2014) reviewed 28 quantitative, qualitative, and q-methodology studies to assess commonly reported barriers to adherence across illnesses. They authors conducted a systematic literature review to

identify common barriers in adolescence. They identified seven families of barriers that were frequently reported across studies and diseases: 1) relations (with peers, parents, and healthcare professionals), 2) adolescent development, 3) health and illness factors, 4) forgetfulness, 5) organization, 6) medicine complexity, and 7) financial costs. Although these frameworks are helpful for understanding the multiple systems related to adherence, the grounded theory approach used in this study argues that these barriers must be elicited directly from patients and family members, rather than imposing a pre-determined set of categories drawn from the literatures.

*Unique Challenges of Adolescence & Young Adulthood.* Across chronic conditions, treatment adherence has been shown to decline in adolescence and young adulthood (Brownbridge & Fielding, 1994; Mellins, Brackis-Cott, Dolezal, & Abrams, 2004; Pai & Ostendorf, 2011; Quittner et al., 2014; Rausch et al., 2012), and barriers to adherence increase during this period (Logan et al., 2003; Modi & Quittner, 2006a; Wysocki et al. 2007). This is particularly true in CF, with adherence rates declining as patients get older (Quittner et al., 2014; Shakkotai et al., 2015). Given that the focus of adolescence is on peer relationships, the stigma of having a chronic illness and deciding whether or not to disclose it to peers is stressful (Modi et al., 2010). Due to the life-limiting nature of CF, disclosure of the condition to potential employers or romantic partners may also result in negative responses or rejection (Modi et al., 2010). Medications need to be taken at school or in front of peers (Sawicki & Tiddens, 2012), which can result in embarrassment or avoidance behaviors. A transition toward independence also occurs during this period, with a natural developmental shift toward

greater autonomy and assumption of responsibility for daily treatments (Modi et al., 2010).

During the transition from adolescence to young adulthood, the disease often progresses, leading to more pulmonary exacerbations and more nutritional and gastrointestinal problems (Konstan, 2007). This decline in health results in additional treatments and more frequent hospitalizations, leading to absences from school and social events. Patients must learn to balance these increased treatment demands and worsening health with their desire to become more independent (Modi et al., 2010; Quittner & Barker, 2010; Sawicki & Tiddens, 2012; Sawicki & Goss, 2015). This transition is complex given that parental supervision has been shown to improve rates of adherence to nebulized treatments (Modi et al., 2008). This leads to tension and uncertainty about how to navigate this transition within the family, juxtaposing parental desires to ensure good adherence with the patient's need to assume these responsibilities. A better understanding of what makes this developmental period difficult for parents and patients is crucial to maintaining adherence and slowing disease progression.

Recently, Sawicki and colleagues (2015) performed a qualitative assessment of barriers and motivators impacting treatment adherence in 18 parent-adolescent dyads with CF. Five important themes emerged during this analysis: 1) Immediate time pressures, 2) Awareness of disease trajectory, 3) Competing priorities, 4) Privacy issues, and 5) Lack of perceived consequences. They also assessed motivations to adhere during these interviews. However, these barriers were not evaluated in relation to a well-validated, objective measure of adherence, such as the Daily Phone Diary (DPD; Quittner

& Opiari, 1994). The current study utilized the DPD to link self-reported barriers with adherence to several aspects of the treatment regimen. Furthermore, Sawicki and colleagues did not assess emotional functioning, health-related quality of life, or parent-child conflict in relation to these barriers.

*Individual and family factors.* Even when family functioning is intact, adherence can be low if an adolescent or family does not have sufficient knowledge of disease management (LaGreca 1990; Modi et al., 2012; Rapoff 2010; Quittner et al., 2012). CF is complex to manage, and the standard treatment regimen has changed significantly over time, necessitating re-education of patients and families (Sawicki & Tiddens, 2012; Sawicki & Goss, 2015). Completing treatments independently also requires motivation and organization.

Negative emotions, including sadness and frustration with diagnosis, can cause difficulties with motivation, and may eventually escalate to symptoms of depression. Depression is consistently associated with lower rates of adherence in those with chronic illnesses (DiMatteo et al., 2003; Ettinger et al., 2014). Parents and other family members provide both emotional and instrumental support for adolescents (Cauce, Reid, Landesman, & Gonzalez, 1990), and psychological distress can reduce their ability to provide effective support. Recently, Quittner and colleagues (2014) conducted a large, international study assessing the prevalence of depression and anxiety in patients and caregivers of children with CF. They found that mothers of children with CF had higher rates of depression and anxiety than community samples, with nearly 37% reporting clinically significant depressive symptoms and 48% reporting elevated anxiety.



Adolescents and adults also reported elevated rates of depression and anxiety. This study included screening measures of depression and anxiety and linked them to barriers and rates of adherence.

Family conflict also plays an important role in the management of chronic illness and tends to be elevated in these families compared to matched, healthy controls (Wysocki et al., 2006; Caplan et al. 2005; DeLambo et al., 2004). In CF, parents often report “burn out” in relation to daily management of the disease and this is related to increased parent-teen conflict about daily treatments (e.g., nagging, arguing) (Modi et al, 2008). DeLambo and colleagues (2004) found that poor observed family relationship quality during discussions of pulmonary treatments was negatively associated with self-reported adherence.

A recent study by Everhart and colleagues (2015) identified higher rates of adherence to oral antibiotics and lower rates of adherence to enzymes in families with lower levels of conflict. Although parent-child conflict is elevated in families living with CF, Sawicki and colleagues (2015) found that adolescents wanted their parents to continue to be involved in their day-to-day disease management. In this study, agreement on the treatment barriers elicited from teens and young adults with CF and their parents was evaluated and linked to both self-reported family conflict and adherence measured via the daily diary (Modi et al., 2006). Patient-caregiver agreement on barriers was expected to be positively related to treatment adherence and negatively related to family conflict.

*Healthcare systems factors.* Managing a chronic disease in our current healthcare system is complex, requiring access to specialty care and copays for clinic visits, hospitalizations and medications (Modi et al., 2012). Families with less education, lower income, and minority status have more difficulty obtaining adequate care and coverage of these expenses, leading to worse adherence (Berquist et al., 2006; Modi, Morita, & Glauser, 2008; Modi, Rausch, & Glauser, 2011; Howell, 2008; Rao et al. 2007). The costs of healthcare visits and medication copays are increasing, making it more difficult for families to afford these costs (Briesacher et al, 2011a; Briesacher et al, 2011b).

As new medications have been developed, costs have accelerated dramatically.. The new disease-modifying drugs have been priced at \$275,000 and \$375,000 per year (Vertex Pharmaceuticals, 2012). Briesacher and colleagues (2011b) examined the costs of healthcare in a national sample of privately insured patients with CF over a 6-year period from 2001 to 2007 and found a 59% average increase in costs over this time, with mean annual costs estimated at \$29,718 per year for a privately insured patient in 2007 (Briesacher et al., 2011b). Little is known about how these increasing costs affect adherence. In this study, barriers related to insurance and healthcare costs were elicited from patients and caregivers.

*Illness-specific factors.* Illness-specific factors are also related to adherence and can include prognosis, treatment complexity, severity, and symptomology (LaGreca & Bearman, 2003, Hanghøj & Boisen, 2014). In CF, complex regimens are associated with worse adherence and worse health outcomes (Rapoff, 2010; Sawicki et al., 2011). Generally, worse disease severity has been associated with worse adherence; however

those who are sicker are also likely to be prescribed more medications and face more barriers to fitting these treatments into their daily lives (e.g., fatigue). Sawicki and colleagues (2013) found that treatment complexity was positively related to age when comparing regimens from childhood through adulthood and that greater complexity was correlated with a higher perception of patient burden. A recent review by Sawicki & Goss (2015) emphasized that treatment complexity in CF will continue to evolve with the introduction of CFTR modulators. Modi and Quittner (2006a) conducted one of the first systematic evaluations of illness-specific barriers to adherence reported by children with CF, and also found that greater treatment complexity was negatively associated with rates of adherence, with different barriers reported for different treatments (e.g., taste, provoked cough).

George and colleagues (2010) conducted a qualitative analysis of illness-specific barriers in adults with CF. A barrier was defined as “anything identified by the subjects as decreasing the likelihood that they will follow a prescribed treatment regimen.” Treatment burden (e.g., frequency, duration, complexity) was the most commonly reported barrier in this study. George and colleagues (2010) generated a diverse list of barriers, including social demands, work demands, forgetting, absence of perceived health benefit, fatigue, and stigma. Higher frequency and severity of barriers were predicted to be negatively associated with health-related quality of life.

#### *Measurement of treatment barriers*

Although several studies have assessed barriers to adherence within and across pediatric chronic conditions, this literature is limited in several ways. First, many studies

have utilized literature reviews to identify which barriers are most common in a particular condition, rather than conducting qualitative interviews with patients, families, or healthcare providers (Griffin et al. 2001; Howell, 2008; Mulvaney et al. 2011; Simon et al., 2012). Second, much of the research assessing barriers is outdated, having been conducted in the early 2000's (Apter et al., 2003; Logan et al., 2003; Griffin et al. 2001; Modi & Quittner, 2006a; Murphy et al., 2003; Nagelkerk, Reick, & Meengs, 2006; Remien et al, 2003; Schafer et al, 1983). This is problematic because new treatments have recently been developed (e.g., gene-modifying drugs), which are likely to present new challenges for patients. Third, the published instruments available to measure barriers have not been utilized in more recent studies, in part, because they include generic barriers (e.g., forgot, don't have time) that do not lend themselves to intervention (Logan et al. 2003; Matza et al., 2008). Although "forgetting" is a common barrier, several studies indicate that when it is operationalized, it reflects an underlying problem, such as embarrassment or denial of disease (Modi & Quittner, 2006a; Quittner, Alpern, & Blackwell, 2013; Sawicki et al., 2015). Thus, this study elicited barriers from adolescents, young adults and parents, using a qualitative method that uncovered greater contextual detail about what "got in the way." This level of detail will be needed to tailor interventions to the barriers that are most relevant to the change process (Graves et al., 2010; Kahana et al., 2008; Kripalani et al., 2007).

### *Qualitative analysis of barriers in CF*

Barriers to adherence in CF were elicited in this study from key stakeholders using a qualitative analytic approach, including patients and their parents. Qualitative

methods are “best suited for asking questions that pertain to understanding the meaning that individuals or groups make out of experiences” (p. 80, Fiese & Bickham, 1998). Given that adolescents are the “experts” in managing their disease, and parents have spent many years supervising and facilitating their management, they are the best sources of information on barriers specific to CF.

Since little is known about this topic, a naturalist approach (Creswell & Miller, 2000) was used for the analytic process, with no a priori hypotheses generated for the qualitative content analysis. Grounded theory (Bryant & Charmaz, 2007; Charmaz, 2006; Charmaz, 2011; Strauss & Corbin, 1994) was utilized to allow concepts related to barriers to emerge organically from the open-ended interviews conducted with patients and parents. This qualitative approach was supplemented by quantitative analyses linking barriers to rates of adherence using the Daily Phone Diary (Quittner & Oipari, 1994), levels of parent-teen conflict, and symptoms of anxiety and depression. Higher rates of depression and anxiety were expected to be negatively associated with adherence, and positively associated with frequency and severity of reported barriers.

### *Specific Aims*

*Aim 1*) To perform a content analysis of 20 videotapes of problem-solving sessions aimed at evaluating barriers and adherence. Barriers were identified from these transcripts and used to create a semi-structured interview to elicit barriers for Aim 2.

*Aim 2)* To elicit patient and parent descriptions of barriers among 17 dyads (17 teens and young adults with CF and their caregivers, plus an additional young adult) using the interview guide developed above to code them for content.

*Aim 3)* To examine how the frequency and difficulty of barriers measured in Aim 2 are related to adherence, parent-teen conflict and symptoms of anxiety and depression.

*Hypothesis 1:* Adolescents/young adults with more frequent and difficult barriers were expected have worse adherence, higher levels of family conflict, elevated levels of psychological distress, and worse health-related quality of life.

*Hypothesis 2:* Caregivers who endorsed more frequent and difficult barriers to their adolescents'/young adults' treatment regimen were expected to report higher levels of family conflict and psychological distress.

*Aim 4)* To assess the extent of agreement between adolescent and parent-reported barriers within dyads.

*Hypothesis 3:* Adolescents/young adults who had lower agreement with their parents regarding the frequency and types of barriers encountered were expected to have lower rates of adherence and higher family conflict

## Chapter 2: Methods

### *Participants*

Data in this study was gathered from two sources: 1) Problem-solving (PS) sessions videotaped with 20 adolescents from the iCARE study, and 2) 17 dyads (adolescents and parents) plus one young adult recruited from CF Centers at the University of Miami (Miami, FL), Joe DiMaggio Children's Hospital (Hollywood, FL), and Rush University Medical Center (Chicago, IL). Participants in iCARE were enrolled at 18 multidisciplinary CF centers across the United States. Inclusion criteria included: 1) age 11-20 years, 2) confirmed diagnosis of CF, 3) attendance at an accredited CF care center, 4) prescription of at least one of the following pulmonary medications (azithromycin, hypertonic saline, dornase alfa, tobramycin inhalation solution, or inhaled, compounded tobramycin) for at least 6 months prior to informed consent, and 5) consent to provide data to the Cystic Fibrosis Foundation Patient Registry. Exclusion criteria included: 1) plan to change CF care teams within the next 2 years, 2) current listing for lung transplantation, or 3) participation in the iCARE pilot study.

Twenty participants for the retrospective review were selected from 325 videotaped PS sessions collected in the iCARE study. Tapes were stratified on the basis of age, gender, and disease severity. Tapes were then chosen at random from within these categories to ensure a representative sampling of iCARE participants. Participants in the retrospective data review had a mean age of 15.2 ( $SD = 2.85$ ), were 55% female, a mean  $FEV_1\%$  predicted of 84.9 ( $SD = 28.9$ ), indicating mild disease severity.

Prospective interview participants included 18 adolescents/young adults with CF and 17 parent/caregivers of adolescents/young adults with CF. This yielded 17 dyads for analyses. Recruitment took place at three hospitals in two major US cities: University of Miami Hospitals, Miami, FL; Joe DiMaggio Children's Hospital, Hollywood, FL; and Rush University Medical Center, Chicago, IL. Recruitment lasted from November 2014 until October 2015 across all three sites.

Participants completed all prospective study procedures. Inclusion criteria were: 1) age between 11 and 25 years, 2) parent/caregiver and/or adolescent willing to complete all components of the study, and 3) diagnosis of CF. Exclusion criteria included: 1) listing for lung transplant and/or dependence on oxygen and 2) developmental disability (i.e. cerebral palsy, autism).

Patients who participated in this study were, on average, 16.9 years ( $SD= 3.9$  years) and mostly female (72.2%). This was a fairly diverse sample racially, with 83.3% of patients identifying as white, 11.1% identifying as black, and 5.6% identifying as Asian. Of the 17 caregivers who completed interviews, 15 were mothers (88%), one was a father (6%), and one was a grandmother (6%). Average lung function for participants fell in the mild range ( $M FEV_1\%$  predicted= 81.5,  $SD= 17.5$ ;  $M BMI = 20.9$ ,  $SD= 3.4$ ). Patients had an average of 0.33 hospitalizations ( $SD= 0.68$ ) and 0.33 IV antibiotic courses ( $SD= 0.49$ ) over the previous year. However, 14 of 18 patients (78%) had not been hospitalized in the previous year, and 12 of 18 (67%) had not had a course of IV antibiotics. Seventeen of 18 patients (94%) were pancreatic insufficient, requiring the use of enzymes with meals and snacks. None of the patients had CF-related diabetes.



## *Procedures*

### *Retrospective analysis of iCARE tapes and development of the open-ended interview guide*

Once the representative sample of PS tapes was selected, they were transcribed by the author and several research assistants. PS sessions in iCARE focused on the elicitation of one barrier to adherence in the context of a single treatment. Analysis of these tapes facilitated a developmentally-appropriate constructivist interview (Glaser, 1978). See the Results section for more information on the analysis and development of the interview guide. (See Appendices A and B for the final interview guides.)

### *Prospective study procedures*

Once developed, the interviews were sent to the IRB for approval. Eligible participants were identified by their healthcare provider and either called prior to their clinic appointment or were approached during their scheduled clinic visit to assess their interest in the study. Participants at the Miami sites had the option to either complete study procedures in clinic after their visit or by phone and mail. Participants at Rush had the option of completing study procedures in a private office after their clinic visit, scheduling a study visit outside of the clinic time, or completing study procedures by phone or mail. Eleven patient interviews and six caregiver interviews were completed in person. Seven patient interviews and 11 caregiver interviews were completed by phone. Informed consent and assent were obtained in person, followed by demographic information, including age, ethnicity, socioeconomic status, and parent's highest level of

education. Medical data (i.e., lung function, BMI %, number of hospitalizations in past year) were extracted from chart reviews.

Participants who completed the study by phone also completed informed consent procedures in person. Contact information was obtained and patients and caregivers were asked to schedule a time to complete a phone interview. Patients were mailed a packet containing the questionnaires and instructed to complete them as soon as possible after the phone interview. Medical data were obtained in the same manner described above.

Interviews were conducted by advanced graduate students. Adolescents generally completed the interview while their parents were completing questionnaires and then the process was reversed. Participants who completed the interviews over the phone were encouraged to find a private place to talk to allow them to be as open as possible. After completing the interview, participants completed study questionnaires; those who completed the interview at home were instructed to complete the questionnaires afterwards. All interviews were audiotaped and transcribed for qualitative content analysis. Participants who reported elevated levels of depression and/or anxiety were provided with appropriate referrals. Interviews averaged 49 minutes ( $SD= 19$  minutes, ranging from 22 minutes to 114 minutes long). Caregivers and adolescents each received a \$25 Amazon gift certificate for their time and effort.

Adolescent/young adult patients were asked to complete the Daily Phone Diary (DPD) to measure their adherence over three days, on two weekdays and one weekend day, in sequence. Participants received an additional \$5 Amazon gift card for each DPD they completed; 15 of 18 (75%) patient participants completed all three days of the diary.

## *Measures*

*Daily Phone Diary (DPD)*. The DPD is a computer-based diary developed by Quittner and colleagues (Modi & Quittner, 2006a; Modi & Quittner, 2006b; Quittner & Espelage, 1999; Quittner & Opiari, 1994), which tracks mood, activities, social interactions, and time spent in all activities over a 24-hour period. It is an ecological momentary assessment (EMA) method to measure all activities occurring over the past 24 hours. It is an unobtrusive measure of adherence, since participants are not aware of which activities are being coded as the interviewer tracks them through their day using a 24-hour clock. In this study, the DPD was used to assess adherence.

The DPD was administered by an interviewer over the phone, with prompts such as, “After you finished dinner at 7 PM, what did you do next?” For each activity lasting 5 minutes or longer, the adolescent described the activity, its duration, companions, and rated his/her mood. The program has a visual clock which counts the time accounted for by these activities up to 24 hours. The DPD has yielded reliable stability coefficients over a 3-week period ( $r$ 's .61 to .71,  $p < .01$ ) and high levels of interrater agreement (over 90% in a CF population; Quittner et al., 1992). Modi & Quittner also found that DPD estimates of adherence converged with electronic measures (Modi & Quittner, 2006b). The DPD has been used to measure adherence to treatment in adolescents with HIV (Wiener et al., 2004) and relationships between treatment adherence and parental spirituality in children with CF (Grossoehme et al., 2012). In this study, adherence rates were calculated using the average 3-day adherence to four aspects of the treatment regimen: airway clearance, dornase alfa, hypertonic saline, and inhaled antibiotics (see Appendix C).

*Prescribed Treatment Plan (PTP).* The PTP was completed by members of the patient's healthcare team and/or via chart review. It measures the prescribed regimen, including frequency and duration of all treatments. The PTP yielded the prescription information required to calculate rates of adherence on the DPD (see Appendix D).

*Rating of barrier severity.* During the interview, each general barrier mentioned was recorded by the administrator to create a barrier count, referred to as the barrier frequency. Adolescents and caregivers were asked to rate each general barrier they mentioned immediately after the qualitative interview. They were presented with a visual analog scale with Likert ratings from 1 indicating "Does not make doing treatments more difficult" to 4 indicating "Makes doing treatments extremely difficult." The interviewer maintained a list of barriers mentioned by the participant throughout the duration of the interview. Immediately upon completion, the participant was asked to rate the severity of the barriers that were generated. These barriers were then coded into categories by the author, and reliability was obtained by having an advanced graduate student perform the second coding. Thirty-eight barrier categories were identified during coding. Inter-rater reliability was excellent (% agreement = 92%, see Appendix E).

*Cystic Fibrosis Questionnaire-Revised (CFQ-R).* Adolescent/young adult patients were asked to complete the CFQ-R, which measures condition-specific health-related quality of life (HRQoL). The CFQ-R is a developmentally appropriate HRQoL measure with versions for children, adolescents, and adults with CF (Quittner, 1998; Quittner et al., 2005; Quittner et al., 2012). In this study, the child and adolescent versions of the CFQ-R were utilized, depending on the participant's age. The Child version has 46 items and the Adolescent/Adult version has 60 items. The CFQ-R has thirteen scales

measuring different domains: Physical Functioning, Role Functioning, Vitality, Emotional Functioning, Social Functioning, Body Image, Eating Disturbances, Treatment Burden, Health Perceptions, Weight, Respiratory Symptoms, Digestive Symptoms, and Sinus Symptoms. All of the scales have demonstrated good internal consistency (Cronbach's alphas = .67-.94), strong test-retest reliability and good convergent validity with health variables, such as lung function and body mass index (BMI) (Quittner et al., 2012, see Appendix F).

*Generalized Anxiety Disorder 7-item (GAD-7).* Adolescent/young adult patients and caregivers both completed the GAD-7. The GAD-7 is a well-validated brief measure for assessing symptoms of anxiety and was developed by Spitzer, Williams & Lowe (2006). This measure has been validated in both clinical and general populations (Lowe et al., 2008) and has been utilized in patients with cancer (Brown et al., 2010). The GAD-7 has good internal consistency (Cronbach's  $\alpha = 0.92$ ) and test-retest reliability (ICC = 0.83) when administered in primary care settings (see Appendix G).

*Patient Health Questionnaire- 8 item version (PHQ-8).* Both patients and caregivers completed the PHQ-8 during this study. The PHQ-8 is eight items and is an edited version of the PHQ-9 (Kronke & Spitzer, 2002). It does not include the final question regarding thoughts of self-harm; the shorter version was selected due to concerns regarding timely risk assessment. The PHQ-8 has been well-validated in both general (Kroenke et al., 2009) and medical populations (coronary artery disease, Razykov et al., 2012), and is highly correlated with scores on the PHQ-9 ( $r = 0.99$ , Razykov et al., 2012). This measure assesses current symptoms of depression based on DSM-IV criteria (see Appendix H).

*Conflict Behavior Questionnaire- 20 item- CF modification (CBQ-20-CF)*. The CBQ-20 is a short measure of perceived conflict between parents and adolescents. Both patients and caregivers completed this measure. There are separate forms for caregivers and adolescents. The CBQ-20 was developed by Prinz and colleagues (1979) to measure dyadic family interactions and dissatisfaction with the behavior of others in the family. The short form correlates well with the full-length CBQ ( $r = .96$ ; Robin & Foster, 1995), and takes about 5 minutes to complete. The CBQ-20 was modified for the purposes of this study to include questions regarding parent-teen conflict related to CF treatments (see Appendix I).

Please note that the current sample was too small to generate reliability estimates for the measures utilized.

#### *Data Analysis*

This study involved multiple phases of data collection and analyses. Please refer to Table 1 for more details regarding the aims and hypotheses for each phase of the study.

*Table 1. Aims and analyses.*

<b>Phase/Aim</b>	<b>Hypotheses</b>	<b>Procedures</b>	<b>Measures</b>	<b>Results</b>
Phase 1/Aim 1: Retrospective analysis of iCARE tapes	None	Grounded theory analysis of 20 iCARE tapes  Interview developed with collaborators at the University of Miami and Johns	None	Results text, page 27

		Hopkins Adherence Research Center		
Phase 2, Aim 2: Prospective qualitative analysis of interviews	None (naturalist approach taken, no a priori hypotheses)	Grounded theory analysis of 35 interviews (18 with patients, 17 with caregivers)	None	Results text, page 27 – 43 Table 2
Phase 3, Aim 3: Analyses of frequency and severity of barriers	<p><i>H1</i>: Adolescents/young adults with more frequent and difficult barriers will have worse adherence, higher levels of family conflict, elevated levels of psychological distress, and worse health-related quality of life.</p> <p><i>H2</i>: Caregivers who endorse frequent and difficult barriers to their adolescents'/young adults' treatment regimen will report higher levels of family conflict and psychological distress.</p>	Simple bivariate correlation analyses, using SPSS	<p>Average barrier frequency</p> <p>Barriers severity ratings</p> <p>DPD results</p> <p>PHQ-8</p> <p>GAD-7</p> <p>CFQ-R scales</p> <p>CBQ-20-CF</p>	Results text, pages 43- 47 Tables 3-18
Phase 3, Aim 4: Analyses of patient-caregiver barrier agreement	<i>H3</i> : Adolescents/young adults who have lower agreement with their parents regarding the frequency and types of barriers encountered will have lower rates of adherence and higher family conflict.	Simple bivariate correlation analyses, using SPSS	<p>Barriers agreement ratings</p> <p>Average barrier frequency ratings</p> <p>Barriers</p>	Results text, page 47-48 Table 19

			severity ratings DPD results CBQ-20-CF	
Post-hoc analyses	None	Simple bivariate correlation analyses, using SPSS	Disease severity Age DPD results Average barrier frequency Average barrier severity	Results text, page 48, Table 20

The aims for this study lent themselves to a mixed-methods analytic approach, which links qualitative and quantitative data to facilitate a deeper understanding of the barriers faced by adolescents with CF and their parents (Morgan, 1998). The qualitative interviews yielded data on the frequency of barriers reported generally and in relation to specific treatments, which were then correlated with the quantitative results (i.e., rates of adherence, psychological distress). The study design included three phases of data collection and analysis. The first and second phases were primarily qualitative, and the third phase linked the qualitative and quantitative results.



The qualitative analysis was based on grounded theory. This method provides structured, yet flexible guidelines for collecting and analyzing data to construct data-driven theories about the process of managing CF (Bryant & Charmaz, 2007; Charmaz, 2006; Charmaz, 2011; LaRossa, 2005; Strauss & Corbin, 1994).

*Phase 1- Specific Aim 1.* The first phase of analysis involved qualitative open coding of the transcribed PS videos selected from the iCARE study. Atlas.ti was utilized to code the text documents produced from these videos. Open coding focused broadly on treatment-level barriers described by the adolescent and parent during the PS session. These codes were analyzed for frequency and saturation, and were then used to construct a first draft of the semi-structured interview for participants in Phase 2. The interview constructed consisted of open-ended questions, divided into three main sections: General Questions, Specific Treatment Questions, and Cross-Cutting Issues. This interview was comprised of open-ended questions, as specified by Charmaz (2006). See the Results section for information on the development of the final interview guide.

*Phase 2- Specific Aim 2.* The second phase of data collection and analysis involved semi-structured interviews using the interview guide. Interviews were conducted by advanced graduate students and then transcribed either by a professional transcription company or trained research assistants. The interview guide facilitated consistency across study participants; however, individualized probes were utilized to elicit more detailed responses. For example, a participant who stated that “forgetting” was a frequent barrier would be encouraged to discuss the situations in which forgetting occurred, allowing for the inclusion of contextual information.

NVivo software was utilized for qualitative analysis in Phase 2 of this study. Transcriptions and coding of interviews were ongoing throughout the study, utilizing a two-step, iterative process (Charmaz, 2006). First, open “line-by-line” coding was conducted to identify introductory codes. In place of “line-by-line” coding, “event-by-event” coding was used to allow for inclusion of longer chunks of data. Memo-writing was utilized as described by Charmaz (2006) and was carefully documented throughout the data collection process. Early memos consisted primarily of free-writing and musings on the interviews themselves. Memos occurring mid-way through the open coding process focused on similarities and differences between the codes, to reduce overlap. Initial open coding was first organized by interview question or medical treatment.

After the initial ten interviews were open-coded, more focused coding began. During this process, repetitive codes were reviewed and combined. Codes were also shifted away from the question/treatment-based organization into a thematically-based organization. For example, codes relating to “forgetting” across treatments were combined into a larger “forgetting” family of codes. As these families emerged, memos were written to reflect the relationships between them. Codes were compared within and across respondents. All major categories were endorsed by a significant portion of both patients and caregivers, and therefore reached theoretical saturation.

Due to the high level of engagement of study participants, reliability was calculated using participant-based triangulation procedures (Charmaz, 2006). Five study participants were called by the principal investigator to discuss the qualitative results and obtain feedback. They all agreed that the major themes accurately represented their

experiences, and they felt nothing major was missing. Two participants emphasized the important role that fatigue plays and encouraged special consideration of that family in the results. In addition, convergent validity was assessed by correlating the CFQ-R Treatment Burden scale with the number of barrier categories reported.

*Phase 3- Specific Aims 3 and 4.* All quantitative analyses were conducted using SPSS software. Descriptive statistics were calculated on the frequency of barriers reported and the ratings of severity completed after the barriers were coded. Descriptive statistics were also calculated for symptoms of depression and anxiety, parent-teen conflict, and health-related quality of life (HRQoL; for patients).

To test the hypothesis that adolescents and parents with more frequent and difficult barriers would have worse adherence, higher family conflict, worse psychological distress and worse HRQoL, correlations were conducted between the number of barrier categories, average difficulty ratings and the questionnaire and diary measures.

Post-hoc power analyses revealed that the quantitative portion of this study was significantly underpowered, with a 25% chance of accurately detecting a 50% average rate of adherence. A priori power analyses suggested that a sample size of  $N=64$  would have been required to detect a correlational effect size of 0.30 ( $\alpha=0.05$ ,  $1-\beta=0.80$ ). Negative associations were expected between the number and difficulty of barriers and adherence. For the analyses relating barriers to conflict, distress and HRQoL, the total number of barriers and average difficulty ratings were correlated with these measures, separately for adolescents and parents. A greater number of barriers and higher severity

ratings were expected to be associated with higher family conflict, more psychological distress and worse HRQoL.

Finally, concordance between parent-teen dyads was calculated via percent agreement. Barriers identified by patients and caregivers during the rating process within dyads were reviewed. The total number of barriers reported by both patients and caregivers within a dyad was determined; this number served as the denominator for the percent agreement calculation. The number of matching barriers was then identified and this number served as the numerator for the percent agreement calculation. These rates of agreement were correlated with treatment-specific adherence and overall adherence on the DPD; higher rates of agreement on these barriers were expected to be related to better rates of adherence and lower family conflict as reported by both adolescents/young adults and parents.

The DPD results were analyzed using the statistical approach published by Modi and Quittner (2006b). Self-reported time spent doing treatments and number of treatments completed daily were divided by the participant's prescription for that treatment obtained from the PTP, then multiplied by 100 to obtain percent adherence for individual treatments. Simple bivariate correlations were conducted between adolescent reports of barrier frequency and their scores on the CBQ-20-CF, GAD-7, PHQ-8, CBQ-20-CF, and CFQ-R. Similarly, simple bivariate correlations were calculated between parent reports of categorical barrier frequency and their scores on the CBQ-20-CF, GAD-7, PHQ-8, and CBQ-20-CF.

### Chapter 3: Results

#### *Aim 1- Analysis of iCARE tapes and development of the qualitative interview.*

Aim 1 analyzed the most common treatments identified during Problem-Solving (PS) sessions in iCARE: airway clearance (e.g. VEST, chest physiotherapy, etc) ( $n= 9$ ) and vitamins ( $n= 4$ ). Adolescents/young adults and parents identified a range of barriers affecting their ability to complete treatments as prescribed, such as: can't find the time ( $n = 11$ ), forgetting ( $n = 6$ ), don't want to do it ( $n= 5$ ), and don't think treatment is needed ( $n= 5$ ). Contextual coding of these barriers highlighted their individualized nature. For example, an adolescent who reported he/she "couldn't find the time" to complete airway clearance stated specifically that he/she did not want to "get up earlier to do it."

These results highlighted the need for a semi-structured interview to allow for further probing after participants reported their "initial" barrier. Since two treatments were chosen most frequently by patients and parents in iCARE, treatment-specific questions were developed to ensure that barriers were elicited across all treatments. In addition, open-ended questions relating to the impact of school, work, friends, family, stress, health insurance, and pharmacy issues were included. This interview was developed with Dr. Quittner and Dr. Kristin Riekert, as part of a larger, national study to develop barriers screeners for CF.

#### *Aim 2- Grounded theory analysis of interviews.*

Charmaz (2006) emphasizes that using grounded theory involves a focus on the *processes* participants experience in their daily lives. Analyses of the semi-structured interviews involved paying particular attention to the description of the day-to-day flow of living with CF. Six major themes emerged, however, it should be noted that these

themes do not exist in a vacuum. They are all interconnected and these connections will be highlighted in the results. As this section proceeds, each theme will be discussed in detail. In keeping with grounded theory methods, quantitative data will be excluded from this section. Themes will be described in the order they typically emerged to reflect the narratives provided by patients and caregivers. Please see Table 2 for the percentages of participants reporting specific themes. In the selected quotes, “P” refers to participant and “I” refers to interviewer.

*Theme 1: Treatment-life balance barriers- “Organization- ha! Yeah. Everything about it is organization.”* Treatment-life balance referred to the daily struggles patients and families faced as they tried to incorporate the demands of their treatment regimen into daily life. These barriers were universally reported by patients and parents, and encompassed several interacting families, including: scheduling challenges, forgetting treatments, being tired, and wanting to do things other than treatments. The following quote sums up the frustrations experienced while trying to balance treatment demands with typical high school life:

*P: ...It was my first year of marching band....And I told you the schedule, twice a week plus competitions.*

*I: Right.*

*P: 3 hour rehearsals, I was worn out with homework and coming home late from rehearsal, I would be tired and I didn't want to do my treatments because I'm working on my homework and it's like one in the morning...And I'm just like, oh my god, like, ma- I'm like marching band, I cannot take this anymore, this is too much.*

*Scheduling challenges.* Scheduling challenges played a crucial role in the progression of treatment-life balance barriers. Successfully fitting the CF treatment

regimen into a daily schedule required organization, planning, and time management. This was a difficult task for most patients and families. Very few teenagers or young adults had these skills, resulting in difficulties scheduling treatments around developmentally “typical” activities. High-achieving students were involved with a number of extracurricular activities in addition to demanding classes. Doing both CF treatments and homework were very time-consuming, as highlighted by this adolescent patient:

*I: ...So how- we talked a little bit about this, but how does school impact your ability to do your treatments the way they're prescribed?*

*P: ... Just in the morning. Like in the evening, it's- I can do it, I've got time. But it does take away from studying, or doing work. And sometimes when I'm on my phone after the treatments, I will just stay on my phone, and then that just totally throws me off. And then I look at the clock, and it's like 9 o'clock, and I start doing my homework and don't get to bed until maybe 1 or 2. And then I'll be like- don't do the treatment in the morning. So that's like- that has effect.*

In addition, caregivers were acutely aware of the scheduling challenges faced by their families. Parents of younger participants reported playing an active role in helping with their adolescent/young adult's treatments. They described an ongoing struggle helping them balance the need to fit in treatments with the desire to participate in typical school activities:

*I: So all in all, what is the most difficult part of getting your teen's treatments done?*

*P: ...I think you know finding the time... that's really the hard part, and sort of finding, knowing when to say okay we can miss this particular treatment, whatever it is, because you need to do this band thing, versus this treatment is so important that nothing else is more important. Um it's, it's kind of always a, a tricky decision to make.*

*Forgetting treatments.* As patients and caregivers worked to overcome these scheduling difficulties, treatments were occasionally forgotten. This was particularly true for quick treatments, such as pills or inhalers. People with CF must take pancreatic enzymes before every meal and snack in order to digest their food; this means that they must have enzymes with them at all times. This posed a challenge for patients while they prepared for a busy day:

*I: ... Um, what kinds of things get in the way of taking your enzymes?*

*P: Um, I mean like, ok, like forgetting to refill them for when I go out to dinner, and um like, I do put a good amount in a little pill bottle I have in my purse in case I go out and I eat somewhere. But, if I check it and I'm like, oh do I have enzymes, and I have like maybe one, I'll either be like, ok, I'll either take something that's not fatty at all or I just take my enzymes when I get home. 'Cause you can do that, but I think sometimes enzymes take like, oh my god, I gotta take this before I eat or I'm gonna like have a problem with my stomach.*

Forgetting treatments has been reported as a key barrier to adherence in CF.

However, note that the examples of forgetting described by participants in this study did not reflect a lack of knowledge or awareness of their treatment regimen. Rather, it was a natural result of juggling multiple demands in the midst of a busy life. Forgetting came up frequently, but many patients and caregivers emphasized that it was a minor, occasional challenge that did not interfere with their ability to complete their treatments as much as other factors, such as being “tired.”

*Being tired.* Working to balance treatment demands with typical life activities inevitably resulted in exhaustion. Being tired was one of the most frequently reported barriers by patients. Patients described a strong connection between fatigue and not wanting to do treatments (see Theme 3). Sleep deprivation is a major concern for many healthy adolescents and young adults; therefore, it was not a surprise that most



adolescents and young adults with CF reported feeling worn out and unable to complete treatments at the end of the day:

*I: Okay. So, tell me what gets in the way of doing your Pulmozyme.*

*P: Um, time. Because usually the time, time is so limited already throughout the day for me. It's just, trying to squeeze it in gets tiring... Like sometimes I'll fall asleep with the machine on because I'm just exhausted.*

*I: What time are you doing it? At night?*

*P: Uh 11, 12, maybe 1.*

*I: Wow, that's pretty late. Yeah.*

Being tired not only affected evening treatment routines; several individuals reported skipping *morning* treatments to sleep in longer after going to bed late. Caregivers described struggling to wake their teens up in the morning to do morning treatments. Parents and patients highlighted morning treatments as particularly challenging given school demands:

*P: Yeah. And also, like staying up late doing homework and stuff, that like affects how you're going to get up the next morning and actually do the treatment or not. Like if I get to be early, there's a 50% chance that I'll do the treatment. If I get to bed around 1, or midnight- there's probably a 25% chance I'll actually do the treatment.*

*Rather do other things.* Even patients who found ways to successfully schedule their treatments into their daily lives struggled to prioritize doing treatments over other, more appealing activities. Patients described this as a conflict between what they knew they needed to do and what they wanted to do. At times, caregivers became exasperated watching their teens skip their treatments in order to engage in other activities:

*I: ...What gets in the way often times of your teen doing her treatments?...*

*P: Wanting to do other things, wanting to be a teenager. Wanting to go play with friends or just do an outside activity that comes up she gets an invite to go do. We have to say no you can't do that right now we have to do a treatment. Or we'll let her go and have to do the treatment later and she'll be up late and tired the next*

*day. There really is just not enough time in the day for a working parent with a child going to school. Especially with a teen.*

*Theme 2: Treatment-related barriers- “She doesn’t like the shaking and it...tickles her nose and makes her itchy.”* Some barriers were related to the mechanism of performing the treatment itself and thus, were not modifiable. These included: side effects, challenges swallowing pills, equipment difficulties, and treatment that tasted bad. Most patients and parents reported having some type of treatment-related annoyance that made adherence more difficult.

*Side effects.* Many patients reported experiencing significant side effects from their treatments. These included coughing caused by hypertonic saline, nausea and gagging from inhaled antibiotics, and joint pain due to oral antibiotics:

*I: Okay, for Zithromax you got joint pain*

*P: And then I took clarithromycin.*

*I: And azithromycin, oh clarithromycin.*

*P: Yeah and that gave me like really bad acne.*

As illustrated by the previous example, some side effects were severe enough to warrant a change in the prescribed regimen. Patients were less likely to adhere to a treatment that was causing them discomfort.

In general, patients were more aware of the side effects they experienced than their caregivers. However, parents mentioned side effects that could also have an impact on the *timing* of treatments:

*I: Describe times and situations when doing inhalers is more difficult for [your son].*

*P: Hmmm. I don’t, sometimes, um, at night, because the albuterol is a stimulant and you have to, and I have to make sure they didn’t do it too close to their bed time...So that would uh sometimes interfere because it would be like, oh god, we forgot to do it but it’s time, you know when they were younger, time to go to bed.*

In this example, the side effects experienced by this patient made scheduling his treatments more challenging, mentioned in Theme 1 (Treatment-life balance barriers).

*Pill swallowing.* Even when treatments did not cause side effects, some people had difficulty swallowing multiple, large pills. Problems with swallowing pills came up frequently with patients, but were less commonly mentioned by parents. Pill swallowing problems may have been overlooked in light of patients who are older. As new, expensive genetic modifiers are developed, pill swallowing presents a significant challenge, even when patients were motivated to take the medication:

*I: And are there times or situations when taking the Kalydeco is more difficult?*

*P: Yeah, Kalydeco has been a bit of an issue. Um first of all, she can't swallow pills, she's tried and tried and can't swallow pills so what we came up with was she can put it in macaroni and cheese and just sort of let it go down with macaroni um and that works fairly well... Um if she doesn't have access to something that has the right texture that she'll be able to swallow it. And occasionally if she's feeling the least bit nauseous she knows that if she tries to force herself to swallow it then it won't have a bad, it won't have good ending, yeah usually it comes back... You know the biggest hurdle is that... it's a tablet... with this it's got an entire coating on it and they're not supposed to break them or crush them so she literally has to find something that has the right consistency so she can just kind of fool herself into just swallowing it.*

*Equipment difficulties.* Even when patients were able to swallow pills without difficulty, they had challenges maintaining their equipment. Aerosolized treatments require the use of a nebulizer, and the VEST is a large, heavy machine used for airway clearance. Many patients and parents reported struggling with discomfort related to using the VEST. The VEST must be sized periodically to ensure a good fit, which is challenging given its high cost and inconsistent reimbursement (see Theme 6). Nebulizers wear out quickly because of their frequent use, which resulted in frustration for patients and caregivers alike:

*P: ... Um, as far as the small things like just not getting her a good nebulizer, we really had to fight hard to get a decent nebulizer. It's really ridiculous the small ones that burn out, that don't really function efficiently. That are so loud. I mean it's just, it's for your everyday asthmatic that might need it a few times a year, and they are giving it to a CF patient.*

*I: Oh my gosh.*

Furthermore, nebulizers require careful cleaning after each use to prevent infection.

Caregivers often reported helping patients clean their nebulizers; however, several patients described it as a frustration, which discouraged them from doing them:

*I: ... So now what's the most difficult part of getting your treatment done?*

*P: Um for me, the thing that really stops me is having to get the nebulizers. Just sometimes I'll forget to wash them and so they're unsanitary and used and whatever. So then you either, I do the vest without them and then just do them later when they're clean or I just don't do the nebulizers and just do the vest and then clean them later, so that's probably the hardest...its like not just one thing and you kinda have to, it involves more responsibility.*

*Treatments taste bad.* Finally, multiple patients reported finding the taste of various nebulized medications unpleasant and difficult to tolerate. Inhaled antibiotics and nutritional supplements were cited as being particularly noxious-tasting, leaving some parents concerned about poor adherence to that treatment:

*P: And um, she's tried the Scandishakes and she hates them to death. Um, she refuses to do them. She doesn't even like ensure or like those kind of shakes, and she thinks that everything else is too thick or too rich or whatever. She doesn't like them so she doesn't take it... It's definitely less invasive than doing a tube feeding, like this past week she was really sick and she lost a lot of weight.... And so this last week I talked to her and I said "look, you know, it's your choice but I think if you add these shakes to your diet it would really help you, but I said I obviously can't force it down your throat..."*

*Theme 3: Negative Emotions Impacting Treatment-* "Yeah um you know like cause when you're depressed you really don't want to do anything." Constantly balancing treatment demands with daily life eventually resulted in burnout and frustration

for patients and caregivers alike. Negative emotions impacted patients' motivation and ability to complete their treatments. The families captured within this theme included: not feeling like doing treatments and feeling down or depressed. It is interesting to note that although anxiety was frequently discussed during these interviews, it was not identified by patients or parents as a significant barrier to adherence. Rather, a few patients reported that feeling anxious made them *more* adherent to their treatment regimen.

*Don't feel like doing treatments.* Patients and families eventually got tired of dealing with CF day in and day out. This was completely normal; however, it posed a significant challenge for patients trying to meet the daily demands of their regimen. Patients frequently admitted to just not feeling like doing treatments, and at times, engaged in "planned nonadherence" to take a break from having CF. A range of cognitions and were emotions associated with not feeling like doing treatments, including wanting to feel "normal," being sick of doing treatments, and being tired (part of Theme 1), leading to a cascade of resistance and negative emotions:

*P: ... Sometimes I get really cranky. Um, like if it's like 12 o'clock and we're still doing it I'm like, "Why am I still here?"*

Many young adults highlighted their teen years as a time when overcoming this feeling felt impossible. Some of these young adults were able to discuss the nuanced cognitive and emotional processes that contributed to the feeling of not wanting to complete their treatments:

*Participant: Um, when, during my teen years, like I mentioned, past when I mentioned that you feel like you know it's kind of taking over your life and you feel like it's taking on things, you start thinking about, like, do I really need this?*

*Is this really helping me? Or I just don't want to do that one, I just want to be a normal kid. Um, or I feel good today, I don't need to do that....Um, I think, just the, it's just the mindset that you put yourself in, is the hardest.*

*Feeling down or depressed.* Most patients who said they did not want to do their treatments also reported being able to push through this feeling when they needed.

However, for some patients, these negative emotions progressed to more symptomatic depression. Once emotional symptoms advanced to this point, patients found themselves struggling to complete basic daily tasks:

*P: Yeah um you know like cause when you're depressed you really don't want to do anything... so I was like failing in school and um I didn't really do my treatments at all. And I was just kind of like moping around the house you know.*

Parents also reported having concerns that their adolescents felt depressed, which could negatively affect adherence; however, their descriptions tended to highlight these symptoms as more mood-related and transient:

*P: I mean there have been times where she's just so tired and exhausted and she just starts crying and doesn't want to finish it, I mean very few and far between but I mean sometimes you just have to say okay, enough is enough and then just let's just stop here you did part of it... You know, we do, we definitely skip every once in a grey while we're not like so crazy, I mean there are times where you have to put your child's mental well-being ahead of her treatment. Missing one treatment is not as bad as you know how she's gonna feel.*

Parents and patients both occasionally engaged in “planned nonadherence,” or a planned break from treatment in an attempt to mitigate these symptoms of feeling down or depressed. This was a challenging barrier for families to overcome without the assistance of professionals.

*Theme 4: Socially-related barriers- “...I'm like “Oh my God what if someone like sees it and thinks I'm selling drugs or something! (laughs).”* For many patients, concerns about specific social situations made completing treatments more difficult. Note that all

participants reported disclosing their disease status to at least some of their friends. Interestingly, social barriers were generally related to not wanting to draw *additional* attention to one's diagnosis, rather than trying to hide it altogether. Two families of social barriers were most commonly reported by patients and parents: sleepover problems and wanting to avoid taking enzymes in front of other people.

*Sleepover problems.* Patients and parents both described sleepovers as uniquely challenging for individuals with CF because they typically last from early evening until the next morning, requiring completing at least one treatment in front of peers. Some patients expressed discomfort about this possibility:

*Participant: Like with the, with the Vest, I never wanted to go on like overnight field trips, like in eighth grade I went to Washington, D.C. which was a week....And all I had, all I had was my old nebulizing machine, which took twice as long, so and it was very loud, it was very annoying. I was embarrassed. My friends didn't mind but it was just like such a pain. So I was, I would never feel comfortable going on family trips or overnight field trips because it's just a pain in the butt to do.*

These social barriers linked closely with Travel barriers (Theme 5); traveling with treatments was difficult and resulted in embarrassment and anxiety. Many patients and parents reported avoiding sleepovers to avoid the stress of doing treatments in front of peers:

*I: ...How about what if has a sleep over with a friend, how does he handle his treatments?*

*P: Um sleepover with a friend, well we've had friends sleep over here but I don't think he has ever slept over somebody else's house.*

Sleepovers are an important social ritual for adolescents, and missing out on these activities may have contributed to the psychological distress discussed in Theme 3.

*Not wanting to take enzymes in front of people.* Although parents were aware of the concerns their teens had about sleepovers, they did not mention their teen's discomfort taking enzymes in front of peers. This is a notable gap between caregivers' and patients' perceptions of social difficulties. Young adults described this barrier as something they faced more frequently as teenagers. Patients worried that peers would ask them why they were taking these medications and have to explain their medical history to people they did not know well:

*I: Okay alright. Um now tell me about times or situations in which taking your eating medicines are, is more difficult?*

*Participant: Um ...probably through high school. ..you know you just take it but all the kids would always ask you why are you taking that all the time or like uh some people would think you're taking drugs or something you know? And it's just like annoying cause you don't want to have to explain yourself to everybody all the time, like you shouldn't have to, you know what I'm saying?*

Even though disclosure to friends was commonly reported by patients, they still did not want to draw attention to being “different” by completing treatments. This linked social barriers closely with negative emotions (Theme 3), as patients sometimes described wanting to feel “normal” as a barrier to taking their medications.

*Theme 5: Travel-related barriers- “And airport security, let me tell ya, I mean even the nebulizer, I think they think I'm going to like blow up the whole airport.”*

Although not a daily event, travel barriers were commonly mentioned by patients and caregivers. Caregivers reported encountering travel barriers more frequently than patients. For younger patients, it appeared that their caregivers dealt with most of the travel challenges, such as planning the trip and carrying equipment. The families



identified within this theme included: traveling with CF treatments is hard and frustrations encountered when going through airport security.

*Traveling with CF treatments is hard.* Participants expressed frustration with lugging heavy equipment along when traveling. A few patients complained they were never able to check a bag because they needed the space for their VEST or nebulizer. Several participants admitted that they skipped treatments while traveling because of these challenges. For patients who travelled for extracurricular or sports-related activities, missed treatments occurred more frequently:

*P: I go, like, out of state, and, or, when I go up, like, up north, and I go to different tournaments and stuff, I'll go to hotels and stay there and stuff, it's hard to go there and bring the machine and equipment with me. So, usually, I don't. I should, but I don't. Like, if I'm going on a trip, like, up north or somewhere, I'm going to be gone for like a week, I don't bring my machine.*

*Air travel security frustrations.* In addition to having to carry heavy equipment on trips, patients and caregivers had to deal with airport security. For many families, this made air travel difficult. Large machines (e.g., VEST, nebulizers) drew additional attention from security personnel and caused delays in boarding the plane. Some participants described avoiding air travel altogether due to these frustrations:

*P: I ... Like if you go to the airport or something, you get a million and two questions about the machine, because all the bombs and everything like that, you get a million and two questions, and it's just not worth the hassle to me to go through all that... they just talk with us all day.*

*Theme 6: Systems-level barriers- "Cost – ha!...As insurance doesn't pay and it's very expensive in the stores."* Systems-level barriers related to the healthcare system. Participants generated two important families within systems level barriers: pharmacy issues and health-insurance. If patients and families did not have access to medications,

they could not do their treatments. Pharmacy issues and health insurance issues were closely linked. Caregivers and older participants were adept at separating issues relating to the pharmacy itself (e.g. delays in medication delivery or the pharmacy's knowledge of medication pre-approvals) from the healthcare system (e.g. denial of certain medications). Parents tended to be more informed about these barriers, mentioning them more frequently and describing them in greater detail. However, a developmental shift was noted for patients, with young adults mentioning these challenges in greater depth than their adolescent counterparts:

*P: Recently, [my insurance] changed to RedSource or now they call themselves Humana, which is totally different for me. So now I have to order [my medication] specifically from that place in order to get my Pulmozyme, and when I came to college, I got really worried because it's delivered, and I'm like oh god, what if they deliver it somewhere else that's wrong and I don't get it. I – I cannot not do my Pulmozyme for a couple days...it kind of worries me sometimes.*

*Pharmacy issues.* Pharmacy issues described by patients and caregivers included frustrations with obtaining frequent re-authorizations from pharmacies and health insurance companies, managing multiple specialty pharmacies, and remembering to mail prescription refills. If a pharmacy refused to cover a prescription, families could be faced with thousands of dollars in costs they had not been expecting. In addition, ordering these medications was time-consuming and frustrating for patients and families:

*P: Um, yeah, I mean it's, um, I have like four different pharmacies I have to order her things for, so it is like a little time consuming...you know insurance is just a, you know specifically wants you to get it from certain places and order sometimes, which is, very stupid but that's what they want.*

*Health insurance issues.* Health insurance issues related to difficulties getting coverage or reimbursement for medical care. If insurance companies refused to cover treatments, patients described either going without medication or struggling with the high

cost. Participants would become animated when discussing insurance problems, and their frustration was visible. Younger participants generally expressed some awareness of financial or insurance problems, but encouraged the interviewers to talk to their parents for more detail. Several participants reported losing access to treatments they had used in the past because of changes in coverage:

*I: So tell me a little bit about her airway clearance.*

*P: A respiratory therapist that comes. Yes, that's what she usually does...I try and do five times a week. Insurance doesn't pay for that so it's very expensive. We used to do more but I had to cut back. And now it actually is like four days one week and five days another week, so it's really like four and a half days, on average and she used to get six to seven.*

New technologies have recently become available that could make doing treatments easier for patients and families (based on identified barriers in Theme 2), such as the Afflo-Vest, which functions wirelessly allowing the wearer to move around; however, insurance companies may not cover time for a long time.

*Aim 3- Barrier frequency and severity analyses.*

*Aim 3- Descriptive statistics.* During these interviews, patients reported an average of 7.56 barriers to adherence ( $SD= 3.28$ ), which was similar to caregivers (caregiver  $M$  number of barriers = 7.50,  $SD= 3.98$ , see Table 3 for more details). Patients and caregivers also reported similar ratings of severity (patient  $M$  barrier severity score = 2.57,  $SD= 0.96$ ; caregiver  $M$  barrier severity score = 2.58,  $SD= 0.92$ , see Table 3).

However, patients and parents differed on which barriers were most frequent and difficult (see Tables 4 and 5). Notably, for both patients and parents, the most frequently reported barriers were not the most severe. For example, forgetting was frequently mentioned by

both patients and caregivers, but was not identified as one of the most difficult barriers by either group. The most severe barriers described by at least 5 patients and caregivers were work scheduling and travel barriers, respectively (see Tables 4 and 5).

Descriptive statistics for the CBQ-20-CF, PHQ-8, GAD-7, and CFQ-R (for patients only) were calculated. Patients and caregivers reported relatively low levels of conflict on the CBQ-20-CF. Out of a minimum score of 20 and maximum score of 40, patients reported an average score of 22.1 ( $SD= 3.50$ ) and caregivers reported an average score of 23.3 ( $SD= 3.83$ , see Table 6).

Although levels of conflict were low, rates of depression and anxiety were high. On the PHQ-8, 35% of patients and 53% of caregivers had scores in the clinically elevated range of depression. The mean caregiver score on the PHQ-8 also fell in the clinically elevated range (see Table 7). On the GAD-7, 35% of patients and 67% of caregivers reported clinically elevated anxiety scores. The mean caregiver score on the GAD-7 fell within the clinically significant range. Thus, both patients and parents reported, on average, a high level of depression and anxiety.

Patients completed the CFQ-R. Four scales of the CFQ-R were analyzed for this study: Emotional Functioning ( $N= 17$ ), Social Functioning ( $N= 17$ ), Health Perceptions ( $N= 14$ ), and Treatment Burden ( $N= 14$ ). The  $N$ s vary because three participants completed the Child version of the CFQ-R (see Tables 8 and 9), which did not include the Health Perceptions or Treatment Burden scales. Of note, this sample scored significantly lower on the Treatment Burden scale than other scales (Treatment Burden  $M = 58.6$ ,  $SD= 14.1$ , see Table 9). Female participants had scores similar to published

norms (Quittner et al., 2012); however, male participants had significantly higher HRQoL scores than gender-matched norms (see Tables 10 and 11). Females reported significantly lower scores on the Emotional Functioning scale than males (see Table 10).

Fifteen patients completed the DPD. Average adherence across treatments over a 3-day period was 44% ( $M$  adherence ratio = 0.45,  $SD$  = 0.30, range 0% - 90%). Rates of adherence to each type of treatment ranged from 0% to 117%. Participants were most adherent to dornase alfa ( $M$  percent adherence = 50%,  $SD$  = 39), and were least adherent to inhaled bronchodilators ( $M$  percent adherence = 9%,  $SD$  = 20, see Table 12).

*Aim 3- Patient correlations.* Patient and caregiver correlation coefficients were calculated separately. For patients, positive correlations were expected between barrier frequency and severity, symptoms of depression and anxiety, and family conflict. A significant correlation was found between average number of barriers and average severity rating ( $r = 0.54$ ,  $p < .05$ ), suggesting that as patients experienced more barriers, their perceptions of severity increased. No significant relationship was found between barrier frequency and family conflict. Average number of barriers was also positively correlated with the PHQ-8 ( $r = 0.48$ ) and the GAD-7 ( $r = 0.42$ ) and indicating that more barriers were related to higher depressive and anxious symptoms. Although not statistically significant, a medium effect size was obtained (Cohen, 1992). ( $r = 0.04$ , see Table 13).

Positive correlations were expected between barrier severity, and family conflict symptoms of depression and anxiety. For patients, average barrier severity was positively correlated with scores on the CBQ-20-CF ( $r = 0.38$ ), PHQ-8 ( $r = 0.46$ ), and

GAD-7 ( $r = 0.41$ ), suggesting that perceptions that barriers to adherence are severe are related to more symptoms of family conflict, depression, and anxiety. Although none of these correlations reached statistical significance; they yielded medium effects (Cohen 1992), suggesting that this sample was underpowered to detect significant effects. Scores on the PHQ-8 and GAD-7 were significantly correlated ( $r = 0.75, p < .01$ ), suggesting a close positive relationship between rates of depression and anxiety. The GAD-7 ( $r = 0.30$ ) and PHQ-8 ( $r = 0.34$ ) were positively correlated with the CFQ-20-CF, indicating that psychological distress is related to family conflict, although the relationship was not statistically significant (See Table 13).

Negative associations were expected between barrier frequency, severity, and scores on the CFQ-R. Four scales were selected for analysis. For patients, average number of barriers was negatively correlated with the Emotional Functioning ( $r = -0.35$ , medium effect size), Social Functioning ( $r = -0.14$ ), Health Perceptions ( $r = -0.21$ ), and Treatment ( $r = -0.16$ ). Average barrier severity was moderately negatively correlated with the Emotional Functioning ( $r = -0.46$ ) and Treatment Burden ( $r = -0.49$ ). However, it was positively correlated with the Social Functioning ( $r = 0.27$ ) and Health Perceptions ( $r = 0.27$ ). (See Table 14).

Negative correlations were expected between frequency and severity of barriers and overall rates of adherence. Rates of adherence for the 15 patients who completed the DPD were correlated with average numbers of barriers and average barrier severity. Overall adherence was positively correlated with average number of barriers ( $r = 0.30$ ) and average severity ( $r = 0.16$ ), but these effect sizes were small to medium (see Table

15). Negative correlations were expected between overall average adherence and symptoms of family conflict, depression, and anxiety. Adherence rates were also correlated with scores on the CBQ-20-CF, PHQ-8, and GAD-7. Again, positive correlations were found between rates of adherence and the CBQ-20-CF ( $r = 0.19$ ), PHQ-8 ( $r = 0.40$ , medium effect), GAD-7 ( $r = 0.30$ , medium effect, see Table 16), indicating that participants with better adherence had more family conflict, symptoms of anxiety, and symptoms of depression. Finally, positive correlations were expected between overall adherence and the CFQ-R. Adherence was correlated with the four selected subscales of the CFQ-R, with negative relationships between the Emotional Functioning ( $r = -0.17$ ), Social Functioning ( $r = -0.39$ ), Health Perceptions scale ( $r = -0.62, p < .05$ ), and Treatment Burden scale ( $r = -0.37$ , see Table 17).

*Aim 3- Caregiver correlations.* For caregivers, positive associations were expected between frequency of barriers, severity of barriers, family conflict, symptoms of depression, and symptoms of anxiety. Results indicated that for caregivers, average number of barriers was *negatively* correlated with scores on the CBQ-20-CF ( $r = -0.29$ ), PHQ-8 ( $r = -0.40$ ), and GAD-7 ( $r = -0.36$ ), indicating caregivers who perceived their teens as having more barriers to adherence experienced lower rates of family conflict, depression, and anxiety. Again, none of these correlations reached statistical significance; however, they had a medium effect size (Cohen, 1992). There was a slight positive correlation between caregiver average barriers severity and the CBQ-20-CF ( $r = 0.18$ ). Similarly, the average barriers severity for caregivers was negatively correlated with the GAD-7 ( $r = -0.43$ ) and PHQ-8 ( $r = -0.45$ ), both to a medium effect. Caregivers demonstrated a significant positive correlation between the PHQ-8 and GAD-7 ( $r = 0.88$ ,

$p < .01$ ). They also demonstrated a medium positive correlation between scores on the PHQ-8 and CBQ-20-CF ( $r = 0.44$ ), suggesting that more parental symptoms of depression were related to increased family conflict. There was a non-significant correlation between caregiver scores on the CBQ-20-CF and scores on the GAD-7 ( $r = 0.17$ , see Table 18).

*Aim 4. Patient/caregiver agreement on barriers.*

Positive associations were expected between rates of agreement regarding barrier frequency and patient adherence. Negative correlations were anticipated between rates of barrier agreement and family conflict. Sixteen patient-caregiver dyads completed barrier frequency and severity ratings. The average percent agreement between patients and caregivers was 0.37 ( $SD = 0.18$ ). For adolescents, there was a non-significant positive correlation between average adherence and percent agreement ( $r = 0.13$ ). However, there was a non-significant positive correlation, with a medium effect size, between percent agreement and family conflict ( $r = 0.37$ , see Table 19). This indicates that families with higher agreement on barrier type and frequency had slightly higher rates of adherence and family conflict.

*Post-hoc analyses.*

Because the directionality of several correlations was unexpected, post-hoc analyses were conducted to assess the relationship between participants' disease severity (FEV<sub>1</sub>% predicted), adherence, and other measures. Average rates of adherence were negatively correlated with disease severity ( $r = -0.49$ ,  $p = 0.07$ ), suggesting that better adherence was associated with lower lung function. Rates of adherence were positively



correlated with average number of barriers ( $r = 0.30$ , medium effect size) and average barrier severity ( $r = 0.16$ , see Table 20).

Age was also correlated with average rates of adherence, disease severity, average number of barriers, and average barrier severity. Participant age was positively correlated with both average number of barriers reported ( $r = 0.44$ ,  $p = 0.06$ , medium effect), and average severity ( $r = 0.33$ , medium effect). There was no relationship between age and adherence or disease severity.

## Chapter 4: Discussion

This study was the first mixed-methods analysis of barriers to adherence for adolescents and young adults with CF that included both qualitative and quantitative assessments of barrier frequency, severity, and adherence. Few other studies have measured these barriers using qualitative methods (George et al., 2010; Modi & Quittner, 2006a; Sawicki et al., 2015), providing a more in-depth assessment of this topic. Furthermore, we recruited patients from three separate CF centers in three cities across two states, allowing for a diverse patient population and likely more generalizable results. This contrasts with Sawicki et al. (2015) and George et al. (2010), which were conducted at a single CF center. This study also introduced a novel way of capturing the frequency and severity of barriers identified by patients and caregivers. The barrier severity rating scale, developed for this study, has not been utilized in previous research and provides important data on what gets in the way for people living with CF.

### *Qualitative discussion of barriers to adherence.*

Individuals with CF and their caregivers identified a range of barriers to adherence during the semi-structured interviews. To illustrate this, the common narrative and lifestyle evident in these interviews is outlined here. The majority of participants were the only member of their family with CF, and most participants were active in school, work, and their communities. One participant was caring for his ill mother and another was about to propose to his girlfriend. The people with CF who participated in this study were generally high-functioning and relatively healthy.

Patients and parents caregivers described a similar pattern of challenges. All patients reported having a treatment regimen that needed to be completed at least twice

daily and a few had a third set of treatments prescribed during the middle part of the day. Completion of the full regimen would take more than two hours each day. Some participants admitted that they were so tired at the end of the day that they were unwilling to set the alarm early enough to complete their morning treatments; others described missing out on needed sleep to fit their evening regimen in. Younger participants adapted their treatment schedule to their demanding extracurricular activities, and one high-school aged participant eschewed all extracurricular activities to complete her treatment regimen as prescribed. Navigating the issues of disclosure and the visible elements of the treatment regimen resulted in social challenges, which caused distress for some patients and caregivers.

The treatments themselves caused a range of aversive side effects that made adherence more difficult. Understandably, many participants described feeling frustrated and discouraged about their attempts to balance their treatment regimen with daily life. At times, these feelings became so severe that the participant chose not to do his/her treatments, or felt so unmotivated that they could not complete them. Frustrations with the health care system were common, including obtaining insurance authorizations and cooperation from pharmacies. Travel presented its own set of challenges, with heavy equipment and intrusive security personnel causing treatments to be skipped when away from home. These barriers were similar to those identified in previous literature (George et al., 2010; Sawicki et al., 2015), with a few notable exceptions.

For example, Sawicki and colleagues (2015) highlighted two themes that failed to emerge in this study: awareness of disease trajectory and lack of perceived

consequences. In this study, several participants discussed an awareness of their disease trajectory as a *motivating* factor for completing their treatments rather than a barrier. One young adult highlighted a recent hospitalization as a “wake up call” for her to improve her adherence. Several young adults wished they could “go back in time” to encourage their younger self to be more adherent so that they could ensure better health in the future. Participants had difficulty articulating why adherence was more difficult when they were teens, highlighting social factors and “just not wanting to do it” as common struggles. This suggests that although lack of perceived consequences did not emerge as a barrier in these interviews, it may have influenced barriers they mentioned.

The gap between the barriers described by younger teens and young adults was evident throughout the interviews. Young adults universally admitted to periods of poor adherence during adolescence, particularly around the ages of 14 and 15. Few of the younger teens in this study admitted to struggling with current adherence difficulties; however, some said that they had issues when they were “younger” (e.g. 12 or 13 years old). More interviews with younger participants would help clarify the developmental transition that appears to occur during later stages of adolescence. Understanding this shift might point to ages at which transfer of responsibility might be best accomplished. Sawicki et al. (2015) found early development of self-care skills was a motivator that increased adherence.

An important similarity between Sawicki et al., 2015 and this study was the description of time pressures and forgetting. Earlier research on barriers in CF identified “forgetting” (George et al., 2010) as a common theme that emerged for adolescents and

young adults. In the current study, patients described forgetting as more common in the context of busy schedules. Sawicki and colleagues (2015) identified an analogous description of “forgetting,” suggesting that the *context* in which it occurs must be understood. For example, patients do not simply need reminders or alarms to help them *remember* to take their enzymes; rather, they need assistance establishing plans to ensure their enzymes are with them at all times, regardless of changes in schedule.

The qualitative data generated by this study has important intervention implications. Each theme presents a target for intervention. For example, treatment-life balance barriers could be addressed by having a more detailed understanding of each patient and family’s schedule, followed by tailored problem-solving to address scheduling challenges. Treatment-related barriers could be addressed both on the individual and systems level. Individuals who struggle with the taste of inhaled antibiotics could try sucking on strong candies to mask the taste (e.g., Jolly Ranchers). At the same time, drug companies can focus on these patient preferences as they develop newer treatments. The types of intervention highlighted by these themes correspond with Modi et al.’s (2012) model of self-management, and reflect the multiple processes which interact to impact adherence. Results of this study clarified the context in which these barriers occur, which will allow for more nuanced and individualized adherence interventions.

#### *Depression and anxiety.*

This sample reported high rates of clinically significant symptoms of depression (35% of patients and 53% of caregivers) and anxiety (35% of patients and 67% of

caregivers). The prevalence in this sample was higher than that reported in the international TIDES study in 9 countries (Quittner et al., 2014). Negative emotions were identified as a major qualitative theme affecting patients' ability to complete their treatments. These results emphasize the need for standardized screening of depression and anxiety in both patients and their caregivers. International guidelines on mental health in CF were recently published, recommending annual screening in individuals with CF beginning at age 12 and all parent caregivers of patients from birth to age 17 (Quittner et al., 2015). This study added to the growing body of literature indicating depression and anxiety are significant problems for both patients and their caregivers (Barker & Quittner, in press; Quittner et al., 2014; Smith et al., 2010).

*Barrier frequency and severity.*

Although patients and caregivers generally reported similar themes, the specific types of barriers they reported differed. Patients identified fatigue as the most frequent barrier, which converged with the feedback received from participants during the "debriefing," triangulation process. During the follow-up discussions, several participants emphasized that fatigue was the most difficult barrier for them to overcome. In contrast, caregivers were more concerned about forgetting. In fact, fatigue was not identified as one of the top six barriers reported by caregivers. These differences highlighted the need to elicit barriers from both types of respondents (Modi & Quittner, 2006a; Sawicki et al., 2015).

Patients and caregivers also differed in terms of the relationships between barrier severity, frequency, and other measures. Patients describing more barriers also described

them as more severe. As hypothesized in Aim 3, patients reporting more frequent barriers also had more symptoms of depression and anxiety, and higher severity ratings were also related to higher conflict and more symptoms of depression and anxiety. This is consistent with the literature on adherence in CF (Modi & Quittner, 2006a; Quittner et al., 2014). As hypothesized, more frequent barriers were related to worse HRQoL, however, higher severity was *positively* associated with social functioning and health perceptions. Patients reporting more severe barriers reported lower HRQoL in emotional functioning and treatment burden. This distinction highlighted the importance of measuring barrier frequency and severity.

Analyses of rates of adherence raised more questions. Rates of adherence in this study were consistent with previous literature, with an average 3-day adherence rate of 44% (Johnson & Carlson, 2004; Quittner et al., 2014; Rapoff 2010; Sabaté, 2003; Sackett & Snow, 1979). Few of the directional predictions about adherence in relation to the other measures were supported. Better adherence was associated with more family conflict and greater symptoms of depression and anxiety. Better adherence was also associated with lower HRQoL, particularly worse perceptions of treatment burden. In contrast to this study, prior studies have found that better adherence is associated with fewer symptoms of emotional distress (Barker & Quittner, in press; Ettinger et al., 2014). In this study, better adherence was associated with *more* barriers, *higher* severity ratings, and worse psychological distress.

This finding was unexpected and spurred several post-hoc analyses. Disease severity likely played an important role in this relationship, since adherence increased as

disease severity worsened. Saez-Flores and colleagues (2015) recently found a much more complex pattern of results in a larger, national study. After controlling for disease severity, adolescents who were prescribed more treatments had better adherence as measured by medication possession ratios.. This was seen as a “paradoxical” effect and contrasted directly with previous findings that worse disease severity and more complex regimens were associated with worse adherence (Sawicki et al., 2011). Patients who are sicker may be more motivated to do their treatments, which may be moderated by their awareness of their disease trajectory and consequences for poor adherence, such as exacerbations, which require intravenous treatments in hospital. The paradoxical effects of treatment complexity and the role of motivation should both be pursued in future research.

Caregivers presented with a markedly different pattern of associations. In contrast to the hypothesis in Aim 3, caregivers who reported more barriers had lower conflict, and lower symptoms of depression and anxiety. Similarly, parents reporting higher severity also endorsed slightly lower family conflict, and fewer symptoms of depression and anxiety. This was an unexpected finding. One possible explanation is that parents who were more engaged with their teens/young adults were more aware of their daily challenges. This engagement might have improved their relationship, increasing parents’ awareness of barriers, while decreasing feelings of depression and anxiety. Research on these parental perceptions is currently limited (Modi & Quittner, 2006a; Bregnballe et al., 2011; Sawciki et al., 2015); this is the first study to examine parental perceptions of barriers and psychological distress in this patient age range.



*Agreement on barriers.*

On average, patients and caregivers agreed on about a third of barriers reported during the interviews (37%). Higher agreement was positively associated with family conflict, which was unexpected. No relationship was found between agreement on barriers and adherence. Thus, our hypotheses were not supported. It should be noted that rates of patient-caregiver conflict in this sample were very low, and patients' health was relatively high. The direction of these findings may have been influenced by these factors as well as the small sample size.

*Limitations.*

The primary limitation of this study was the small sample size that was obtained, despite recruiting at three major CF centers. Many of the correlations in this study were unexpected and will require replication in a larger sample. The small sample size also increased the chance of Type II error rates, failing to detect an effect where one existed, especially in the case of non-significant correlations which had medium effect sizes.

Additionally, the qualitative results have limitations which are similar to other qualitative research and thus, these findings may not be generalizable to the larger CF population. One individual (author) conducted the entire grounded theory analysis, and her bias may have influenced the results of the study (Charmaz, 2006). However, a notable strength of this qualitative analysis was that it took place across multiple sites and cities, allowing for a broader range of participants.

Participants in this study were somewhat different from the general CF population. More females than males participated, and the male participants tended to report higher HRQoL than age- and gender matched norms (Quittner et al., 2012). Rates of depression and anxiety were higher in caregivers than previously reported in the TIDES study, but the screening measures used in these two studies differed, which may explain the discrepancy (Quittner et al., 2014). Because this study used a convenience sample, it is possible that there were important differences between those who did vs. did not participate.

#### *Future directions.*

The qualitative analysis in this study focused on the barriers patients and caregivers encountered. Constructing effective adherence interventions will require an understanding of both the barriers to and motivators for adherence (Sawicki et al., 2015). During these interviews, patients mentioned both, but motivating factors were not the focus of the coding process. Sawicki and colleagues (2015) assessed these motivators and identified several key factors contributing to adherence: 1) symptoms of CF, 2) having a positive relationship with the CF team, 3) feeling as if they were treated like an adult by the CF team and their parents, 4) early development of self-care skills and 5) establishment of a structure or routine for doing these treatments. Future research should closely examine what motivates individuals with CF to fit their treatments in, and the paradoxical results found by Saez-Flores in the iCARE study suggest that there are resilience factors that enable some teens to be highly adherent in the face of high complexity. Several patients in this study were adherent to their regimens, at a rate of

88% over three days, in addition to conducting very busy, productive lives.

Understanding the unique strengths that helped them maintain their treatment regimen will be an important step in designing future interventions.

The results of this study suggest that developing a brief, in-clinic assessment of barriers to adherence is critical. It should be noted that when rating severity, participants utilized the entire range of the scale (1-4), indicating that it is possible to measure type of barrier, its frequency and severity. Currently, Quittner and Riekert are developing two types of barrier measures that will be launched nationally once the development and psychometric testing has concluded (grant awarded by CFF, 2014).

Finally, the negative associations between disease severity and adherence contrast with the work of Saez-Flores (2015). These results indicate that adherence in CF is a complex construct which takes into account both level of disease severity, complexity of the prescribed regimen, and psychological distress. Additional research is needed to understand how these variables interact with disease trajectory and developmental age.

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## Tables

*Table 2. Percent of participants reporting major themes during grounded theory analysis.*

Major theme	Patients % reporting (N = 18)	Caregivers % reporting (N = 17)
Treatment-life balance barriers	100	100
Treatment-related barriers	89	88
Negative emotions impacting treatment	67	88
Social barriers	78	71
Systems-level barriers	78	88
Travel barriers	56	82

*Table 3. Descriptive statistics for number of barriers reported and barrier severity.*

	Mean number of barriers (SD)	Range of number of barriers	Mean barrier severity (SD)
Patients (N= 18)	7.56 (3.28)	2-15	2.57 (0.96)
Caregivers (N= 16)	7.50 (3.98)	1-18	2.58 (0.92)

*Table 4. Most frequent barriers identified during barrier rating procedure.*

	#1 frequent barrier	#2 frequent barrier	#3 frequent barrier	#4 frequent barrier	#5 frequent barrier	#6 frequent barrier
Patients (N= 18)	Tired (78%)	School scheduling (61%)	Doesn't feel like it (56%)	Forgetting (56%)	Rather do other things (56%)	Scheduling issues (56%)
Caregivers (N= 16)	Forgetting (67%)	Doesn't feel like it (56%)	Side effects (50%)	Time (50%)	Travel barrier (50%)	Pharmacy issues (44%)

*Table 5. Barriers identified as most severe by patients and caregivers (reported by at least 5 participants, or about 30% of the sample).*

	#1 severe barrier	#2 severe barrier	#3 severe barrier	#4 severe barrier	#5 severe barrier	#6 severe barrier
Patients (N= 18)	Work schedule (28%), M= 3.40	Time (44%), M= 3.00	Pharmacy issues (28%), M= 2.80	Scheduling issues (56%), M= 2.55	Tired (78%), M= 2.50	Side effects (44%), M=2.50
Caregivers (N= 16)	Travel barriers (50%), M= 3.00	Time (50%), M= 2.89	School scheduling (38%), M= 2.83	Health insurance issues (31%), M= 2.80	Side effects (50%), M= 2.63	Doesn't feel like it (56%), M= 2.50

*Table 6. CBQ-20-CF descriptive results.*

	CBQ-20-CF Mean (SD)
Patients (N= 17)	22.1 (3.50)
Caregivers (N= 15)	23.3 (3.83)

*Table 7. PHQ-8 and GAD-7 descriptive results.*

	PHQ-8 mean (SD)	% scoring above clinical cutoffs on PHQ-8	GAD-7 mean (SD)	% scoring above clinical cutoffs on GAD-7
Patients (N= 17)	3.65 (4.14)	35%	3.35 (3.55)	35%
Caregivers (N= 15)	5.73 (4.80)	53%	7.60 (6.34)	67%

*Table 8. Older Child CFQ-R descriptive results compared to norms from Quittner et al., 2012 (for selected scales).*

Scale (N= 3 patients)	Scale Mean (SD)	Normative Scale Mean (SD)
Emotional Functioning	79.2 (16.7)	73.9 (14.8)
Social Functioning	77.8 (7.3)	67.9 (18.0)

*Table 9. Teen/Adult CFQ-R descriptive results compared to norms from Quittner et al., 2012 (for selected scales).*

Scale (N= 14 patients)	Scale Mean (SD)	Normative Scale Mean (SD)
Emotional Functioning	80.0 (16.7)	76.4 (20.0)
Social Functioning	75.8 (13.7)	72.4 (17.9)
Health Perceptions	75.0 (18.6)	67.2 (24.1)
Treatment Burden	58.6 (14.1)	61.5 (21.0)

*Table 10. Teen/Adult CFQ-R descriptive results by gender (for selected scales).*

Scale (N= 14 patients)	Female Scale Mean (SD), N= 9	Male Scale Mean (SD) N= 5	Significant Difference?
Emotional Functioning	72.6 (20.1)	93.3 (0.0)	Y ( $t(12) = -2.26, p = .03$ )
Social Functioning	70.4 (13.9)	85.6 (6.3)	N
Health Perceptions	69.8 (18.2)	84.4 (16.8)	N
Treatment Burden	55.0 (12.2)	65.0 (12.4)	N

Table 11. Teen/Adult CFQ-R descriptive results by gender with normative comparisons (for selected scales).

Scale (N patients)	Female Scale Mean (SD), N= 12	Female Scale Norms (SD)	Male Scale Mean (SD), N= 5	Male Scale Norms (SD)
Emotional Functioning	72.6 (20.1)	75.0	93.3 (0)	77.7
Social Functioning	70.4 (13.9)	70.7	85.6 (6.3)	73.9
Health Perceptions	69.8 (18.2)	66.0	84.4 (16.8)	68.3
Treatment Burden	55.0 (12.2)	60.0	65.0 (12.4)	62.9

Table 12. Average adherence by treatment type.

	Mean adherence % (SD)	Adherence range %
Airway clearance	36 (34)	0-100
Dornase alfa	50 (39)	0-100
Hypertonic saline	33 (45)	0 – 117
Inhaled antibiotics	29 (38)	0-100
Inhaled bronchodilators	9 (20)	0-67
Overall	44 (30)	0-90

Table 13. Patient correlations- average number of barriers and barriers severity ratings.

	Average number of barriers	Average barrier severity	PHQ-8	GAD-7	CBQ-20-CF
Average number of barriers	—	.54*	.48	.42	.04
Average barriers severity		—	.46	.41	.38
PHQ-8			—	.75**	.34
GAD-7				—	.30
CBQ-20-CF					—

\*Indicates correlation is significant  $p < .05$



**\*\*Indicates correlation is significant  $p < .01$**

*Table 14. Patient correlations- average number of barriers and barriers severity ratings and CFQ-R scales.*

	Average number of barriers	Average barrier severity	CFQ-R Emotional Functioning Scale	CFQ-R Social Functioning Scale	CFQ-R Health Perceptions Scale	CFQ-R Treatment Burden Scale
Average number of barriers	_____	.54*	-.35	-.14	-.21	-.16
Average barriers severity		_____	-.46	.27	.27	-.49
CFQ-R Emotional			_____	.20	.35	.52
CFQ-R Social				_____	.76**	-.23
CFQ-R Health					_____	-.09
CFQ-R Treatment Burden						_____

**\*Indicates correlation is significant  $p < .05$**

**\*\*Indicates correlation is significant  $p < .01$**

*Table 15. Correlations between barrier frequency, severity, and rates of adherence.*

	Average number of barriers	Average barrier severity	Average adherence
Average number of barriers	_____	.27	.30
Average barriers severity		_____	.16
Average adherence			_____

**\*Indicates correlation is significant  $p < .05$**

**\*\*Indicates correlation is significant  $p < .01$**

Table 16. Correlations between rates of adherence, PHQ-8, GAD-7, and CBQ-20-CF.

	Average rates of adherence	PHQ-8	GAD-7	CBQ-20-CF
Average rates of adherence	_____	.40	.30	.19
PHQ-8		_____	.82**	.42*
GAD-7			_____	.26
CBQ-20-CF				_____

\*Indicates correlation is significant  $p < .05$

\*\*Indicates correlation is significant  $p < .01$

Table 17. Correlations between rates of adherence and selected scales of the CFQ-R.

	Average rates of adherence	CFQ-R Emotional Functioning Scale	CFQ-R Social Functioning Scale	CFQ-R Health Perceptions Scale	CFQ-R Treatment Burden Scale
Average rates of adherence	_____	-.17	-.39	-.62*	-.37
CFQ-R Emotional		_____	.20	.35	.52
CFQ-R Social			_____	.76**	-.23
CFQ-R Health				_____	-.09
CFQ-R Treatment Burden					_____

\*Indicates correlation is significant  $p < .05$

\*\*Indicates correlation is significant  $p < .01$

Table 18. Caregiver correlations- average number of barriers and barriers severity ratings.

	Average number of barriers	Average barrier severity	PHQ-8	GAD-7	CBQ-20-CF
Average number of barriers	_____	.01	-.40	-.36	-.29
Average barriers severity		_____	-.45	-.43	.18
PHQ-8			_____	.88**	.44
GAD-7				_____	.17
CBQ-20-CF					_____

\*Indicates correlation is significant  $p < .05$

\*\*Indicates correlation is significant  $p < .01$

Table 19. Correlations between percent agreement, average adherence, and family conflict (for patients)

	Percent agreement	Average adherence	Family conflict
Percent agreement	_____	.13	.37
Average adherence		_____	.19
Family conflict			_____

\*Indicates correlation is significant  $p < .05$

\*\*Indicates correlation is significant  $p < .01$

Table 20. Correlations between rates of adherence, FEV<sub>1</sub>% predicted, barrier frequency, and barrier severity.

	Average rates of adherence	FEV <sub>1</sub> % predicted	Average number of barriers	Average barrier severity
Average rates of adherence	—	-.49	.30	.16
FEV <sub>1</sub> % predicted		—	-.11	-.08
Average number of barriers			—	.27
Average barrier severity				—

\*Indicates correlation is significant  $p < .05$

\*\*Indicates correlation is significant  $p < .01$

## Appendices

### Appendix A. Barriers Interview for Teens/Young Adults with CF

#### Barriers Interview

#### Open-Ended Interview Guide: Teen/Young Adult Participant with CF

##### Introduction

Thank you for agreeing to be in this study and taking the time to speak with me today. As explained in the informed consent you signed, the purpose of this study is to speak to people with CF and their parents about the impact of CF on their daily lives. We are interested in how you are able to fit in your CF treatments, as well as what gets in the way. Today, we are particularly interested in the barriers, aside from time and forgetting, you encounter when getting your CF treatments done. None of this information will be shared with your CF team, and this conversation will be kept strictly confidential.

**[Ask for permission to audiotape the interview; begin recorder.] *First, can I confirm with you that it is okay for me to record this conversation? [While recording, confirm participant ID and date]***

##### General Questions

Please tell me a bit about your family (e.g., parents, brothers, sisters, children).

- Does anyone else in your family have CF?

We know that you are prescribed several treatments to manage your CF. We have found that it is very hard for most people to get all of their treatments done. What can we do to help you manage this challenging set of tasks? What would be most helpful to you in managing your treatment regimen more easily?

What often gets in the way of doing your treatments?

What is setting up your inhaled/nebulized treatments like for you?

How about for your VEST or other types of treatments?

Who, if anyone, assists you with setting up treatments?

Who, if anyone, is around when you do your treatments and when you clean the equipment afterwards?

What are your easiest treatments to get done? What makes it easy for you? [If response is "pills"] Other than pills, what are your easiest treatments to get done?

What is the most difficult part of getting your treatments done? What gets in the way?

### **Specific Treatment Questions (adapt these questions based on their regimen)**

Now, I'm going to ask questions about specific treatments you might do. Let me know if I forget any treatments you are doing or if there are any you don't do.

Tell me about doing your airway clearance. What type of airway clearance do you do (Acapella/Flutter/VEST/Chest physiotherapy)? How often do you do it? What makes it difficult to fit in your airway clearance (Acapella/Flutter/VEST)? Any issues with equipment? If yes, what are some of the issues you face with equipment?

Where do you store your acapella/vest/flutter?

What types of nebulized treatments do you do? (Prompt for Pulmozyme/TOBI/Cayston/Hypertonic Saline)

- Tell me about what gets in the way of doing your Pulmozyme.
  - Describe times or situations when taking your Pulmozyme is more difficult.
- Tell me about what gets in the way of doing your hypertonic saline.
- Describe times or situations when doing your hypertonic saline is more difficult.
- 
- What gets in the way of doing your inhaled antibiotics?
  - What makes this more difficult? Describe the times or situations when doing your inhaled antibiotics is more difficult.
- 
- Tell me about what gets in the way of taking your oral antibiotics (such as Zithromax/Azithromycin)?
  - Describe times or situations when taking your oral antibiotics is more difficult.

Now, let's talk about enzymes (if they are pancreatic insufficient). What gets in the way of taking your enzymes?

- What gets in the way of taking your enzymes with meals? How about with snacks?
- Describe times or situations when taking your enzymes is more difficult. (*Prompt for social situations with friends/going out, lunch at school or work etc.*)
- Does anyone remind you to take your enzymes? If yes, who reminds you?
- Do you use any other strategies for remembering them? If yes, what other strategies do you use?

Do you take any nutritional supplements, such as Scandishakes or tube feedings? What gets in the way of doing those?

- Describe times or situations when taking your nutritional supplements is more difficult.

Do you take any medications for digestive problems like acid reflux (antacids), such as Prevacid, Prilosec, or over-the-counter medications like Zantac? What gets in the way of doing those?

- Describe times or situations when taking these medications is more difficult.

What inhalers do you use (Albuterol/Advair/etc.)? Tell me about what gets in the way of doing those.

- Describe times or situations when doing your inhalers is more difficult.

Tell me about what gets in the way of doing your vitamins each day?

- Describe times or situations when taking your vitamins is more difficult.

Are you taking Kalydeco? (if not, skip this section)

- Describes times or situations when taking Kalydeco is more difficult.
- (probe about weight gain; needing to eat with fat-containing food)

Do you have CF-related diabetes? (*If no, skip this question*) If yes, tell me about managing your CFRD. What gets in the way of managing your CFRD?

- Tell me about diet challenges?
- What about testing your blood sugar/glucose? Giving yourself insulin?
- Describe times or situations when managing your CFRD is more difficult.

Tell me about what gets in the way of exercising ?

- What types of exercise do you like to do?
- Describe times or situations when [doing named exercise] is more difficult.

What other treatments do you take? What gets in the way? Describe times or situations when doing (specific treatment) is more difficult.

### **Cross-Cutting Issues**

In what way do the following affect your ability to follow your treatment plan?

- Work/school/career
- Family
- Friends

- Stress, psychological distress (burn out?)
- Finances
- Health insurance
- Pharmacy issues

What other types of issues have you faced?

For each challenge endorsed ask:

- How do you work around these challenges?
- What has been helpful?

Do you feel comfortable telling other people about your CF? If so, who do you feel comfortable talking about your CF with? Who do you NOT feel comfortable discussing it with?

Everyone has times in their lives when they are really good about following their regimen and times when it's hard to get all of their treatments done. Think about a day when getting all of your treatments done was fairly easy and it all worked. Tell me about that day. What was going on?

*(Probe if unclear to participant)*

- How were your daily activities different during these times?
- What made things easier?
- What helps you get your treatments done the most?

Now think about a day when getting your treatment regimen done was difficult. Tell me about that day. What was going on when things were harder?

*(Probe if unclear to participant)*

- How were your daily activities different during these times?
- What made things harder?

How do you get your treatments done when you're traveling?

What about other times when you aren't at home at treatment time, for example you are at a sleepover? What about other social/church/community/work functions? Adolescents only: Do you ever attend camp? How are treatments done there?

Are there times where you just don't feel like doing your treatments? When?

For many people, emotions have an effect on doing their treatments. How do your emotions affect how you do your treatments?

Probe if further needed

- What about when you've felt down or sad – does this affect your ability to do your treatments?
- What about when you've felt worried or anxious – does this affect your ability to do your treatments?

How do you deal with those feelings?



## Appendix B. Barriers Interview Guide for Parent of Teen/Young Adult with CF

### Barriers Interview

#### Open-Ended Interview Guide: Parent of Teen/Young Adult with CF

##### Introduction

Thank you for agreeing to be in this study and taking the time to speak with me today. As explained in the informed consent you signed, the purpose of this study is to speak to people with CF and their parents about the impact of CF on their daily lives. We are interested in how you and your teen/adult are able to fit in your CF treatments, as well as what gets in the way. Today, we are particularly interested in the barriers you encounter when getting your CF treatments done. None of this information will be shared with your CF team, and this conversation will be kept strictly confidential.

**[Ask for permission to audiotape the interview; begin recorder.] *First, can I confirm with you that it is okay for me to record this conversation? [While recording, confirm participant ID and date]***

##### General Questions

Please tell me a bit about your family (e.g., parents, brothers, sisters, children).

- Does anyone else in your family have CF?

We know that your teen/adult is prescribed several treatments to manage their CF. We have found that it is very hard for most people to get all of their treatments done. What can we do to help your teen/adult manage this challenging set of tasks? What would be most helpful to your teen/adult in managing their treatment regimen more easily?

What often gets in the way of your teen/adult doing their treatments?

What is setting up your inhaled/nebulized treatments like for your teen/adult?  
How about for your teen/adult's VEST or other types of treatments?  
Who, if anyone, assists your teen/adult with setting up treatments?

Who is around when your teen/adult does their treatments, if anyone? How about when he/she cleans the equipment afterwards?  
What are your easiest treatments for your teen/adult to get done? What makes it easy for them? [If response is "pills"] Other than pills, what are their easiest treatments to get done?

What is the most difficult part of getting your teen/adult's treatments done? What gets in the way?

### **Specific Treatment Questions (adapt these questions based on their regimen)**

Now, I'm going to ask questions about specific treatments your teen/adult might do. Let me know if I forget any treatments you are doing or if there are any they don't do.

Tell me about their airway clearance. What type of airway clearance do they do (Acapella/Flutter/VEST)? How often do they do it?

What makes it difficult to fit in their airway clearance (Acapella/Flutter/VEST)? Any issues with equipment? If yes, what are some of the issues your teen/adult faces with equipment?

Where does he/she store their acapella/vest/flutter?

What types of nebulized treatments does your teen/adult do? (Prompt for Pulmozyme/TOBI/Cayston/Hypertonic Saline)

- Tell me about what gets in the way of doing their Pulmozyme.
  - Describe times or situations when taking their Pulmozyme is more difficult.
- Tell me about what gets in the way of doing their hypertonic saline.
  - Describe times or situations when doing their hypertonic saline is more difficult.
- What gets in the way of doing their inhaled antibiotics?
  - What makes this more difficult? Describe the times or situations when doing their inhaled antibiotics is more difficult.
  - Any side effects or problems with these?

Now, let's talk about enzymes (if they are pancreatic insufficient). What gets in the way of taking their enzymes?

- What gets in the way of taking their enzymes with meals? How about with snacks?
- Describe times or situations when taking their enzymes is more difficult. (*Prompt for social situations with friends/going out, lunch at school or work etc.*)
- Does anyone remind your teen/adult to take their enzymes? If yes, who reminds them?
- Does your teen/adult use any other strategies for remembering them? If yes, what other strategies does he/she use?

Does your teen/adult take any nutritional supplements, such as Scandishakes or tube feedings? What gets in the way of doing those?

- Describe times or situations when taking their nutritional supplements is more difficult.

Does your teen/adult take any medications for digestive problems like acid reflux (antacids), such as Prevacid, Prilosec, or over-the-counter medications like Zantac? What gets in the way of doing those?

- Describe times or situations when taking these medications is more difficult.

What inhalers do your teen/adult use (Albuterol/Advair/etc.)? Tell me about what gets in the way.

- Describe times or situations when doing their inhalers is more difficult.

Is your teen/adult able to take their vitamins each day? What makes it more difficult to take them?

- Describe times or situations when taking their vitamins is more difficult.

How about your teen/adult's oral antibiotics (like Zithromax/Azithromycin)?

- Describe times or situations when taking their oral antibiotics is more difficult.

Is your teen/adult taking Kalydeco? (if not, skip this section)

- What gets in the way of taking this?
- (probe about weight gain; needing to eat with fat-containing food)

Does your teen/adult have CF-related diabetes? (*If no, skip this question*) If yes, tell me about managing their CFRD. What gets in the way of managing their CFRD?

- Tell me about diet challenges?
- What about testing their blood sugar/glucose? Giving themselves insulin?
- Describe times or situations when managing their CFRD is more difficult.

Tell me about what gets in the way of exercising?

- What types of exercise does your teen/adult like to do?
- Describe times or situations when [doing named exercise] is more difficult.

What other treatments does your teen/adult take? What gets in the way?

### **Cross-Cutting Issues**

In what way do the following affect your teen/adult's ability to follow their treatment plan?

- Work/school/career

- Family
- Friends
- Stress, psychological distress (burn out?)
- Finances
- Health insurance
- Pharmacy issues

What types of issues has your teen/adult faced?

For each challenge endorsed ask:

- How do you work around these challenges?
- What has been helpful?

Does your teen/adult feel comfortable telling other people about their CF? If so, who does he/she feel comfortable talking about their CF with? Who does he/she NOT feel comfortable discussing it with?

Everyone has times in their lives when they are really good about following their regimen and times when it's hard to get all of their treatments done. Think about a time when getting all of your teen/adult's treatments done was fairly easy.

What was going on?

*(Probe if unclear to participant)*

- How were your teen/adult's daily activities different during these times?
- What made things easier?

Now think about a time when getting your treatment regimen done was difficult.

What was going on when things were harder?

*(Probe if unclear to participant)*

- How were your teen/adult's daily activities different during these times?
- What made things harder?

How does your teen/adult get their treatments done when they are traveling?

What about other times when your teen/adult is not at home at treatment time, for example he/she is at a sleepover? What about other

social/church/community/work functions? (For parents of adolescents only):

Does your teen ever attend camp? How are treatments done there?

What helps your teen/adult get your treatments done the most?

Are there times where your teen/adult just doesn't feel like doing their treatments? When?


For many people, emotions have an effect on doing their treatments. How do your teen/adult's emotions affect how they do their treatments?

Probe if further needed

- What about when they have felt down or sad – does this affect their ability to do their treatments?
- What about when they have felt worried or anxious – does this affect their ability to do their treatments?

How does your teen/adult deal with those feelings?

## Appendix C. Daily Phone Diary

DAILY PHONE DIARY	
<h1>DPD</h1> <p>DEPARTMENT OF PSYCHOLOGY UNIVERSITY OF MIAMI</p>	
<p>5 group</p> <p>miami site</p>	<p>0029-8 participant id</p> <p>Andre participant name</p> <p>Andre interviewer</p> <p>treatment 3 assessment point</p> <p>diary number</p>
<p>activity date</p> <p>activity day</p> <p>2 activity number</p> <p>[ start now ]</p>	<p>4:10 PM start time</p> <p>4:10 PM activity start time</p> <p>5:50 PM activity end time</p> <p>100 activity duration</p>
<p>Basic Child Care</p> <p>Medical Care</p> <p>Household Tasks</p> <p>Meals</p> <p>Recreation - Home</p> <hr/> <p>Medical Care</p> <p>Preparing/Giving Enzymes</p> <p>Preparing/Giving Medications</p> <p>Doing Airway Clearance</p> <p>Picking up Prescriptions</p> <hr/> <p>Preparing/Giving Enzymes</p>	<p>Preparing/Giving Enzymes</p> <p>selected activity - or enter other activity</p> <p><input checked="" type="checkbox"/> Adult Friends <input type="checkbox"/> Relatives</p> <p><input type="checkbox"/> Alone <input type="checkbox"/> Spouse/Partner</p> <p><input type="checkbox"/> Co-Workers <input type="checkbox"/> Younger Sib 1</p> <p><input checked="" type="checkbox"/> Entire Family <input type="checkbox"/> Younger Sib 2</p> <p><input type="checkbox"/> Older Sib 1 <input type="checkbox"/> Younger Sib 3</p> <p><input type="checkbox"/> Older Sib 2</p> <p><input checked="" type="checkbox"/> Older Sib 3</p> <p><input checked="" type="checkbox"/> Other Kids</p> <p>4 companion count</p>
	
	<p>mood</p> <p>purpose</p>
Administrator	

## Appendix D. Prescribed Treatment Plan

1

### PRESCRIBED TREATMENT PLAN

To be completed by a healthcare professional

Today's Date:...../...../.....

ID: \_\_\_\_\_

Recommended Order, CFF Guidelines

	Dose	Freq/Day	Duration
<b>Inhaled Bronchodilator:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Albuterol/Xopenex®	_____ puffs/vials	PRN * 1 2 3 4	_____ min
Other:	_____ puffs/vials	PRN 1 2 3 4	_____ min
<b>Hypertonic Saline:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Hypertonic Saline	_____ mL	1 2 Other:	_____ min
<b>Pulmozyme®:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Pulmozyme®	1 ampule	1 2	_____ min
<b>Airway Clearance:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no	
CPT		1 2 3 4	_____ min
The Vest®		1 2 3 4	_____ min
Flutter®/Acapella®		1 2 3 4	_____ min
PEP Device		1 2 3 4	_____ min
Other:		1 2 3 4	_____ min
<b>Inhaled Antibiotic:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no	
TOBI®** <small>(Tobramycin Inhalation Solution)</small>	1 ampule	1 2	_____ min
Cayston®		1 2 3	_____ min
Other:			
<b>Oral Antibiotics:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Zithromax® 250/500mg	1 ampule	2	
Other:		1 2 3	
Other:		1 2 3	
<b>Enzymes:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Creon®	_____ strength	(1-12)	
Zenpep®	_____ strength	(1-12)	
Other:	_____ strength	(1-12)	
<b>Vitamins:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Calcium	_____ tablets	1 2	
ADEKs®	_____ tablets	1 2	
AquADEKs™	_____ tablets	1 2	
VITAMAX®	_____ tablets	1 2	
Other:			
<b>Digestive Medications:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Zantac®	_____ mg	1 2 3	
Prevacid®	_____ mg	1 2 3	
Prilosec™	_____ mg	1 2 3	
Other:	_____ mg	1 2 3	

\* PRN = as needed

\*\* TOBI and ALZI are taken in repeated cycles of 28 days on and 28 days off

	Dose	Freq/Day
<b>Disease Modifying (Oral):</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no
Kalydeco™	150 mg	2
Other:		
<b>Nutritional Supplements:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no
<b>Tube Feedings:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no
	_____ CC/hr	_____ hrs/day
	_____ CC/hr	_____ hrs/day
<b>Inhaled Steroids:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no
Pulmicort® mcg	_____ puffs/vials	PRN 1 2 3 4
Flovent® mcg	_____ puffs/vials	PRN 1 2 3 4
Other:	_____ puffs/vials	PRN 1 2 3 4
<b>Combination Inhaler:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no
Advair®/Symbicort® mcg	_____ puffs	2
<b>Allergy Medications/Antihistamines:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no
Claritin®/Zyrtec®/Allegra®	_____ mg	PRN 1 2
Flonase®/Rhinocort®/Nasonex®	_____ sprays	PRN 1 2
Other:		
<b>Leukotriene Modifiers:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no
Singulair®	_____ mg	1
<b>Blood Glucose Monitoring:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no
Glucose Monitoring		1 2 3
<b>Insulin:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no
	_____ units	Meal Bedtime
	_____ units	Meal Bedtime
<b>Other Medications:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no
Prednisone	_____ mg	1 2 taper
Other:		
Other:		
<b>Exercise:</b>	<input type="checkbox"/> yes	<input type="checkbox"/> no
	_____ min	1 2 3 4
	_____ min	1 2 3 4

<b>NOTES:</b>			
CURRENT:	FEV <sub>1</sub> : _____%	BMI: _____	Weight: _____lb/ _____kg
Goals:	FEV <sub>1</sub> : _____%	BMI: _____	Weight: _____lb/ _____kg      Date of next visit:...../...../.....
My SOLUTION:			
We commit to this plan together. By signing this document, we agree to follow the Treatment Plan outlined above			
X	X	X	
Patient Signature	Parent Signature	Provider Signature	

## Appendix E. Barriers Severity Scale

### Barriers Severity Scale

Think about what gets in the way of doing your/your child's treatments. For each barrier discussed, please rate it on a scale from 1, meaning "Does not make doing treatments more difficult," to 4, meaning "Makes doing treatments very difficult." Use this chart to help you rate the barriers as we talk about them.

<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>
Does not make doing treatments more difficult	Makes doing treatments a little bit difficult	Makes doing treatments somewhat difficult	Makes doing treatments very difficult



## Appendix F. Cystic Fibrosis Questionnaire- Revised



**Adolescents and Adults (Patients 14 Years Old and Older)**

CYSTIC FIBROSIS QUESTIONNAIRE – REVISED (WITH DIGESTIVE/SINUS ITEMS)

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

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

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

### Section I. Demographics

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

- A. What is your date of birth?  
Date 

Mo	Day	Year				
- B. What is your gender?  
 Male     Female
- C. During the **past two weeks**, have you been on vacation or out of school or work for reasons **NOT** related to your health?  
 Yes     No
- D. What is your current marital status?  
 Single/never married  
 Married  
 Widowed  
 Divorced  
 Separated  
 Remarried  
 With a partner
- E. Which of the following best describes your racial background?  
 Caucasian  
 African American  
 Hispanic  
 Asian/Oriental or Pacific Islander  
 Native American or Native Alaskan  
 Other (please describe) \_\_\_\_\_  
 Prefer not to answer this question
- F. What is the highest grade of school you have completed?  
 Some high school or less  
 High school diploma/GED  
 Vocational school  
 Some college  
 College degree  
 Professional or graduate degree
- G. Which of the following best describes your current work or school status?  
 Attending school outside the home  
 Taking educational courses at home  
 Seeking work  
 Working full or part time (either outside the home or at a home-based business)  
 Full time homemaker  
 Not attending school or working due to my health  
 Not working for other reasons





Section II. Quality of Life

Please check the box indicating your answer.

Table with 5 columns: Question, A lot of difficulty, Some difficulty, A little difficulty, No difficulty. Rows 1-5: Performing vigorous activities, Walking as fast as others, Carrying or lifting heavy things, Climbing one flight of stairs, Climbing stairs as fast as others.

Table with 5 columns: Question, Always, Often, Sometimes, Never. Rows 6-12: You felt well, You felt worried, You felt useless, You felt tired, You felt energetic, You felt exhausted, You felt sad.

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

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

- 13. To what extent do you have difficulty walking?
1. You can walk a long time without getting tired
2. You can walk a long time but you get tired
3. You cannot walk a long time because you get tired quickly
4. You avoid walking whenever possible because it's too tiring for you
14. How do you feel about eating?
1. Just thinking about food makes you feel sick
2. You never enjoy eating
3. You are sometimes able to enjoy eating
4. You are always able to enjoy eating
15. To what extent do your treatments make your daily life more difficult?
1. Not at all
2. A little
3. Moderately
4. A lot




**Adolescents and Adults (Patients 14 Years Old and Older)**
**CYSTIC FIBROSIS QUESTIONNAIRE – REVISED (WITH DIGESTIVE/SINUS ITEMS)**

16. How much time do you currently spend each day on your treatments?
1. A lot
  2. Some
  3. A little
  4. Not very much
17. How difficult is it for you to do your treatments (including medications) each day?
1. Not at all
  2. A little
  3. Moderately
  4. Very
18. How do you think your health is now?
1. Excellent
  2. Good
  3. Fair
  4. Poor

*Please select a box indicating your answer.*

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

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


**Adolescents and Adults (Patients 14 Years Old and Older)**

CYSTIC FIBROSIS QUESTIONNAIRE – REVISED (WITH DIGESTIVE/SINUS ITEMS)

**Section III. School, Work, or Daily Activities**
*Questions 35 through 38 are about school, work, or other daily tasks.*

35. To what extent did you have trouble keeping up with your schoolwork, professional work, or other daily activities during the past two weeks?
1. You have had no trouble keeping up
  2. You have managed to keep up but it's been difficult
  3. You have been behind
  4. You have not been able to do these activities at all
36. How often were you absent from school, work, or unable to complete daily activities during the last two weeks because of your illness or treatments?
- Always       Often       Sometimes       Never
37. How often does CF get in the way of meeting your school, work, or personal goals?
- Always       Often       Sometimes       Never
38. How often does CF interfere with getting out of the house to run errands such as shopping or going to the bank?
- Always       Often       Sometimes       Never

**Section IV. Symptom Difficulties**
*Please select a box indicating your answer.*
*Indicate how you have been feeling during the past two weeks.*

- |  | A great deal             | Somewhat                 | A little                 | Not at all               |
|--|--------------------------|--------------------------|--------------------------|--------------------------|
| 39. Have you had trouble gaining weight? .....   | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 40. Have you been congested in your chest? ..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 41. Have you been coughing during the day? ..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 42. Have you had to cough up mucus? .....        | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
- Go to Question 44
43. Has your mucus been mostly:     Clear     Clear to yellow     Yellowish-green     Green with traces of blood     Don't know

*How often during the past two weeks:*

- |   | Always                   | Often                    | Sometimes                | Never                    |                          |
|---|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| 44. Have you been wheezing? .....                                       | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |
| 45. Have you had trouble breathing? .....                               | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |
| 46. Have you woken up during the night because you were coughing? ..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |
| 47. Have you had problems with gas? .....                               | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |
| 48. Have you had diarrhea? .....  | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |
| 49. Have you had abdominal pain? .....                                  | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |
| 50. Have you had eating problems? .....                                 | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Doesn't Apply            |
| 51. Have you forgotten to take your enzymes? .....                      | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |




**Adolescents and Adults (Patients 14 Years Old and Older)**
**CYSTIC FIBROSIS QUESTIONNAIRE – REVISED (WITH DIGESTIVE/SINUS ITEMS)**
*How often during the past two weeks:*

	<b>Always</b>	<b>Often</b>	<b>Sometimes</b>	<b>Never</b>
52. Have you been constipated? .....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
53. Have you had acid reflux? .....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
54. Have you felt bloated? .....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
55. Have you had to use the bathroom frequently (bowel movements)? .....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
56. Have you felt congestion in your nose? .....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
57. Have you had sinus headaches? .....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
58. Have you had post-nasal drip? .....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
59. Have you had facial pain? .....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
60. Have you felt pressure in your ears? .....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

*Please be sure you have answered all the questions.*

**THANK YOU FOR YOUR COOPERATION!**

## Appendix G. Generalized Anxiety Disorder-7

<b>GAD-7</b>				
Over the <u>last 2 weeks</u> , how often have you been bothered by the following problems?  <i>(Use "✓" to indicate your answer)</i>	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

*(For office coding: Total Score T \_\_\_ = \_\_\_ + \_\_\_ + \_\_\_)*

## Appendix H. Patient Health Questionnaire- 8

## PATIENT HEALTH QUESTIONNAIRE-8 (PHQ-8)

Over the last 2 weeks, how often have you been bothered by any of the following problems?

(Circle your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself- or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite- being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
	___ +	___ +	___ +	Total score =

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all <input type="checkbox"/>	Somewhat difficult <input type="checkbox"/>	Very difficult <input type="checkbox"/>	Extremely Difficult <input type="checkbox"/>
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Adapted from Spitzer, Williams, Kroenke, et al. (PHQ-9)

## Appendix I. Conflict Behavior Questionnaire- 20: CF Modification

### Conflict Behavior Questionnaire- CF Adolescent to complete (for Mother)

*In this questionnaire, the term “mother” refers to a woman who is raising you.*

Think back over the last 2 weeks at home. The statements below have to do with you and your mother. Read the statement, and then decide if you believe the statement is true. If it is true, check the box marked true, and if you believe the statement is not true, check the box marked false. For each item, please check either true or false, but never both for the same item. Please answer all items. Your answers will not be shown to your parents if you don't want them to be.

	True	False
1. My mom doesn't understand me.	<input type="checkbox"/>	<input type="checkbox"/>
2. My mom and I sometimes end our arguments about CF treatments calmly.	<input type="checkbox"/>	<input type="checkbox"/>
3. My mom understands me.	<input type="checkbox"/>	<input type="checkbox"/>
4. We almost never seem to agree about how to fit in my CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
5. I enjoy the talks we have.	<input type="checkbox"/>	<input type="checkbox"/>
6. When I state my own opinion, she gets upset.	<input type="checkbox"/>	<input type="checkbox"/>
7. At least three times a week, we get angry at each other about my treatments.	<input type="checkbox"/>	<input type="checkbox"/>
8. My mother listens when I need someone to talk to about my CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
9. My mom is a good friend to me.	<input type="checkbox"/>	<input type="checkbox"/>
10. She says I have no consideration for her.	<input type="checkbox"/>	<input type="checkbox"/>
11. At least once a day, we get angry at each other about my treatments.	<input type="checkbox"/>	<input type="checkbox"/>
12. My mother is bossy when we talk.	<input type="checkbox"/>	<input type="checkbox"/>
13. The talks we have about CF treatments are frustrating.	<input type="checkbox"/>	<input type="checkbox"/>
14. My mom understands my point of view, even when she doesn't agree with me.	<input type="checkbox"/>	<input type="checkbox"/>
15. My mom always seems to be complaining about my CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
16. In general, I don't think we get along very well.	<input type="checkbox"/>	<input type="checkbox"/>
17. My mom screams a lot.	<input type="checkbox"/>	<input type="checkbox"/>
18. My mom puts me down.	<input type="checkbox"/>	<input type="checkbox"/>
19. If I run into problems planning my CF treatments, my mom helps me out.	<input type="checkbox"/>	<input type="checkbox"/>
20. I enjoy spending time with my mother.	<input type="checkbox"/>	<input type="checkbox"/>



## Conflict Behavior Questionnaire CF — Adolescent to complete (for Father)

*In this questionnaire, the term “father” refers to a man who is raising you.*

Think back over the last 2 weeks at home. The statements below have to do with you and your father. Read the statement, and then decide if you believe the statement is true. If it is true, check the box marked true, and if you believe the statement is not true, check the box marked false. For each item, please check either true or false, but never both for the same item. Please answer all items. Your answers will not be shown to your parents if you don't want them to be.

	True	False
1. My dad doesn't understand me.	<input type="checkbox"/>	<input type="checkbox"/>
2. My dad and I sometimes end our arguments about CF treatments calmly.	<input type="checkbox"/>	<input type="checkbox"/>
3. My dad understands me.	<input type="checkbox"/>	<input type="checkbox"/>
4. We almost never seem to agree about how to fit in my CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
5. I enjoy the talks we have.	<input type="checkbox"/>	<input type="checkbox"/>
6. When I state my own opinion, he gets upset.	<input type="checkbox"/>	<input type="checkbox"/>
7. At least three times a week, we get angry at each other about my treatments.	<input type="checkbox"/>	<input type="checkbox"/>
8. My father listens when I need someone to talk to about my CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
9. My dad is a good friend to me.	<input type="checkbox"/>	<input type="checkbox"/>
10. He says I have no consideration for her.	<input type="checkbox"/>	<input type="checkbox"/>
11. At least once a day, we get angry at each other about my treatments.	<input type="checkbox"/>	<input type="checkbox"/>
12. My father is bossy when we talk.	<input type="checkbox"/>	<input type="checkbox"/>
13. The talks we have about CF treatments are frustrating.	<input type="checkbox"/>	<input type="checkbox"/>
14. My dad understands my point of view, even when he doesn't agree with me.	<input type="checkbox"/>	<input type="checkbox"/>
15. My dad always seems to be complaining about my CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
16. In general, I don't think we get along very well.	<input type="checkbox"/>	<input type="checkbox"/>
17. My dad screams a lot.	<input type="checkbox"/>	<input type="checkbox"/>
18. My dad puts me down.	<input type="checkbox"/>	<input type="checkbox"/>
19. If I run into problems planning my CF treatments, my dad helps me out.	<input type="checkbox"/>	<input type="checkbox"/>
20. I enjoy spending time with my father.	<input type="checkbox"/>	<input type="checkbox"/>

## Conflict Behavior Questionnaire CF — Parent

In this questionnaire, the term “mother” or “father” refers to a woman or man who is a primary caregiver for this teenager.

You are the teenager’s:  mother  father (check one)

You are filling this questionnaire out regarding your:  male teen  female teen who is \_\_\_\_\_ years old.

Think back over the last 2 weeks at home. The statements below have to do with you and your teenager. Read the statement, and then decide if you believe the statement is true. If it is true, check the box marked true, and if you believe the statement is not true, check the box marked false. For each item, please check either true or false, but never both for the same item.

Answer for yourself, without talking it over with your partner.

	True	False
1. My teenager is easy to get along with.	<input type="checkbox"/>	<input type="checkbox"/>
2. My teenager is receptive to criticism.	<input type="checkbox"/>	<input type="checkbox"/>
3. My teenager is well behaved in our discussions about his/her CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
4. For the most part, my teenager likes to talk to me about his/her CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
5. We almost never seem to agree about how to manage his/her CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
6. My teenager usually listens to what I tell him/her.	<input type="checkbox"/>	<input type="checkbox"/>
7. At least three times a week, we get angry at each other about his/her CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
8. My teenager says that I have no consideration of his/her feelings.	<input type="checkbox"/>	<input type="checkbox"/>
9. My teenager and I compromise during arguments about his/her CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
10. My teenager often doesn’t do what I ask.	<input type="checkbox"/>	<input type="checkbox"/>
11. The talks we have about his/her CF treatments are frustrating.	<input type="checkbox"/>	<input type="checkbox"/>
12. My teenager often seems angry at me.	<input type="checkbox"/>	<input type="checkbox"/>
13. My teenager acts impatient when I talk.	<input type="checkbox"/>	<input type="checkbox"/>
14. In general, I don’t think we get along very well.	<input type="checkbox"/>	<input type="checkbox"/>
15. My teenager almost never understands my side of an argument about his/her CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
16. My teenager and I have big arguments about little things.	<input type="checkbox"/>	<input type="checkbox"/>
17. My teenager is defensive when I talk to him/her about his/her CF treatments.	<input type="checkbox"/>	<input type="checkbox"/>
18. My teenager thinks my opinions don’t count.	<input type="checkbox"/>	<input type="checkbox"/>
19. We argue about a lot of rules.	<input type="checkbox"/>	<input type="checkbox"/>
20. My teenager tells me she/he thinks I am unfair.	<input type="checkbox"/>	<input type="checkbox"/>