Caregiver Personality Effect on Health Status and Adherence in Children With Cystic Fibrosis

Caregiver Personality Effect on Health Status and Adherence in Children With Cystic Fibrosis

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Abstract

Although there have been multiple studies that have assessed the effect of individual personality on health outcomes and adherence to prescribed treatment, few studies have examined the impact of a caregiver personality on health outcomes, and adherence for their child with a chronic disease. This study investigated the relationship between a caregiver's personality type and its effect on two key health status measures and treatment adherence measured for a child with cystic fibrosis (CF) by examining (i) caregiver personality type, based on the NEO-FFI-3 (Neuroticism, Extraversion, Openness, Agreeableness, and Conscientiousness Five Factor Inventory), and its relationship to their child's body mass index percentile (BMI%) and percent predicted forced expiratory volume in one second (FEV_1% predicted) (ii) caregivers' personality type and its relationship to adherence to prescribed daily treatment regiments. It was hypothesized that caregivers who score higher for neuroticism would have children with lower FEV_1% predicted, BMI%, and adherence scores, while parents who score higher for conscientiousness would have children with higher FEV_1% predicted, BMI%, and adherence scores.

Participants were recruited after conducting a medical chart review of children that were followed at Boston Children Hospital's (BCH) CF Center. Caregivers of the children that met the inclusion criteria were asked to complete the self-report NEO-FFI-3 and the TAQ- CF (Treatment Adherence Questionnaire – Cystic Fibrosis) during a scheduled clinical visit. A total of 29 participants completed both questionnaires. The results showed no significant relationship between caregiver personality type and FEV_1%

predicted, BMI%, and adherence to prescribed treatment for the child. The results indicated that there was no significant relationship between caregiver personality trait and health outcomes for children with CF. Further study using a larger sample size across multiple CF centers would be beneficial to elaborate on our findings.

Dedication

I dedicate this thesis to my wife Devika, my children Jeevan and Darshan, my parents, and in-laws whom all have supported me in this important educational journey.

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Without the strong guidance from Dr. Greg Sawicki, Dr. Devika Rao, Jonathan Greenberg, Emma McWilliams, Dr. Dante Spetter, and Chuck Houston, this work would not have been possible. I offer them my deepest gratitude and thanks.

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Chapter I

Introduction

Cystic fibrosis (CF) is an autosomal recessive disease that is caused by a mutation of the cystic fibrosis transmembrane conductance protein regulator (CFTR) gene on the long arm of chromosome 7. Mutations in the CFTR protein cause normally thin airway surface liquid to thicken leading to chronically inflamed and obstructed airways prone to chronic bacterial infection. This mutation also impairs the pancreas's ability to release key digestive enzymes needed to break down food and absorb vital nutrients (What is cystic fibrosis, n.d.). Thus, dysfunction of CFTR leads to abnormalities of the respiratory tract, gastrointestinal tract, sweat glands, and reproductive tract (Schechter & O'Sullivan, 2011). The largest population of individuals with CF are Caucasian, but Asian, African-American, and Hispanic individuals can be affected as well. According to the Cystic Fibrosis Foundation, there are more than 29,000 people with cystic fibrosis living in the United States.

Signs and symptoms of cystic fibrosis include pulmonary manifestations such as chronic cough and lung infection, gastrointestinal manifestations such as fatty stools, constipation and poor weight gain (Spoonhower & Davis, 2016). The two most common primary health outcome measures used by clinicians are lung function as measured by the percent predicted forced expiratory volume in 1 second (FEV_1% predicted) and nutritional status as measured by BMI percentile (BMI%; Callaghan, et al., 2005; Com, et al, 2014; Hulzebos et al., 2014; Kulich et al., 2005; van der Spuy et al., 2011; Wiedemann et al., 2007). FEV_1% predicted is a clinical assessment of disease

progression based on lung function. Test results are typically presented as a percent of predicted level based on age, gender, height and race. Individuals who have an FEV_1% predicted ≥ 70% are considered to have mild CF lung disease. Individuals who have FEV_1% predicted between 40% and 69% are considered have moderate lung disease and once below 40% are considered to have severe lung disease (Cystic Fibrosis Foundation [CFF], 2016).

Similar to lung function, nutritional status is also a key measure used by clinicians to understand overall health. For children with CF, maintaining a BMI% at the 50th percentile or greater is recommended because a lower percentile is associated with an increased frequency of pulmonary exacerbations and more rapid decline in lung function. Children with a BMI% less than the 25th percentile are considered nutritionally at risk and a child with a BMI% less than the 10th percentile is considered to be in nutritional failure (Bowser & Wagner, 2011; CFF, 2016).

Treatment

People with CF are at an increased risk of malnutrition, (Stallings, Stark, Robinson, Feranchak, & Quinton, 2008) which is associated with accelerated lung disease progression. Consequently, children with CF must adhere to a strict treatment regimen (Lai, Shoff, & Farrell, 2009; van der Spuy, Cader, van der Spuy & Westwood, 2011; Woestenenk, Stellato, Terheggen-Largo, van der Ent, Houwen, 2014). Commonly prescribed treatments for individuals with CF include inhalation of steroids and antibiotics, aerosols to thin and clear mucus, oral intake of pancreatic enzymes to help break down fats, chest physiotherapy, increased consumption of calories to maintain BMI, vitamins, supplements, and oral antibiotics. The high treatment burden is thought

to contribute to low adherence rates in patients with CF. Even with advances in care, which have resulted in improved survival, treatment regimens have become increasingly complex and time intensive, thereby decreasing the likelihood of complete adherence (Sawicki, Heller, Demars, & Robinson, 2015, Sawicki et al., 2013).

Life Expectancy and Effects of Non-adherence

The life expectancy for individuals with CF has steadily increased over the last several decades and evidence shows that early detection of CF using newborn screening and prior to onset of CF symptoms increases the likelihood of better nutritional status and lung function. In the United States, 52.7% of people with CF are under 18 years of age, and the curve has remained skewed toward the pediatric population despite gains in survival. The median predicted survival is approaching 40 years of age, although the primary cause of death is cardiorespiratory complications, and the median age at death is 29.6 years, indicating that there is significant morbidity and mortality in even very young patients (CFF, 2016).

A possible predictor of positive health outcomes in cystic fibrosis is adherence to clinician recommended treatment (CFF, 2016; Borowitz, et al., 2009). Several studies have shown that nonadherence to clinician recommended treatment has deleterious effects on health and quality of life and can lead to increased pulmonary exacerbations (Com et. al, 2014; Eakin, Bilderback, Boyle, Mogayzel, & Riekert, 2011; Sawyer & Aroni, 2003), lower than predicted FEV_1% predicted and BMI% scores, and increased use of health care resources (Hommel & McGrady, 2013). Eakin, Bilderback, Boyle, Mogayzel, & Riekert (2011) conducted a longitudinal retrospective review of medication adherence and is relationship to the frequency of antibiotics to treat pulmonary

exacerbations and change in FEV_1% predicted over a 12-month period for individuals with CF (ages ≥7). Results indicated that participants on average had poor adherence to all pulmonary medications and individuals that were less adherent very more likely to experience a pulmonary exacerbation.

Adherence to CF Treatment

Adherence to medical treatment has been defined as the active, voluntary, and collaborative involvement of the patient in a mutually acceptable course of behavior to produce a therapeutic result (Meichenbaum, 1987). It is estimated that approximately 50% of individuals with chronic diseases are adherent to prescribed treatment with lower rates of adherence seen in developing countries (WHO, 2003). Multiple factors have been shown to affect adherence across disease populations including socioeconomic status (SES), and parental involvement and monitoring (Rapoff, 2010). Higher SES has been shown to be associated to increased adherence and better health outcomes in children with CF (Oates, Stepanikova, Gamble, Gutierrez, & Harris, 2015; Schechter, Shelton, Margolis, & Fitzsimmons, 2001). However, regardless of SES, parents who are more involved in treatment regimens have children who are more adherent (Butcher & Nasr, 2014; Modi, Marciel, Slater, Drotar, & Quittner, 2008).

Methods to measure adherence include clinician ratings, validated questionnaires, patient diaries, structured interviews, electronic monitoring and biochemical assays. The Treatment Adherence Questionnaire-Revised (TAQ-CF) is a questionnaire that has been specifically designed to measure adherence behavior of individuals with CF and can be administered to parents of preadolescent children. The TAQ-CF is a well-established method to measure adherence in CF patients and has shown strong test-retest reliability

(Quittner, Espelage, Ievers-Landis, & Drotar, 2000; Quittner, Modi, Lemanek, Ievers-Landis, & Rapoff, 2008; Dziuban, Saab-Abazeed, Chaudry, Streetman, & Nasr, 2010).

Adherence to recommended treatment in the CF population remains relatively high for children then decreases from adolescences into adulthood. Although adherence is often suboptimal amongst the broader population of individuals with CF, in younger children it is higher. The drop in adherence rates happens generally in the transition from childhood to adolescence, and is likely due to parental involvement in the early stages (Leeman, Sandelowski, Havill, & Knafl, 2015). As children move into adolescence, they become more independent and are made responsible for their own treatment regimens. In a retrospective analysis of medication adherence and health outcomes as measured by BMI% and FEV_1% predicted, Shakkottai, Kidwell, Townsend and Nasr (2015) studied children between 0-21 years of age. Adherence to medication usage was highest amongst children in the 0-5 age range, followed by the 6-12 age range. It was lowest amongst adolescents, and pre-adolescent children had higher overall BMI% and FEV_1% predicted scores than adolescents. The primary conclusion of these findings was that children in the 0-12 age range were still supervised and guided by parents to adhere to the prescribed treatment. These findings were corroborated by Butcher and Nasr (2015) in a study that found parental presence, positive attention and direct instruction were significantly associated with higher treatment adherence amongst children between 6-12 years of age. It is well established that parental involvement in prescribed treatment seems to have a positive effect on adherence rates amongst children with chronic diseases (Leeman et al., 2015; O'Hara & Holmbeck, 2013). Even when researchers controlled for factors such as the complexity of treatment, and barriers to treatment amongst children and adolescents with CF, parental involvement has remained an important predictor of better adherence

rates (Arias-Lorente, Bousono-Garcia, & Diaz-Martin, 2008). Rapoff (2010) suggests that parental monitoring and involvement of treatment regimens is fundamental in increasing adherence rates amongst children and adolescents.

Several studies also have examined caregiver psychosocial factors such as depression, anxiety, and stress and the effect on adherence, health status, and quality life assessment within the CF population but no study has looked at caregiver personality as determinant of health status. Besier and Goldbeck (2011) examined the anxiety and depression in adolescents (age 12-17 years) with CF and their caregivers. An important study hypothesis was that lung function would be lower in dyads reporting high levels of psychological symptoms than in psychologically unaffected dyads. The results indicated that there was no significant association between psychological symptoms affecting the adolescent-caregiver dyads and lung function as measured by FEV_1% predicted. When screening for symptoms of depression and anxiety amongst adolescents with CF and caregivers, Modi et al. (2011) found low rates of depressive symptoms in adolescents but high-levels of anxiety. However, caregivers of adolescents with CF had clinically elevated levels of depressive and anxiety symptoms. Low levels of depression and moderate levels of anxiety have also been reported for children between 7 and 14 years of age (Bregnballe, Thatsum, & Schiotz, 2006).

Overall, better adherence is related to better outcomes in CF, and prior to reaching adolescence and adulthood, parents are likely the key drivers for treatment adherence in children (Modi, et. al, 2008, Zindani, Streetman, Streetman, & Nasr, 2006). Because parents play a critical role in their children's treatment regimen, it is important to investigate factors that predict treatment adherence and treatment outcomes.

Studies in the adult population have shown that the personality traits of neuroticism and conscientiousness are associated to adherence to antibiotic usage, renal dialysis adherence and nebulizer usage within that same individual (Axelsson, 2013; Axelsson et.al, 2009; Christensen, & Smith, 1995). Understanding a link between parental personality traits and treatment adherence would allow physicians the ability to predict which patients are at risk for poor adherence.

Personality and Health Outcomes

In the adult population, one enduring factor shown to be related to an individual's health across a lifespan is personality (Aldwin, Spiro, Levenson, & Cupertino, 2001). Amongst adults with chronic diseases, personality traits have been implicated in adherence to recommended treatment, perceptions of health, and quality of life (Bruce, Hancock, Arnett, & Lynch, 2010; Goodwin & Engstrom, 2002; Yamada et. al, 2012).

Personality refers to our individual differences in how we think, feel, and behave (APA, n.d.). However, there are multiple methods and theories to classify and conceptualize personality. The Five Factor Model (FFM) is one theory that places special emphasis on natural language and how individuals describe themselves and others (John, Robins, & Pervin, 2008; McCrae & Costa, 2006; Hoffstee, Kiers, De Raad, Goldberg, Ostendorf, 1997). It organizes personality traits into five broad dimensions: neuroticisms, extraversion, openness to experience, conscientiousness, and agreeableness (McCrae & John, 1992). There are a multiplicity of questionnaires to assess personality traits, but the Neuroticism, Extraversion, Openness Five-Factor Inventory (NEO-FFI) developed by Costa and McCrae has been used in a number of studies regarding

personality traits and its relationship to health outcome measures and adherence behavior (Yamada et. al, 2012; Marsh et. al, 2010). Overall, the NEO questionnaires represent one of the best-validated measures for the big five personality traits (McCrae & Costa, 2006). Each personality trait has a broad definition and the questionnaire categorizes an individual's traits based on their response to the self-report NEO-FFI.

Neuroticism is defined as negative emotionality, or more simply, feeling anxious, nervous, sad, and tense. Behavioral manifestation includes difficulty coping and poor reaction to illness. Conscientiousness is defined as having strong impulse control, being goal-directed, organized, planned, prioritizing tasks, and thinking prior to taking action. Behavior manifestation includes arriving early to appointments, to scheduled events in general and adhering to medical treatment, (John, Robins, & Pervin, 2008).

Several studies have established that neuroticism and conscientiousness can be predictors of adherence behavior and overall health status for people with chronic diseases. In a large random sample epidemiological study that included individuals with a diagnosed chronic disease, Axelsson, Brink, Lundgren and Lotvall (2011) found that neuroticism was inversely related to medication adherence, while conscientiousness was positively related to medical adherence for adults. Wheeler, Wagaman and McCord (2012) compared how personality traits are related to adherence behavior in adolescents with type 1 diabetes. High conscientiousness scores were associated with higher self-reported adherence and high neuroticism scores were associated with lower self-reported adherence. Isolation of the conscientiousness personality trait in a study of adults that required renal dialysis found individuals who score high on conscientiousness were more adherent with treatment. A strength of study this was the use of biological markers,

serum potassium and phosphorus levels rather than patient self-report to measure adherence to dietary restrictions and medication intake (Christensen & Smith,1995).

In one of the few long-term studies, adherence rates to medications were shown to be related to both neuroticism and conscientiousness. This study was a six-year randomized placebo-controlled trial of 771 subjects over the age of 72 in which Jerant, Chapman, Duberstein, Robins and Frank (2011) compared medication non-adherence to personality traits as measured by the NEO-FFI. Study participants were randomized to use of ginkgo balboa or placebo. All participants completed the NEO-FFI and adherence was measured using pill counts at each 6-month follow-up until study completion. The data analysis revealed with every 1 standard deviation increase in neuroticism measure, that there was a 6.4% increase in non-adherence. Similarly, higher scores for neuroticism were in seen in those with decreased adherence with regards to short term antibiotic use (Axelsson, 2013). Overall, studies of personality and CF are lacking in the present literature.

CF, Adherence and Personality

In people with CF, Zindani, Streetman, Streetman, and Nasr (2006) studied adherence to dornase alpha, an inhaled mucolytic, and an oral multivitamin in children with CF. There were 44 participants in the study, including 22 children under 12 years of age and 22 adolescents 12 years of age and older. The results showed that younger children had higher rates of adherence and higher FEV_1% predicted scores indicative of mild lung disease. The researchers concluded parental supervision was likely a contributing factor for the higher reported adherence rates in the younger children, even though this was not verified empirically. Also, the higher FEV% predicted scores for the

younger children could be due to the level of disease progression. Similar results were seen when Modi et. al (2008) studied preadolescent and adolescent children. Their study demonstrated that children were more adherent to treatment when supervised by parents. In the pediatric CF population, researchers have studied all facets of how parents affect adherence to treatment including parental depression, supervision, routines, and behaviorally-based group parent-training intervention (Happ, Hoffman, DiVrgillo, Higgins, Orenstein, 2013; Modi et. al, 2008; Modi, Driscoll, Montag-Leifling, & Acton, 2011; Sheehan, Hiscock, Massie, Jaffe, & Hay, 2014).

Study Aims and Hypothesis

This study aimed to examine associations between personality, health outcomes, and self-reported adherence.

Aim 1

The primary aim of this study was to understand the association between specific personality traits found in the parents/primary caregivers of children with CF and lung function (measured by FEV_1% predicted) and nutritional status (measured as BMI%) in their child. Specifically, is there a relationship between a caregiver's personality traits of neuroticism and conscientiousness and the child's FEV_1% predicted and BMI% in the setting of childhood cystic fibrosis? It was hypothesized that caregivers who score higher for neuroticism will have children with lower FEV_1% predicted and BMI% and caregivers that scored higher for conscientiousness would have children with higher FEV_1% predicted and BMI%. As characteristics of neuroticism trait include fear, embarrassment, anger, guilt, disgust, feeling anxious, nervous, sad and tense versus

characteristics of the conscientiousness trait include task and goal-directed behavior, thinking before acting, delaying gratification, following rules, planning, organizing and prioritizing tasks (McCrae & Costa, 2010; John, & Srivastava, 1999).

Aim 2

The secondary aim of this study is to characterize the association between adherence to prescribed treatment and personality traits of the parents/primary caregivers of children with CF. It was hypothesized that caregivers who score higher for neuroticism will have children that were less adherent and caregivers that scored higher for conscientiousness would have children that were more adherent

To date, no studies have evaluated the relationship between a caregiver's personality has on a child's adherence and health outcome. The literature suggests that there is a negative relationship between highly neurotic individuals and adherence behavior and a positive relationship between highly conscientious individuals and adherence behavior (Axelsson, Brink, Lundgren, & Lötvall, 2011). Studying this relationship further in CF is important because if improved adherence predicts better health outcomes, and if personality is related to adherence, clinicians may be able to target high risk families for more specific interventions and may be able to improve health outcomes.

Chapter II

Method

The study was conducted at Boston Children's Hospital (BCH) Cystic Fibrosis Center in Boston, Massachusetts. All components of the study were created in the BCH REDCap (Research Electronic Data Capture; Harris, et al., 2009) application, which included the consent to participate, the NEO-FFI-3 and the TAQ-CF. The target sample was 50 participants who met the inclusion criteria. When participants met the inclusion criteria and had a routine clinical follow-up during the data collection period of this study, they were asked to participate. Once the consent to participate and all questionnaires were completed, the participant would be given a ten-dollar Target gift card.

Participants

The inclusion criteria for this study followed a two-step process. Step one was to conduct a medical chart review to find children that met the following criteria: between 6 and 12 years of age, had 4 or more documented visits to the BCH CF center and had a scheduled appointment during the data collection period. Exclusion criteria included whole organ transplantation, foster care status, and having an open case with child protective services. Caregivers of children that met the inclusion criteria were asked to participate in the study during a scheduled clinical visit at the BCH CF center. In clinic, a research assistant provided a brief synopsis and goals of the study. Caregiver's who

agreed to participate were given an iPad to provide consent, complete the NEO-FFI-3 and the TAQ-CF within the REDCap application. Once complete, they were given a Target gift card for 10 dollars. Further medical chart review was conducted on participants. The following medical chart data was collected for each child: parental gender, child's gender, FEV_1% predicted, BMI%, and prescribed treatment for airway clearance, aerosols to thin mucus, and pancreatic enzymes. All data was de-identified. Only BCH staff involved in the study had access to the confidential data. One participant who completed both questionnaires was excluded from the study upon further review of their child's medical chart, as they did not have an established CF diagnosis.

A total of 29 caregivers (of 39 approached) completed the study during the data collection period. Based on the inclusion criteria, 28 children and 28 caregivers were included in the study.

Measures

Several measures were included in this study to understand personality type, adherence, lung function, and nutritional status. Personality and adherence were measured using self-report questionnaires. Both lung function and nutritional status were derived from medical charts for each child included in the study protocol.

Personality Assessment

Personality Type: The NEO-FFI is a personality index that can be administered as a self-report or as an interview. The NEO-FFI measures the five broad domains of personality, proposed by the Five Factor Model of personality. Based on responses to 60 questions within a personality domain (Neuroticism, Extraversion, Openness to

Experience, Agreeableness and Conscientiousness), an individual's personality traits are determined (Costa, & McCrae, 1992). The NEO-FFI-3 is the second revised version of the NEO-FFI and is the current recommended version (McCrae & Costa, 2010). Once completed, the NEO-FFI-3 is scored for each domain, and the domain score is then compared to a t-score table. Based on the t-score and individual fits in the following categories of each respective domain; very low, low, average, high, and very high (McCrae & Costa, 2010). For the current study only the Neuroticism and Conscientious domains were scored for statistical analysis to test the validity of the primary hypothesis.

Adherence

Treatment Adherence: The TAQ-CF consists of 12 domains of common treatment regimens prescribed to individuals with CF. Respondents answer how often they have done a recommended treatment over the last week. The 6-point Likert scale asks how often a particular treatment regimen was completed, and the respondent can answer "not all" to "3 or more times daily". The measure takes approximately 5 to 15 minutes (Quittner, Modi, Lemanek, Ivers-Landis, Rapoff, 2008). The TAQ-CF covers a broad set of treatment regimens prescribed to individuals with CF. Based on disease specific characteristics, a subset of the treatment regimens may be prescribed. For this study three treatment regimens were measured for adherence; airway clearance, aerosols to thin mucus, and pancreatic enzymes. Children were classified as adherent, non-adherent, or not prescribed, based on the responses of the TAQ-CF. On the TAQ-CF if caregivers selected one of the following; "occasionally", "three-times a week", "once a day", "3 or more times a day", their child was classified as adherent for the respective treatment. If parents selected one of the following; "not at all" or "does not apply to me" on the TAQ-

CF, their child was classified as non-adherent or not prescribed. Medical chart review indicated which treatments each child was prescribed.

Health Indicators

Lung Function: The FEV_1% predicted is measured after the maximum inhalation of air is taken into the lungs and forcefully exhaled with the mouth tightly closed around a mouth piece and with the nose breathing ceased with nose clips. Subjects exhale until no further volume can be exhaled. The volume exhaled in the first second of this maneuver is the FEV_1% predicted (Blaisdell, 2011). Test results from the FEV_1 predicted are presented as percent predicted based on the child's age, height, sex, and race. For each enrolled participant, the highest FEV_1% predicted for the year 2016 was used in the final analysis as a baseline measure.

Nutritional Status:

BMI is the weight in kilograms over the height in meters squared (weight in kg/ [height in m2]) and is the overall assessment of a child's weight for their height (Bowser & Wagner, 2011). The Centers for Disease Control (CDC) recommends that BMI scores be expressed relative to other children of the same sex and age, based on national survey data collected in the United States (CDC, 2015). BMI% is commonly used to assesses the overall health status of individual with CF (Hulzebos et al., 2014). The highest BMI% for 2016 was used to understand the overall health status of enrolled participants.

Procedure

The study was divided into several processes; Intuitional Review Board (IRB), recruitment, REDCap, data collection and medical chart review, scoring and data analysis.

IRB Process

Initially an IRB application was submitted to the Harvard IRB, to allow for cede agreements with the respective CF centers. Upon further analysis of the study and that the investigator did not have an official affiliation with either institution, the Harvard IRB indicated that the that separate IRB submissions were needed. In order to move forward with the study protocol in the time allotted, the decision was made to submit an IRB application to the BCH IRB. After the study protocol was approved by the BCH IRB the next steps were to review medical charts for recruitment and to create the NEO-FFI-3, the TAQ-CF, and consent to participate within the REDCap web application.

Recruitment

An initial medical chart review was conducted on all patients on November 14th, 2017 that were followed at the BCH CF center and met the inclusion criteria. Caregivers of any child that met the inclusion criteria and had a scheduled appointment between November 15th, 2017 and January 31st, 2018 were asked to participate. Conducting a medical chart review prior to enrolling participant was necessary to ensure they met the inclusion criteria for the study and provided a method to screen out a large number of individuals that have CF like diseases. Of all possible participants, ten individuals declined to participate in the study.

REDCap

REDCap is a commonly used (Health Insurance Portability and Accountability Act of 1996) HIPPA secure web application used to build and manage online surveys, questionnaires, and databases. The REDCap application provides an intuitive interface, audit trails, and data downloads (Harris, et al., 2009), therefore it was an excellent platform to have a smooth process to consent to participate and for administration of questionnaires. Both the NEO-FFI-3 and the TAQ-CF were created within the REDCap application once copyright permission was obtained.

Data Collection and Medical Chart Review

Participants (in clinic) were handed an iPad with the REDCap application open for this study. All participants were asked to provide consent, once consent participants were led through the questions for the NEO-FFI-3 and the TAQ-CF for approximately 15 minutes. Each participant was given a Study Identification (ID). The Study ID corresponded to a separate spreadsheet that contained personal information, which was managed by an internal BCH Team approved by the BCH IRB. Further medical chart review was conducted on participant's gender and their child's age, gender, BMI%, FEV1% predicted and prescribed treatment pertinent for this study. This data then was uploaded into the REDCap application for the corresponding Study ID.

Scoring

All raw data was exported from the REDCap application, imported into and scored within the Microsoft Excel application than exported to SPSS version 24. For the NEO-FFI-3, answers were tabulated according to the questionnaire instructions and raw

scores were obtained for each of the 5 domains. Domain raw scores range ≥ 1 and ≤ 37. Domain raw scores for Neuroticism and Conscientiousness, pertinent for this study, were used to derive gender based t-scores (provided for the NEO-FFI-3) and assigned a value of very low, low, average, high and very high for the total domain score (McCrae, & Costa, 2010).

Non responses to any questions on the NEO-FFI-3 were coded as neutral, as per the guidance of the test creators (McCrae, & Costa, 2010). One participant of all 28 did not answer one question on the NEO-FFI-3, which was coded neutral.

Responses for the TAQ-CF, were scored as adherent, non-adherent, or not prescribed for airway clearance, aerosols to thin mucus, and pancreatic enzyme usage. The TAQ-CF was scored using the criteria as outlined in the measures section of this paper.

Data Analysis

In order to understand if the primary and secondary hypothesis proved valid, data analysis was conducted separately for each. Due to the limited sample size, key trends were also analyzed to understand if further research or extending the study would elicit different results. All data was loaded and analyzed using SPSS version 24 licensed to Harvard University.

Aim 1

To examine whether the personality traits of neuroticism or conscientiousness were associated with the child's lung function (FEV_1% predicted), or nutritional status (BMI%), a two-way ANOVA were conducted, one for each of the dependent variables.

The two-way ANOVA evaluates the association of two different categorical on one continuous dependent variable. Upon further review of the ANOVA results, a Spearman's rank order was conducted between the conscientiousness personality trait and BMI%.

Aim 2

To examine if the personality trait of neuroticism or conscientiousness was associated with adherence, a Pearson's chi-square test was conducted.

Aim 3

To examine whether treatment adherence is associated with lung function and nutritional status, an independent sample T-Test was conducted.

Chapter III

Results

At the conclusion of the data collection period, the final sample size included in this study protocol was 28 individuals from a total of 29 originally enrolled. Demographic data are shown in Table 1. There was an equal number of female (n = 14) and male (n = 14) children who were included in the analytic cohort. There were 28 total caregivers who completed all components of the study (one per child). The breakdown of caregivers was 19 females (67.9%) and 9 males (32.1%). The mean age of the children enrolled was 9.39 (SD = 2.10).

Table 1
Participant Demographic Data

Variables		*n*	Percent
Child Gender	Male	14	50.0
	Female	14	50.0
	Total	28	100.0
Caregiver Gender	Male	9	32.1
	Female	19	67.9
	Total (*N*)	28	100.0

In the current study only one caregiver was asked to participate during a scheduled interview. However, it is interesting to note that the number of female caregivers is two times the number of male caregivers.

Table 2
Descriptive Statistics of Variables Included in Study

	N=(28)	Minimum	Maximum	*M*	*SD*
Child Age		6	12	9.39	2.06
Neuroticism Raw Score		3.00	31.00	18.43	8.74
Neuroticism t-score		27	65	46.00	11.55
Conscientiousness Raw Score		22.00	44.00	35.64	5.39
Conscientiousness t-score		33.00	67.00	54.68	8.41
BMI%		13.21	99.50	68.13	27.21
FEV_1% predicted		78.00	134.00	104.00	11.27

Two personality domains were scored; raw scores for each participant were compared to t-scores for the NEO-FFI-3 (McCrae & Costa, 2010) to understand how strongly a participant possessed the personality trait of Neuroticism or Conscientiousness. The t-scores for Neuroticism (M = 46, SD = 11.55) and Conscientiousness (M = 54, SD = 8.41) corresponded to the following ordinal variables (very low, low, average, high, and very high).

Table 3
Caregiver Neuroticism Profiles

Neuroticism Category	t-score Range	Caregiver Gender		
		Male	Female	Total
Very Low	≥25-34	2	4	6
Low	35-44	1	6	7
Average	45-55	2	5	7
High	56-65	4	4	8
Total		9	19	28

Based on the NEO-FFI-3 responses and t-score analysis none of the caregivers were categorized as very high for the neuroticism trait.

Table 4
Caregiver Conscientiousness Profiles

Conscientiousness Category	t-score Range	Caregiver Gender		
		Male	Female	Total
Very Low	≥25-34	1	0	1
Low	35-44	0	2	2
Average	45-55	4	7	11
High	56-65	3	9	12
Very High	65-≥75	1	1	2
Total		9	19	28

Only 3 caregivers were in the very low to low category for the conscientiousness trait. Most of the caregivers (n = 23) were average to high category for conscientiousness trait.

A test of normality was conducted on the interval/ratio variables in this protocol to understand if the sample size was normally distributed. Due to the small sample size the Shapiro-Wilks (SW) test for normality was used to examine if the variables in the study were normally distributed. Variables that have p-values above 0.05 are considered normally distributed. The SW test for normality indicated that the age of the child (p = .012) and BMI% (p = .017*)* were not normally distributed. Further examination of the histogram and Q-Q plot for BMI% demonstrated that BMI% was approximately normally

distributed. The FEV_1% predicted (p = .775), t-scores for neuroticism (p = .155), and t-scores for conscientiousness (p = .127), were normally distributed.

Table 5
Test for Normality for Interval/Ratio Variables

	Shapiro-Wilk		
	Statistic	*df*	*p*
Child Age	.901	28	.012
Neuroticism t-score	.946	28	.155
Conscientiousness t-Score	.942	28	.127
FEV_1% Predicted	.977	28	.775
BMI%	.907	28	.017

Adherence behavior for children was measured for airway clearance, usage of aerosols to thin mucus (pulmozyme) and usage of pancreatic enzymes (Creon or Ultrase). All parents of children prescribed airway clearance (n = 27) and pancreatic enzymes (n = 26) reported 100% adherence on the TAQ-CF questionnaire. Regarding adherence to aerosols to thin mucus, only 3 parents of children of the 24 reported non-adherence on the TAQ-CF.

Table 6
Adherence to Airway Clearance

	n	Percent	Valid Percent	Cumulative Percent
Adherent	27	96.4	100.0	100.0
Not-Prescribed	1	3.6		
Total(*N*)	28	100.0		

Twenty-seven of the 28 children included in the study were prescribed airway clearance. Overall the results indicated that adherence to airway clearance was very high for the current cohort.

Table 7
Adherence to Pancreatic Enzyme Usage

	n	Percent	Valid Percent	Cumulative Percent
Adherent	26	92.9	100.0	100.0
Not-Prescribed	2	7.1		
Total (*N*)	28	100.0		

Results for adherence to pancreatic enzyme usage was also very high for the current cohort.

Table 8
Adherence to Aerosol Usage

	n	Percent	Valid Percent	Cumulative Percent
Non-Adherent	3	10.7	12.5	12.5
Adherent	21	75.0	87.5	100.0
Total	24	85.7	100.0	
Not-Prescribed	4	14.3		
Total (*N*)	28	100.0		

Personality and Health Outcomes

The primary aim of this study was to determine if caregiver personality traits were associated with FEV_1% predicted, BMI% and adherence behavior. A one-way ANOVA

was used to determine if a significant effect could be observed for each of the independent variables. It was hypothesized that the mean FEV_1% predicted, or BMI% would be different for at least one level of personality trait. Tables 9 and 10 summarize the ANOVA results both personality traits and their effect on FEV_1% predicted, and BMI% health indicators, respectively. There was no significant association between neuroticism and FEV_1% predicted, ($F(3,24) = 0.134$, $p = .939$) or BMI% ($F(3,24) = 0.077$, $p = .972$).

Table 9
Effect of Neuroticism on Health Indicators

		df	*F*	*p*
FEV_1% predicted	Between Groups	3	.134	.939
	Within Groups	24		
	Total	27		
BMI%	Between Groups	3	.077	.972
	Within Groups	24		
	Total	27		

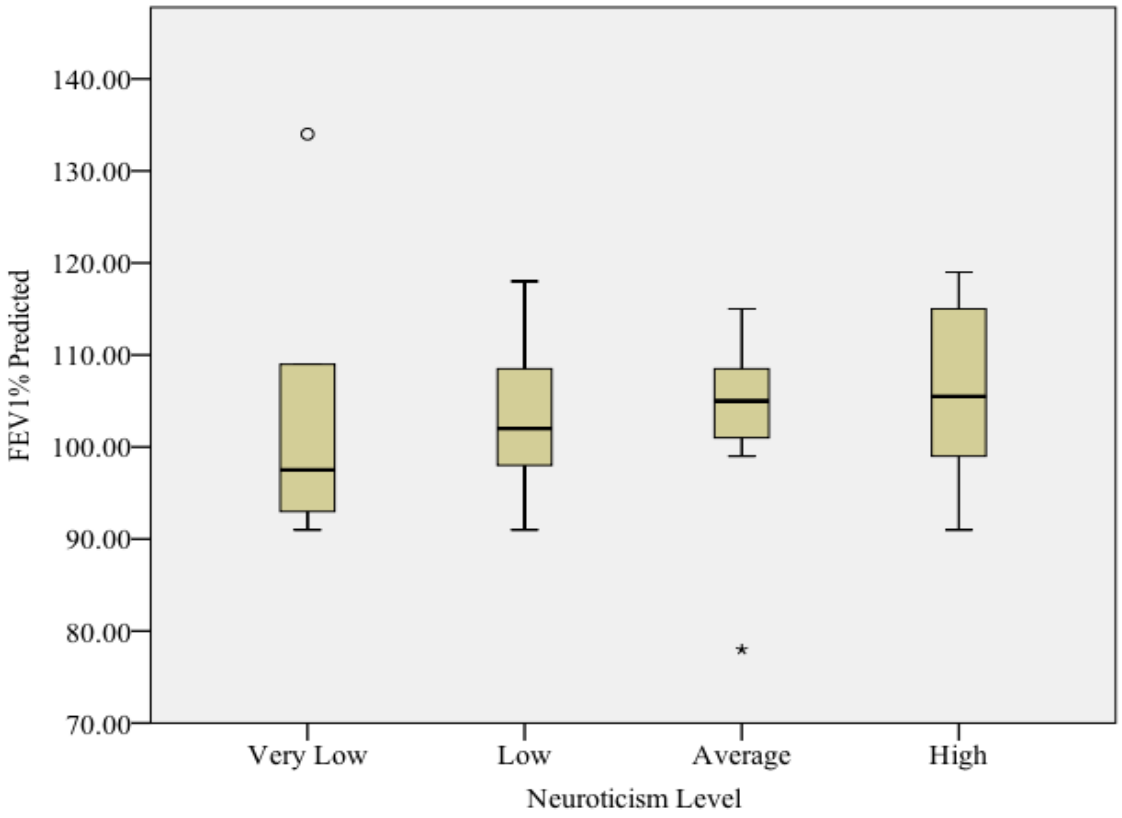

Figure 1. Boxplot for FEV_1% predicted by. caregiver neuroticism level.

Although, FEV_1% predicted mean values for each level of neuroticism were above 100%, within each neuroticism level there were children that had FEV_1% predicted scores lower than 100%. For example, one child had a FEV% predicted score of 78%, whose caregiver exhibited an average level of neuroticism. Further review of the dataset revealed all children that had caregivers that exhibited either high or low levels of neuroticism had FEV_1% predicted scores above 90%. Overall, for the primary hypothesis to be valid, caregivers that exhibited high levels of neuroticism were expected to have children with lower FEV_1% predicted scores.

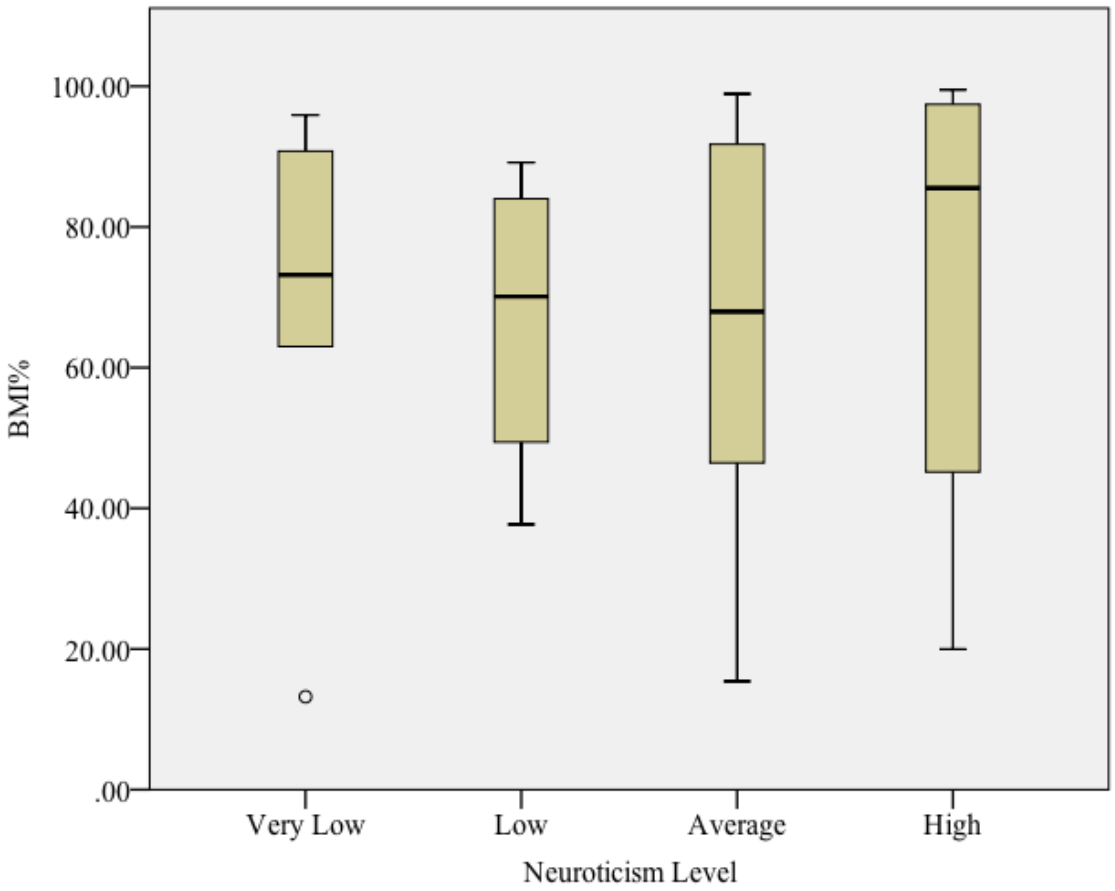

Figure 2. Boxplot for BMI% by caregiver neuroticism level.

The mean BMI% results appeared to follow the same trend as the FEV_1% predicted findings for each level of neuroticism. Caregivers that exhibited high levels of neuroticism had children with BMI% that ranged from 20% to 99% but 5 of the 8 children with caregivers at this level had a mean BMI% of 93%. When reviewing the results for caregivers that exhibited average levels of neuroticism, BMI% ranged from 15% to 99%. Overall, for the primary hypothesis to be valid, caregivers that exhibited high levels of neuroticism were expected to have children with lower BMI% scores.

The personality trait of conscientiousness was not significantly associated with FEV_1% predicted ($F(4,23) = 0.433$, $p = .783$) or BMI% ($F(4,23) = 1.638$, $p = .199$).

Table 10
Effect of Conscientiousness on Health Indicators

		df	*F*	*P*
FEV_1% predicted	Between Groups	4	.433	.783
	Within Groups	23		
	Total	27		
BMI%	Between Groups	4	1.638	.199
	Within Groups	23		
	Total	27		

Only one caregiver exhibited very low level of conscientiousness, whose child had a FEV_1% predicted score of 100%. The largest number of caregivers exhibited an average ($n = 11$) or high ($n = 12$) level of conscientiousness. Caregivers that exhibited high levels of conscientiousness had children with FEV_1% predicted scores that ranged from 78% to 134%. Overall, for the primary hypothesis to be valid, caregivers that exhibited high levels of conscientiousness were expected to have children with higher FEV_1% predicted scores.

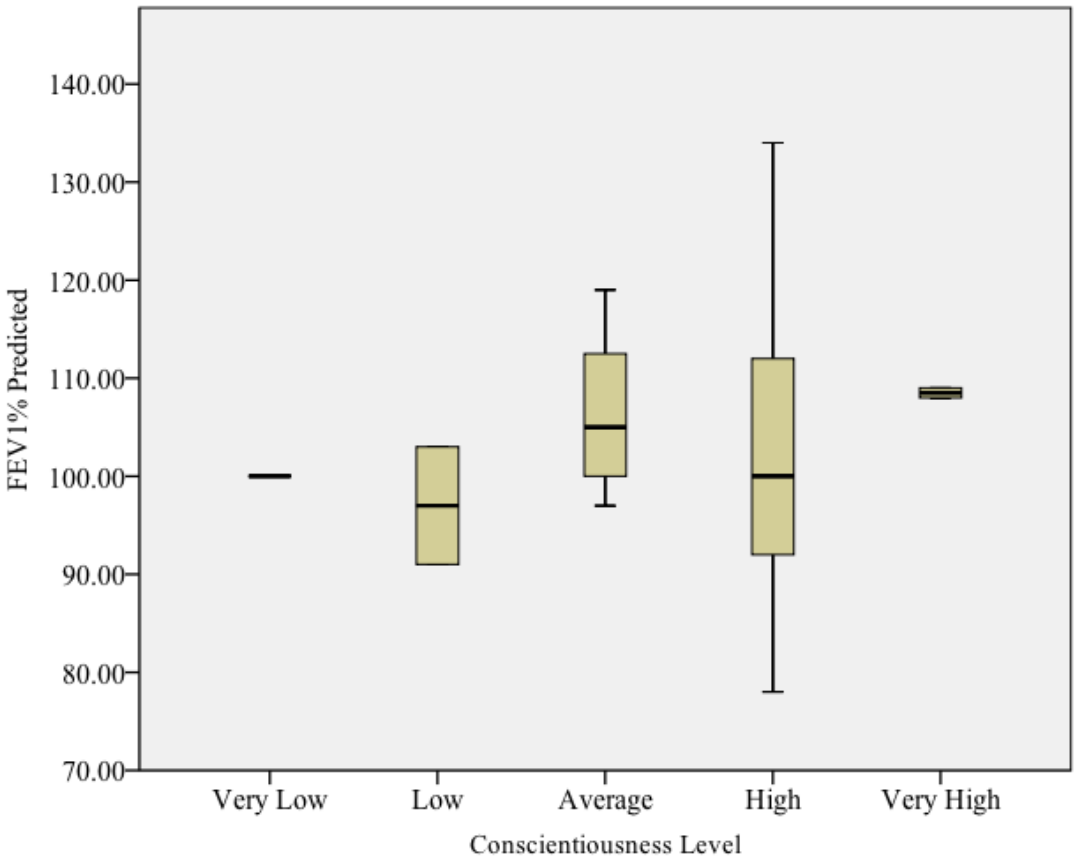

Figure 3. Boxplot for FEV_1% predicted by caregiver conscientiousness level.

Only one caregiver exhibited a very low level of conscientiousness, whose child had a BMI% score of 20%. Caregivers that exhibited high levels of conscientiousness had children with BMI% scores that ranged from 15% to 96%. For caregivers that exhibited average levels of conscientiousness, had children with BMI% scores that ranged from 13% to 99%. As the level of conscientiousness increased BMI% means also increased, eliciting a positive slope. However, it cannot be stated conclusively that a caregiver's level of conscientiousness is associated with BMI%. Overall, for the primary hypothesis to be valid, caregivers that exhibited a very high or high level of

conscientiousness were expected to have children with higher BMI% scores. In order to examine if possible association between the level of conscientiousness and BMI% a Spearman's correlation was conducted. The Spearman's correlation measures the strength and direction of; two continuous variables, or two ordinal variables, or one continuous and one ordinal variable. Three assumptions are required for the Spearman's correlation statistical test. Variables being tested for association are measured using continuous and/or ordinal scales, the variables represent paired observations, and the variables have a monotonic relationship. Two variables have a monotonic relationship when the value of one variable increase and the value of the second variable also increases or when one variable increases and the value of the second variable decreases.

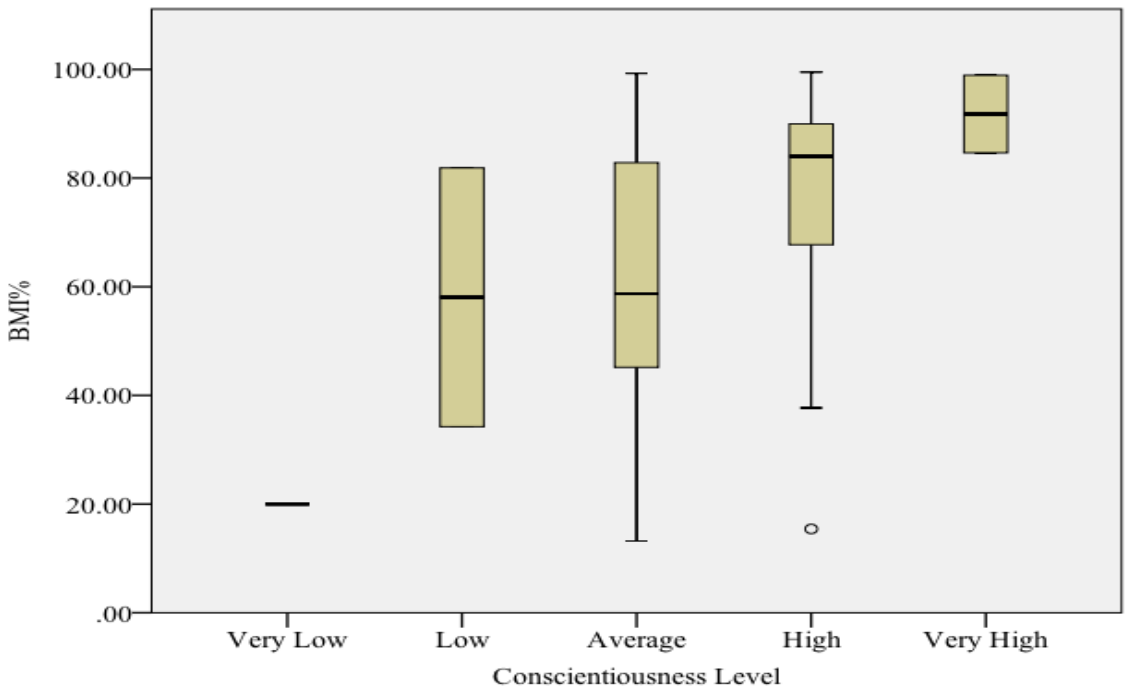

Figure 4. Boxplot for BMI% by caregiver conscientiousness level.

A Spearman's correlation was conducted between conscientiousness t-scores and BMI% to further explore the relationship between the variables ($r = .375$, $p = .049$). The results show that while the sample does not give sufficient evidence to support a statistically significant association between conscientiousness and BMI%, this may be due to the small sample size and lack of power in the overall study.

Table 11
Relationship between Conscientiousness and BMI%

			C t-score	BMI%
Spearman's rho $p < 0.05$	Conscientiousness t-score	Correlation Coefficient	1.000	.375*
		Sig. (2-tailed)	.	.049
		N	28	28
	BMI%	Correlation Coefficient	.375*	1.000
		Sig. (2-tailed)	.049	.
		N	28	28

Adherence and Health Outcomes

Analysis of the adherence data revealed that caregivers reported high-levels of adherence on the TAQ-CF for all three treatment regimens which generally matched the prescribed medical chart data for frequency (i.e., not at all, occasionally, three times a week, once a day, twice a day, 3 or more times a day, and does not apply to me). For example, all caregivers reported complete adherence to for the pancreatic enzyme treatment regimen with a frequency of 3 or more times a day and only one child was not prescribed this treatment regimen, whose caregiver reported not at all.

As stated amongst the three treatment regimens included for adherence, non-adherence was only observed in the aerosols to thin mucus treatment regimen. It was

hypothesized that there was a relationship between the personality traits (neuroticism and conscientiousness) and adherence to the aerosols to thin mucus treatment regimen. The null hypothesis was that there is no relationship between either personality trait (neuroticism & conscientiousness) and adherence to the aerosol to thin mucus treatment. The alternate hypothesis was that there is a relationship between the personality traits and adherence to aerosols to thin mucus treatment. Pearson's chi-square results indicated for neuroticism ($X^2(3) = 3.102$, $p = .376$) and conscientiousness ($X^2(4) = 4.80$, $p = .308$) that the null hypothesis cannot be rejected and the study sample does not give sufficient evidence that there is a relationship between either personality trait and adherence to the aerosols to thin mucus treatment regimen.

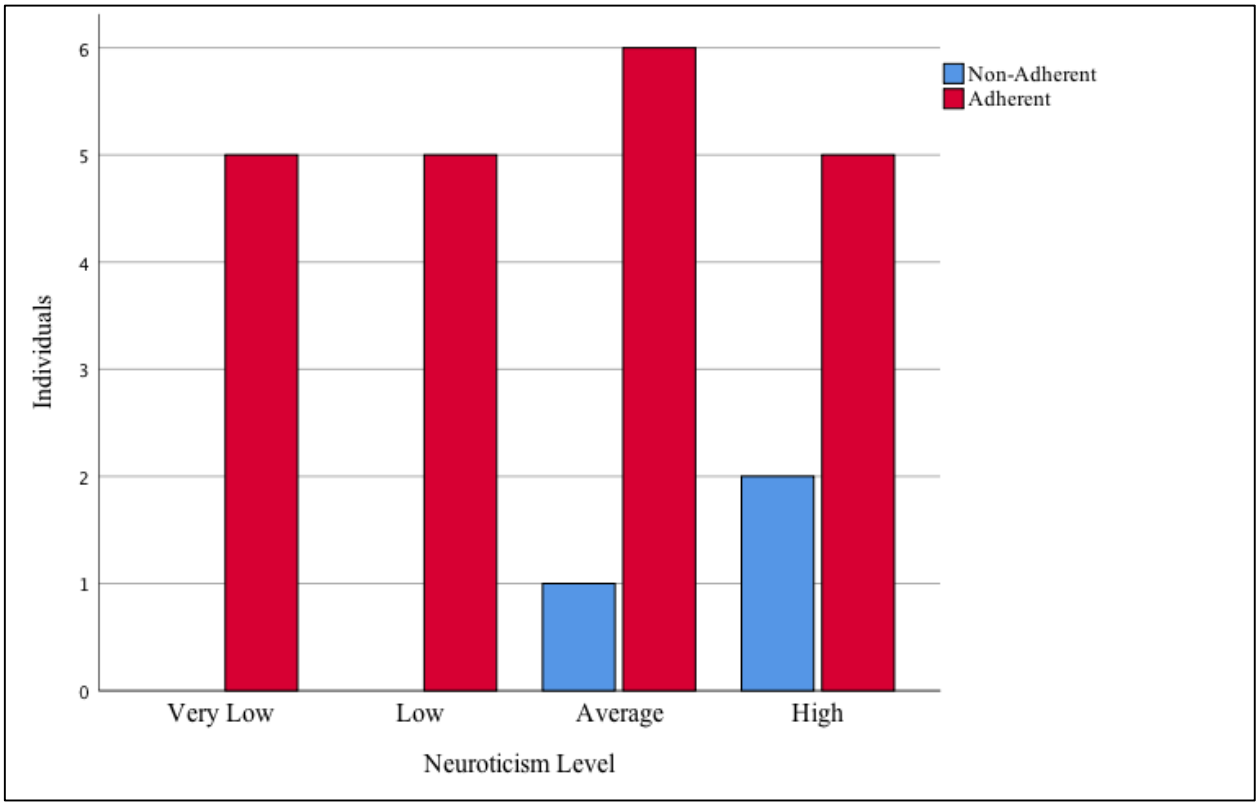

Figure 5. Adherence to aerosols to thin mucus by caregiver neuroticism level.

Caregivers that exhibited a high level of neuroticism were expected to have children that were less adherent, however only two caregivers reported non-adherence, thus an association, even if present, was not detected.

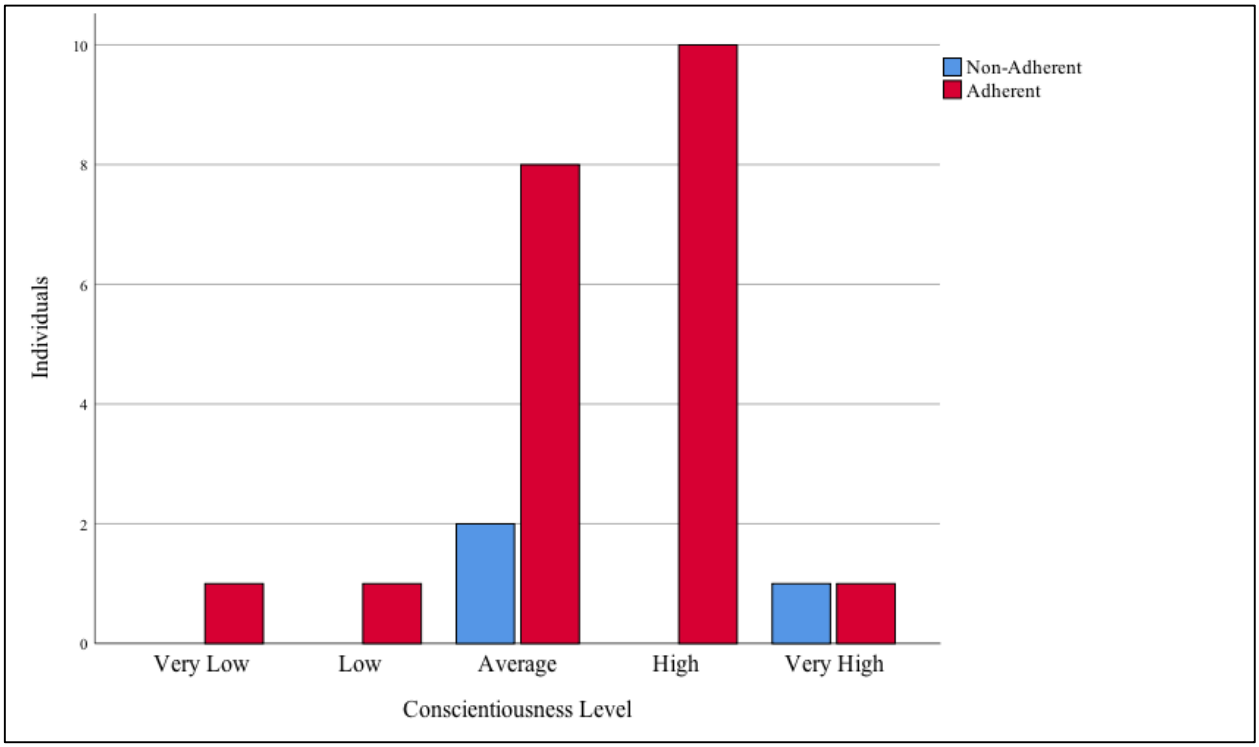

Figure 6. Adherence to aerosols to thin mucus by caregiver conscientiousness level.

Finally, to examine if adherence behavior were associated with nutritional status (BMI%) and lung function (FEV_1% predicted) an independent samples t-test was conducted. From the sample size only three participants reported non-adherence to the prescribed treatment (aerosols to thin mucus). Due to the small sample size, no

significant difference was found for BMI%, t(22) = -.77, p = 0.447, between the adherent patients (M = 71.83, SD = 28.72, n = 21) and non-adherent patients (M=58.34, SD=23.01, n=3). The same was true for FEV_1% predicted, t(22) = .07, p = .946. The results for the adherent patients were (M = 105.86, SD = 11.70, n = 21) and the non-adherent patients were (M=106.33, SD=4.73, n=3).

Chapter IV

Discussion

The primary purpose of the current study was to examine if the caregiver personality traits of neuroticism and conscientiousness were associated with the health status of children with CF. The study results indicated that there is no significant relationship between personality traits and health status, as measured by FEV_1% predicted and BMI%. A possible explanation for why no relationship was not found between personality type and health status was due to the overall healthy population of individuals included in this current study, although it is also possible that caregiver personality is not related to CF health outcomes in this age group.

The results obtained in this study run counter to the initial hypothesis, but may be explained by the fact that children enrolled in the cohort were fairly healthy with very mild lung disease. This is not surprising given that there is ample evidence that overall, outcomes in CF are improving. According to the 2016 CF Foundation Patient Registry Annual Report, the median predicted survival age, pulmonary function measures, and the measures for nutritional status are now trending upwards. The patient registry reports data on 29,497 individuals diagnosed with CF across multiple CF centers in the United States. The registry contains data on individuals with CF from 1986 to 2016 with a median age of 19.1 years of age with 42.3% children (under age 18). For individuals in the registry, the mean percent predict FEV_1% predicted is 77.4%, which is overall consistent with mild lung disease although there are many individuals with far worse lung

disease than the mean. There is strong evidence that newborn screening (NBS) enabling early diagnosis of CF is associated with better lung function and nutritional outcomes amongst the registry population (Borowitz et al., 2009), which likely accounts for improving outcomes in cystic fibrosis, and it is likely that most of the individuals in the current study were diagnosed with newborn screening as the percentage of children diagnosed via NBS has steadily increased from 9.2% in 2001 to 62.4% in 2016 (CFF, 2016). There has also been an increasing number of individuals diagnosed with CF evaluated by a multi-disciplinary team, which includes a respiratory/physical therapist, a dietitian/nutritionist and a social worker, and evaluation by these disciplines may be associated with healthy cohort included in this study (Borowitz et al., 2009; Johnson, Butler, Konstan, Morgan, & Wohl, 2003). Further, the CF Foundation reports that the proportion of people with CF at age 18 who are in the normal/mild category (FEV_1% predicted ≥ 70) has increased from 31.9 percent in 1986 to 73.9 percent in 2016. Also, the proportion in the severe category (FEV_1% predicted < 40) has decreased from 30% in 1986 to 4% in 2016. One key finding from the CF registry population is that FEV_1% predicted is steadily improving and currently above 90% into early adolescence, which corroborates the findings in this study.

It should be noted that lung function as measured by FEV_1% predicted declines with age (Zemanick et al., 2010), and therefore is it plausible to have normal lung function in childhood. Com et al. (2010) has similar findings in a study conducted to understand the relationship between FEV_1 % predicted and frequency of hospitalizations, effect on BMI, and rates of infection. Of the 122 children enrolled in a retrospective study performed at the Arkansas Children's Hospital Cystic Fibrosis Care Center, only

17% of the children were categorized as having low FEV_1% predicted mean at 69% (*SD* = 12%) The remaining 83% of participants had FEV_1% predicted mean above 95% (*SD* = 12%). In the current study, the mean FEV_1% predicted was 104%, within one standard deviation of the findings in the Com et al. (2010) study. When Com et al. (2010) did further statistical analysis, they found that the children with high FEV_1% predicted had faster rates of lung function decline. Similar FEV_1% predicted values were found in a large multi-center retrospective observational study of 946 children with CF who were ≤12 years of age – in this study the mean FEV_1% predicted was 104.4 % *SD* = 15.5 (Cogen et al., 2015). Participants for the Cogen et al. (2015) study were enrolled between 2004 and 2006, with mean age of 5.7 years of age (*SD* = 3.6 years), younger than the participants in our cohort. In an earlier study, Konstan et al. (2007) examined the risk factors for rate of decline in FEV_1% predicted in children and adolescents between 6 and 17 years of age. A total of 4866 children were enrolled in this study and grouped by the following ages; 6 to 8 years of age (*n* = 1811), 9 to 12 years of age (*n* = 1696), and 13 to 17 years of age (*n* = 1359). For the 6 to 8-year-old group, the baseline mean FEV_1% predicted was 88.4% (*SD* = 20.5) and for the 9 to 12-year-old group, the baseline mean FEV_1% predicted was 85.3 (*SD* = 20.8). These studies show that it is entirely plausible to have a young, healthy cohort of children with cystic fibrosis, as was demonstrated in the current study.

Regarding the BMI%s, for the current study the highest BMI% measured for each child in 2016 was used, and the mean BMI% was high at 68.1%. Our findings are in line with other studies and other data. When looking at the broader population of individuals diagnosed with CF (29,497 individuals in the CFF registry), the CF Foundation (2016)

reports the median BMI% to be 55.1 percent. Similar to FEV_1% predicted data, the CF Foundation reports that BMI% has been trending up most notably in youngest cohorts, which the authors attribute to the advent of NBS as well as a multi-disciplinary approach to CF care. Cogen et al. (2015), found that the mean BMI% was 62.7 (*SD* = 24.4) for 946 children who on average 7.9 years of age (*SD* = 2). Our study cohort was within one standard deviation of the larger sample size (68%) and used similar methods to baseline BMI%. The current study did not review medical chart data to examine if the cohort had early diagnosis via NBS.

In reviewing the current literature, there is a strong emphasis from a policy perspective to diagnose CF using NBS or within the first 6 months of life as it leads to better health outcomes (Borowitz et al., 2009; CFF, 2016; Marshall & Campbell, 2009). Also, from a policy perspective, there is a strong emphasis to provide families that have children with CF the proper psychological support to deal with the complex treatment regiments (Lahiri et al. 2016; Borowitz et al., 2009; Marshall et al., 2009). Feelings of disbelief, anger, and anxiety are common when parents are informed of a CF diagnosis for their child. The recommendation is to convey the diagnosis information in a sensitive, empathetic, and positive manner. Another important policy recommendation is to introduce the family to the multi-disciplinary team of CF clinicians, which include the CF nurse, registered dietitian, respiratory therapist, and social worker within the first two visits. An interesting future area of study would be to assess personality type of a caregiver at the initial diagnosis and after the child's sixth birthday, to understand the enduring nature of personality after receiving stressful news about a child's health.

A key principle our study relied upon was the enduring nature of personality traits regardless of life events (McCrae & Costa, 2006). Roy et al. (2017) assessed whether personality traits (measured by the NEO-FFI) are associated with cognitive impairment in patients with multiple sclerosis (MS). A sample of 275 MS patients and 55 healthy controls (HC) completed several neuro-performance tests and the NEO-FFI. The NEO-FFI was also completed by an independent observer. Results indicated that MS patients were higher in neuroticism and lower in extraversion than HCs, but only cognitively impaired patients were significantly lower in conscientiousness. Further analysis revealed that cognitive impairment in individuals with MS, co-occurred with the neuroticism trait. Four years later in a follow-up longitudinal study, 82 MS patients were compared to HCs and the results indicated that that personality changes in extraversion and conscientiousness were more evident in MS patients who experienced cognitive decline. Although, the mechanism of why these changes occurred was not examined, the authors concluded that neuroanatomical changes, or the ability to perform and complete tasks, influenced the change in personality traits. This study shows that anatomical changes were associated with a change in personality, providing evidence that in the absence of these changes, personality is likely to endure even in the setting of a potentially debilitating chronic illness such as MS. It is plausible that for parents of children with CF, unlike what was seen in the MS cohort, personality traits do not influence health behaviors or outcomes to the same extent. It could also be that such factors would play a role for parents of older children, or perhaps that personality traits of adults with CF would impact health outcomes. These hypotheses were beyond the scope of the current study but could be evaluated in future work.

The secondary aim of the study was to determine if personality trait was associated with adherence to the prescribed treatment regimen. Results indicated that adherence was very high for the three prescribed treatment regimens regardless of the caregiver personality, and this is likely why no significant association was found. A similar study by Baker and Quinter (2018) examined the relationship between caregiver reported levels of depression and its effect on children's adherence to pancreatic enzymes. The researchers hypothesized that parental depressive symptoms would contribute to worse adherence. The study included children between age 1 to 13 years of age with cystic fibrosis who were followed for a 3-month period. Adherence was measured using the Medication Event Monitoring System (MEMS), which records the date and time of each prescription bottle opening. The Center for Epidemiological Studies Depression Scale (CES-D) was used to measure depression. A total of 83 participants met the inclusion criteria. Parents were subdivided into three groups, few to no symptoms of depression, subclinical symptoms, and elevated symptoms. Children were also divided into 3 three groups, early childhood (age $\leq$ 5 years, n = 30), middle childhood (ages 5-9 years, n = 35), and preadolescents (age >9, n = 18). At study conclusion, one key finding was that age of the child was significantly related to adherence at home. Older children demonstrated the worst rates of adherence. Younger children in the middle-childhood and early childhood age ranges exhibited higher rates of adherence to pancreatic enzymes. Although, the mentioned studies did not study personality specifically, they examined another psychological factor (e.g. depression) to and understand the association with adherence and the results support our finding that adherence is high in childhood in cystic fibrosis.

In a five-year retrospective analysis of medication adherence in CF, Shakkottai et al. (2015), examined long-term adherence using prescription refill histories. The researchers hypothesized that younger patients with CF would be more adherent. Adherence was measured if the study participants were prescribed one of the following treatments for a minimum of 3 months; pancreatic enzyme replacement therapy (PERT), inhaled hypertonic saline (IHS), dornase alpha, tobramycin solution for inhalation (TSI), and CF multivitamins. Participants were divided into the following groups infant-young (age ≤5 years), older child-preteen (ages 6-12 years), and adolescent-young adult (ages 13-21 years). Data for 204 participants was reviewed, and the results showed significant differences between groups as related to adherence to IHS, PERT, and CF multivitamins. Adherence to IHS and all inhaled medications combined was higher in the infant-young group and the older child-preteen group, further providing evidence to overall high adherence in children with cystic fibrosis.

Modi et al. (2006) examined adherence in the pediatric population (ages 6-13 years) using a multi-method approach by examining self-reported adherence, pharmacy refill data, daily diary, and electronic monitoring (MEMS). Results indicated that parent self-reported adherence was 89.5% to PERT, 88.4% to CF multivitamins, 74.4% to airway clearance, and 82.4% to nebulized medications. The prescription refill data revealed an adherence rate of 46% for PERT, 35% to CF multivitamins, and 68% to nebulized medication. Taken together the Shakottai et al. (2015) and Modi et al. (2006) show that measuring adherence to treatment amongst the CF population continues to be a difficult task. In the current study, self-reported adherence was measured using the TAQ-CF, which could explain the high rates of adherence reported.

A recent study by Quittner et al. (2014) examined associations of adherence to pulmonary medications, health-care use, and cost among patients with CF. Patients with CF (n = 3,287) 6 years of age and above, were identified using the Thomson Reuters MarketScan Commercial Claims and Encounters Database between January 2005 and June 2011. This database contains medical and drug information for active employees and their dependents who have primary coverage through employee sponsored private health insurance. Adherence was measured using a 12-month medication possession ratio (MPR) for each long-term pulmonary medication the averaged for a composite MPR (CMPR) all patients. The study sample had the following age categories; 6 to 10 (n = The mean age was 22.8 years (SD = 13.0 years) and 49% of the patients were female. Quittner et al. (2014) found that age was related to CMPR, and that adherence was highest amongst the patients age 6 to 10 years of age (59%) compared to all other age groups. Further, a large drop in adherence was observed in adolescents and adults. These results are consistent with our study. Although a large body of research has been conducted on what factors are associated with adherence in the pediatric CF population no other studies have examined caregiver personality type and the relationship between adherence to treatment regiments prescribed for their child as we have done.

Finally, the third aim of this study sought to examine if adherence behavior was associated with health status. Like the secondary aim, self-reported adherence behavior was very high amongst this sample size and the results indicated that adherence behavior had no significant relationship with the health indicators. A review of the literature indicates that prior to adolescence, adherence to prescribed treatment is directed by caregivers and disease progression increases with age (Sawicki, Heller, Demars, &

Robinson, 2015; CFF, 2016; Shakkottai et al., 2015; Lahiri et al., 2016). This could explain why no association was observed in the current study focusing on younger children.

One area of focus to increase adherence rates has been to focus on the transition from childhood to adolescence by identifying barriers to treatment and examining psychosocial factors. Barriers to treatment adherence include, lack of adequate training on how to perform a treatment, poor understanding on the importance of treatment, social embarrassment, depression, and difficulty with inhalation techniques, behavior (Sawicki & Tiddens, 2012). As discussed, several research studies have shown that children are more adherent to CF treatment regimens and adherence rates start to decline starting around adolescence. Investigators have focused a great deal of attention on the transition from childhood to adolescence to understand what factors are associated with the decline in adherence rates.

There were several important limitations of the current study. One weakness of our study we did not evaluate any other psychosocial or physiological factors experienced by caregivers, such as the presence of depression in the parents, which could potentially affect the quality of care given, independent of caregiver personality. Only a baseline NEO-FFI-3 was administered to caregivers at the initial visit, however a follow-up NEO-FFI-3 would be helpful to confirm previous studies such as the one by Roy et. al showing that personality traits are constant regardless of disease state. Such a design would perhaps even allow for the discovery of results contrary to the study by Roy et al. (2017), such as a study conducted on patients who have undergone lung transplantation, nothing less than a significant life event. A study by Goetzmann et al. (2005) found that patients

who underwent lung transplantation scored higher on the conscientiousness trait than a representative normal sample of 1908 Germans. In other words, there are some drastic life events that surely influence personality change, and it is possible for caregivers and patients alike to experience these changes. Overall, the complex nature of personality and its relationship to health status needs further analysis and better study designs, namely that include personality assessment at regular intervals over a longer period of time.

One weakness of the NEO-FFI-3 is that it provides a broad classification of personality traits unlike the longer form Neuroticism, Extraversion, Openness to Experience Profession Inventory 3 (NEO-PI-3). The NEO-PI-3 has 240 questions and takes approximately 30 minutes to complete. When time is not an issue, it is advised to use the NEO-PI-3 to get a detailed understanding of the trait scores and specific facets within a trait that individuals possess. Our data showed 89% of the caregivers had average to very high scores for the conscientiousness trait and that 54% of the caregivers had average to high scores for the neuroticism trait. Two caregivers scored high for both neuroticism and conscientiousness trait and had children with FEV_1% predicted above 90% and BMI% above 89%. Key to the primary hypothesis was that the caregiver level of neuroticism or conscientiousness was associated to the health outcome measures. With a caregiver scoring high for both personality traits, it is difficult to assess which trait, if at all, have influenced the health outcome measures. It is not uncommon for individuals to score high for multiple traits (McCrae & Costa, 2010), but understanding the specific facets of a trait may provide further detail on what is driving these health outcomes. Alternatively, one caregiver scored low for the neuroticism trait and high for

the conscientiousness trait, but had a child with FEV_1% predicted above 90% and BMI % at 37.7%. The low BMI % value could be due to multiple factors, but shows why significance between personality and health outcomes was not found. The NEO-PI-3 may have been helpful in this regard to understand the nuances of each major personality trait to better explain the relationship between personality and health outcome.

Another weakness of the current study is that the CF mutation type was not examined, and genotype may have had a confounding impact on the overall health status of individuals with CF. Certain genotypes are associated with more severe phenotypes including worse lung disease. The CF Foundation (2016) groups individuals with CF into 5 classes, based on where the CFTR defect occurs at the cellular level. Although our study did not use mutation type as a baseline inclusion criterion, the majority of patients that are in the CF registry are in the mutation class I-III grouping (CFF, 2016), which typically amounts to little CFTR function. Given that lung function was largely normal in our cohort, it is not clear as to whether genotype had a confounding effect therefore knowing the participants genotype would help to explore this possibility.

This study had additional weaknesses that could have affected the results. In particular, the small sample size limits the power of the study to detect associations. If the study should be conducted across multiple CF centers to increase the sample size, this would improve generalizability and potentially identify more variation in health and adherence outcomes. Additionally, we did not control for the effect that genotype had on severity of lung disease or nutritional status. Regardless of the level of adherence or the personality traits of a caregiver, CF genotype may be the primary determinant of overall health status. Also, we relied upon caregiver self-report to determine adherence, and

recall bias could have affected our results, especially since most caregivers responded that their children were adherent to the prescribed treatment (Daniels et al., 2011). Further, the TAQ-CF measures adherence across a broad spectrum of treatment regimens but each child has an individualized treatment plan. Finally, the effect of three other personality domains measured in the NEO-FFI-3 (Extraversion, Openness to Experience, & Agreeableness) should be examined as it was not included in the current study.

In summary, it is possible that an association between personality and health outcomes, personality and adherence, and adherence and health outcomes was not identified in the present study due to a healthy preadolescent population, which has previously been proven to be highly adherent with minimal lung disease and optimal nutritional status. Several studies have shown the preadolescent population have relatively high adherence rates (Butcher & Nasr, 2014; Modi, et al., 2008; Shakkottai, et al., 2015). Children included in this study were relatively healthy based on the BMI% and FEV_1% predicted data, and very adherent to prescribed treatment regimens (based on the self-report TAQ-CF). Finally, all children enrolled in the study were regularly followed large tertiary care center with a relatively healthy population who were closely monitored by clinicians.

Overall, this study was one of the first to evaluate how a caregiver's personality could affect health and adherence outcomes for their child with CF. In this small, overall healthy sample of children with CF, no association was found. Future studies should focus on a larger sample size with varying degrees of lung function severity, nutritional deficiency, age, and adherence levels in different CF centers, as well as to follow

personality traits of caregivers over a longer period of time in order to confirm the results of this current study.

References

Aldwin, C. M., Spiro, A., Levenson, M. R., & Cupertino, A. P. (2001). Longitudinal findings from the normative aging study: III. personality, individual health trajectories, and mortality. *Psychology and Aging, 16*(3), 450-465. doi:10.1037/0882-7974.16.3.450

American Psychological Association. (n.d.). In Personality. Retrieved on January 12, 2016, from http://www.apa.org/topics/personality/index.aspx

Arias-Llorente, R. P., Bousoño-García, C., & Díaz-Martín, J. J. (2008). Treatment compliance in children and adults with cystic fibrosis. Journal of Cystic Fibrosis, 7(5), 359-367. doi:10.1016/j.jcf.2008.01.003

Axelsson, M. (2013). Report on personality and adherence to antibiotic therapy: A population-based study. BMC Psychology, 1(1), 1-6. doi:10.1186/2050-7283-1-24

Axelsson, M., Brink, E., Lundgren, J., & Lötvall, J. (2011). The influence of personality traits on reported adherence to medication in individuals with chronic disease: An epidemiological study in west Sweden. Plos One, 6(3) doi:10.1371/journal.pone.0018241

Axelsson, M., Emilsson, M., Brink, E., Lundgren, J., Torén, K., & Lötvall, J. (2009). Personality, adherence, asthma control and health-related quality of life in young adult asthmatics. Respiratory Medicine, 103(7), 1033-1040.

Barker, D., & Quittner, A. (2016). Parental Depression and Pancreatic Enzymes Adherence in Children With Cystic Fibrosis. Pediatrics, 137(2), E20152296.

Besier, & Goldbeck. (2011). Anxiety and depression in adolescents with CF and their caregivers. Journal of Cystic Fibrosis, 10(6), 435-442.

Blaisdell, C. J. (2011). Pulmonary function testing. In Light, M. J., Blaisdell, C. J., & Homnick, D. N. (Eds.). Pediatric Pulmonology, AAP Section on Pediatrics. Pediatric Pulmonology (p.92). New York, NY: American Association of Pediatrics.

Borowitz, D., Robinson, K., Rosenfeld, M., Davis, S. D., Sabadosa, K. A., Spear, S. L., Michel, S. H., Parad, R. B., White, T. B., Farrell, P. M., Marshall, B. C., & Accurso, F. J. (2009). Cystic fibrosis foundation evidence-based guideline for management of infants with cystic fibrosis. The Journal of Pediatrics. 155(6), 73-93.

Bowser, E. K., & Wagner, M. H. (2011). Nutritional aspects of pulmonary conditions. In Light, M. J., Blaisdell, C. J., & Homnick, D. N. (Eds.). Pediatric Pulmonology, AAP Section on Pediatrics. Pediatric Pulmonology (p.979-981). New York, NY: American Association of Pediatrics.

Bregnballe, V., Thastum, M., & Schiøtz, P. O. (2007). Psychosocial problems in children with cystic fibrosis. Acta Paediatrica, 96(1), 58-61. 10.1111/j.1651-2227.2006.00014.x

Bruce, J., Hancock, L., Arnett, P., & Lynch, S. (2010). Treatment adherence in multiple sclerosis: Association with emotional status, personality, and cognition. Journal of Behavioral Medicine, 33(3), 219-227. doi:10.1007/s10865-010-9247-y

Butcher, J. L., & Nasr, S. Z. (2015). Direct observation of respiratory treatments in cystic fibrosis: Parent– child interactions relate to medical regimen adherence. Journal of Pediatric Psychology, 40(1), 8-17. doi:10.1093/jpepsy/jsu074

Callaghan, B. D., Hoo, A. F., Dinwiddie, R., Balfour-Lynn, I., & Carr, S. B. (2005). Growth and lung function in Asian patients with cystic fibrosis. Archives of Disease in Childhood, 90(10), 1029. doi:10.1136/adc.2004.067264

Centers for Disease Control and Prevention. (n.d.). In About Child and Teen BMI. Retrieved on December 01, 2016, from https://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/about_childrens_bmi.html

Christensen, A., & Smith, T. (1995). Personality and patient adherence: Correlates of the five- factor model in renal dialysis. Journal of Behavioral Medicine, 18(3), 305-313. doi:10.1007/BF01857875

Cogen, J., Emerson, J., Sanders, D., Ren, C., Schechter, M., Gibson, R., Morgan, W., Rosenfeld, M. (2015). Risk factors for lung function decline in a large cohort of young cystic fibrosis patients. Pediatric Pulmonology, 50(8), 763-770.

Com, G., Carroll, J. L., Castro, M. M., Tang, X., Jambhekar, S., & Berlinski, A. (2014). Predictors and outcome of low initial forced expiratory volume in 1 second measurement in children with cystic fibrosis. The Journal of Pediatrics, 164(4), 832-838. doi:http://dx.doi.org.ezp-prod1.hul.harvard.edu/10.1016/j.jpeds.2013.11.064

Costa, P. T., & McCrae, R. R. (1992). Revised NEO personality inventory (NEO-PI-R) and NEO five-factor inventory (NEO-FFI) professional manual. Odessa. Fl: Psychological Assessment Resources.

Cystic Fibrosis Foundation. (2016). 2016 CF Foundation Patient Registry Annual Data Report. Retrieved from https://www.cff.org/Research/Researcher-Resources/Patient-Registry/2016-Patient-Registry-Annual-Data-Report.pdf

Daniels, T., Goodacre, L., Sutton, C., Pollard, K., Conway, S., & Peckham, D. (2011). Accurate assessment of adherence: Self-report and clinician report vs electronic monitoring of nebulizers. CHEST Journal, 140(2), 425-432. doi:10.1378/chest.09-3074

Dziuban, E. J., Saab- Abazeed, L., Chaudhry, S. R., Streetman, D. S., & Nasr, S. Z. (2010). Identifying barriers to treatment adherence and related attitudinal patterns in adolescents with cystic fibrosis. Pediatric Pulmonology, 45(5), 450-458. doi:10.1002/ppul.21195

Eakin, M., Bilderback, A., Boyle, M., Mogayzel, P., & Riekert, K. (2011). Longitudinal association between medication adherence and lung health in people with cystic fibrosis. Journal of Cystic Fibrosis: Official Journal of the European Cystic Fibrosis Society,10(4), 258-64.

Goetzmann, L., Scheuer, E., Naef, R., Klaghofer, R., Russi, E., Buddeberg, C., & Boehler, A. (2005). Personality, illness perceptions, and lung function (FEV1) in 50 patients after lung transplantation. GMS Psycho-Social Medicine, 2, Doc06.

Goodwin, R., & Engstrom, G. (2002). Personality and the perception of health in the general population. Psychological Medicine; Psychol.Med., 32(2), 325-332. doi:10.1017/S0033291701005104

Harris, P.A., Taylor, R., Thielke, R., Payne, J., Gonzalez, & N., Conde, J.G. . (2009). Research electronic data capture (REDCap) – A metadata-driven methodology and workflow process for providing translational research informatics support. Journal of Biomedical Information; 42(2), 377-381.

Happ, M. B., Hoffman, L. A., DiVirgilio, D., Higgins, L. W., & Orenstein, D. M. (2013). Parent and child perceptions of a self-regulated, home-based exercise program for children with cystic fibrosis. Nursing Research, 62(5), 305-314. doi:10.1097/NNR.0b013e3182a03503

Hobbs, S., Schweitzer, J., Cohen, L., Hayes, A., Schoell, C., & Crain, B. (2003). Maternal attributions related to compliance with cystic fibrosis treatment. Journal of Clinical Psychology in Medical Settings, 10(4), 273-277. doi:10.1023/A:1026349303930

Hoffstee, W.K.B., Kiers, H.A.L., De Raad, B., Goldberg, L.R., & Ostendorf, F. (1997). A Comparison of Big-Five Structures of Personality Traits in Dutch, English, and German. European Journal of Personality, 11(1), 15-31.

Hommel, K. A., & McGrady, M. E. (2013). Medication adherence and health care utilization in pediatric chronic illness: A systematic review. (report). Pediatrics, 132(4), 730.

Hulzebos, J., E., Bomhof-Roordink, B., Weert, V. D., Twisk, M., J., Arets, K.,H.G., Van, D. E., & Takken, K., T. (2014). Prediction of mortality in adolescents with cystic fibrosis. Medicine & Science in Sports & Exercise, 46(11), 2047-2052. doi:10.1249/MSS.0000000000000344

Jerant, A., Chapman, B., Duberstein, P., Robbins, J., & Franks, P. (2011). Personality and medication non- adherence among older adults enrolled in a six- year trial. British Journal of Health Psychology, 16(1), 151-169. doi:10.1348/135910710X524219

John, O. P., Robins, R. W., & Pervin, L. A. (2008). Handbook of personality : Theory and research. New York: The Guilford Press.

Johnson, C., Butler, S. M., Konstan, M. W., Morgan, W., & Wohl, M. E. B. (2003). Factors Influencing Outcomes in Cystic Fibrosis: A Center-Based Analysis: A Center-Based Analysis. Chest, 123(1), 20-27.

Konstan, M., Morgan, W., Butler, S., Pasta, D., Craib, M., Silva, S., Stokes, D., Wohl, M. E., Wagner, J., Regelmann, W., Johnson, C. (2007). Risk Factors For Rate of Decline in Forced Expiratory Volume in One Second in Children and Adolescents with Cystic Fibrosis. The Journal of Pediatrics, 151(2), 134-139.e1.

Kulich, M., Rosenfeld, M., Campbell, J., Kronmal, R., Gibson, R. L., Goss, C. H., & Ramsey, B. (2005). Disease- specific reference equations for lung function in patients with cystic fibrosis. American Journal of Respiratory and Critical Care Medicine, 172(7), 885.

Lahiri, T., Hempstead, S. E., Brady, C., Cannon, C. L., Clark, K., Condren, M. E., Guill, M. F., Guillerman, R. P., Leone, C. G., Maguiness, K., Monchil, L., Powers, S. W., Rosenfeld, M., Schwarzenberg, S. J., Tompkins, C. L., Zemanick, E. T., Davis, S. D. (2016). Clinical practice guidelines from the cystic fibrosis foundation for preschoolers with cystic fibrosis. Pediatrics, 137(4), E20151784-e20151784.

Lai, H. J., Shoff, S. M., & Farrell, P. M. (2009). Recovery of birth weight z score within 2 years of diagnosis is positively associated with pulmonary status at 6 years of age in children with cystic fibrosis. Pediatrics, 123(2), 714-722. 10.1542/peds.2001-3089

Leeman, J., Sandelowski, M., Havill, N. L., & Knafl, K. (2015). Parent- to- child transition in managing cystic fibrosis: A research synthesis. Journal of Family Theory & Review, 7(2), 167-183. doi:10.1111/jftr.12070

Marsh, H. W., Ludtke, O., Muthen, B., Asparouhov, T., Morin, A. J. S., Trautwein, U., & Nagengast, B. (2010). A new look at the big five factor structure through exploratory structural equation modeling. Psychological Assessment, 22(3), 471-491. doi:10.1037/a0019227

Marshall, & Campbell. (2009). Improving the Care of Infants Identified through Cystic Fibrosis Newborn Screening. The Journal of Pediatrics, 155(6), S71-S72.

McCrae, R. R., & Costa, P. T. J. (2007). Brief versions of the NEO-PI-3. Journal of Individual Differences, 28(3), 116-128. 10.1027/1614-0001.28.3.116

McCrae, R.R., Costa, & P. T. (2010) NEO inventories for the NEO Personality Inventory-3 (NEO-PI-3), NEO Five-Factor Inventory-3 (NEO-FFI-3), NEO Personality Inventory-Revised (NEO PI-R): professional manual Lutz, FL : PAR,

McCrae, R. R., & Costa, P. T. (2006). Personality in adulthood: A five-factor theory perspective [Kindle Edition ISBN 978146506224]. Retrieved from Amazon.com.

McCrae, R. R., & John, O. P. (1992). An introduction to the five-factor model and its applications. Journal of Personality, 60(2), 175-215. doi:10.1111/j.1467-6494.1992.tb00970.x

McDonald, C. M., Haberman, D., & Brown, N. (2013). Self-efficacy: Empowering parents of children with cystic fibrosis. Journal of Cystic Fibrosis, 12(5), 538-543. doi:10.1016/j.jcf.2012.11.014

Meichenbaum, D. (1987). In Turk D. C. (Ed.), Facilitating treatment adherence: A practitioner's guidebook. New York: Plenum Press.

Modi, A. C., Driscoll, K. A., Montag-Leifling, K., & Acton, J. D. (2011). Screening for symptoms of depression and anxiety in adolescents and young adults with cystic fibrosis. Pediatric Pulmonology, 46(2), 153. doi:10.1002/ppul.21334

Modi, A., Marciel, K., Slater, S., Drotar, D., & Quittner, A. (2008). The influence of parental supervision on medical adherence in adolescents with cystic fibrosis: Developmental shifts from pre to late adolescence. Children's Health Care, 37(1), 78-92. doi:10.1080/02739610701766925

Oates, G. R., Stepanikova, I., Gamble, S., Gutierrez, H. H., & Harris, W. T. (2015). Adherence to airway clearance therapy in pediatric cystic fibrosis: Socioeconomic factors and respiratory outcomes. Pediatric Pulmonology, 50(12), 1244-1252. doi:10.1002/ppul.23317

O'Hara, L. K., & Holmbeck, G. N. (2013). Executive functions and parenting behaviors in association with medical adherence and autonomy among youth with spina bifida. Journal of Pediatric Psychology, 38(6), 675-687. doi:10.1093/jpepsy/jst007

Quittner, A., Espelage, D., levers-Landis, C., & Drotar, D. (2000). Measuring adherence to medical treatments in childhood chronic illness: Considering multiple methods and sources of information. Journal of Clinical Psychology in Medical Settings, 7(1), 41-54. doi:10.1023/A:1009545319673

Quittner, A. L., Modi, A. C., Lemanek, K. L., Ievers-Landis, C., & Rapoff, M. A. (2008). Evidence- based assessment of adherence to medical treatments in pediatric psychology. Journal of Pediatric Psychology, 33(9), 916-936. doi:10.1093/jpepsy/jsm064

Quittner, A.L., Zhang, J., Marynchenko, M., Chopra, P.A., Signorovitch, J., Yushkina, Y., & Riekert., K. A. (2014). Pulmonary Medication Adherence and Health-care Use in Cystic Fibrosis. Chest, 146(1), 142-151.

Rapoff, M. A. (2010). Adherence to pediatric medical regimens: 2nd edition. Boston, MA: Springer-Verlag US.

Roy, S., Drake, A., Fuchs, T., Dwyer, M., Zivadinov, R., Chapman, B., Wienstock-Guttman, B., Benedict, R. (2018). Longitudinal personality change associated with cognitive decline in multiple sclerosis. Multiple Sclerosis Journal, Multiple Sclerosis Journal, 2018.

Sawicki, G. S., Heller, K. S., Demars, N., & Robinson, W. M. (2015). Motivating adherence among adolescents with cystic fibrosis: Youth and parent perspectives. (report).50(2), 127.

Sawicki, G. S., Ren, C. L., Konstan, M. W., Millar, S. J., Pasta, D. J., & Quittner, A. L. (2013). Treatment complexity in cystic fibrosis: Trends over time and associations with site-specific outcomes. Journal of Cystic Fibrosis, 12(5), 461-467.

Sawicki, G., & Tiddens, H. (2012). Managing treatment complexity in cystic fibrosis: Challenges and Opportunities. Pediatric Pulmonology, 47(6), 523-533.

Sawyer, S. M., & Aroni, R. A. (2003). Sticky issue of adherence. Journal of Pediatrics and Child Health, 39, 2-5.

Schechter, M. S., Shelton, B. J., Margolis, P. A., & Fitzsimmons, S. C. (2001). The association of socioeconomic status with outcomes in cystic fibrosis patients in the united states. American Journal of Respiratory and Critical Care Medicine, 163(6), 1331.

Schechter, M.S., & O'Sullivan, B. P. (2011). Cystic fibrosis. In Light, M. J., Blaisdell, C. J., & Homnick, D. N. (Eds.). Pediatric Pulmonology, AAP Section on Pediatrics. Pediatric Pulmonology (p.717-724). New York, NY: American Association of Pediatrics.

Shakkottai, A., Kidwell, K. M., Townsend, M., & Nasr, S. Z. (2015). A five- year retrospective analysis of adherence in cystic fibrosis. Pediatric Pulmonology, 50(12), 1224-1229. doi:10.1002/ppul.23307

Sheehan, J., Hiscock, H., Massie, J., Jaffe, A., & Hay, M. (2014). Caregiver coping, mental health and child problem behaviours in cystic fibrosis: A cross- sectional study. International Journal of Behavioral Medicine, 21(2), 211. 10.1007/s12529-013-9289-y

Spoonhower, K. A., & Davis, P. B. (2016). Epidemiology of cystic fibrosis. Clinical Chest Medicine, 37(1), 1-8. doi: 10.1016/j.ccm.2015.10.002.

Stallings, V. A., Stark, L. J., Robinson, K. A., Feranchak, A. P., & Quinton, H. (2008). Evidence- based practice recommendations for nutrition- related management of children and adults with cystic fibrosis and pancreatic insufficiency: Results of a systematic review. Journal of the American Dietetic Association, 108(5), 832-839. 10.1016/j.jada.2008.02.020

van, d. S., Cader, S., van, d. S., & Westwood, A. T. (2011). Improving nutritional status of children with cystic fibrosis at red cross war memorial children's hospital. Journal of Paediatrics & Child Health, 47(5), 282-286. doi:10.1111/j.1440-1754.2010.01954.x

What is cystic fibrosis. (n.d). In About Cystic Fibrosis. Retrieved on January 10, 2016, from https://www.cff.org/What-is-CF/About-Cystic-Fibrosis/

Wheeler, K., Wagaman, A., & McCord, D. (2012). Personality traits as predictors of adherence in adolescents with type I diabetes. Journal of Child & Adolescent Psychiatric Nursing, 25(2), 66-74. doi:10.1111/j.1744-6171.2012.00329.x

Wiedemann, B., Paul, K. D., Stern, M., Wagner, T. O., & Hirche, T. O. (2007). Evaluation of body mass index percentiles for assessment of malnutrition in children with cystic fibrosis. European Journal of Clinical Nutrition, 61(6), 759-768. doi:10.1038/sj.ejcn.1602582

Woestenenk, J. W., Stellato, R. K., Terheggen-Lagro, S., Ent, C. K., & Houwen, R. H. J. (2014). The relationship between body growth and pulmonary function in children with cystic fibrosis. Acta Paediatrica, 103(2), 162-167. 10.1111/apa.12462

World Health Organization. (2003). Adherence to long-term therapies. Evidence for action. Retrieved from http://www.who.int/chp/knowledge/publications/adherence_report/en/

Yamada, A., Kato, M., Suzuki, M., Suzuki, M., Watanabe, N., Akechi, T., & Furukawa, T. A. (2012). Quality of life of parents raising children with pervasive developmental disorders. BMC Psychiatry, 12, 119. doi:10.1186/1471-244X-12-119

Zemanick, E. T., Harris, J. K., Conway, S., Konstan, M. W., Marshall, B., Quittner, A. L., Retsch-Bogart, G., Saiman, L., Accurso, F. J. (2010). Measuring and improving respiratory outcomes in cystic fibrosis lung disease: Opportunities and challenges to therapy. Journal of Cystic Fibrosis, 9(1), 1-16.

Zindani, G. N., Streetman, D. D., Streetman, D. S., & Nasr, S. Z. (2006). Adherence to treatment in children and adolescent patients with cystic fibrosis. Journal of Adolescent Health, 38(1), 13-17. doi:10.1016/j.jadohealth.2004.09.013