Published in final edited form as:

Health Psychol. 2015 May ; 34(5): 496–504. doi:10.1037/hea0000136.

Medication Beliefs Mediate Between Depressive Symptoms and Medication Adherence in Cystic Fibrosis

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Abstract

Objective—Depression is a known barrier to regimen adherence for chronic conditions. Despite elevated depression rates and complex regimens for people with cystic fibrosis (CF), little is known about associations between depressive symptoms and CF adherence. One possibility is that depressive symptoms distort beliefs about medications, which may influence adherence.

Method—Adolescents and adults ($N = 128$; mean age = 29 ± 11 years, range = 16–63, 93% Caucasian) with CF reported on depressive symptoms and medication beliefs (self-efficacy, motivation, perceived importance, and outcome expectancies related to taking medications). Medication adherence was assessed objectively through pharmacy refill data. Cross-sectional structural equation models evaluated medication beliefs as a mediator between depressive symptoms and medication adherence.

Results—Twenty-three percent of participants exceeded clinical cutoffs for depressive symptoms. Participants took less than half of prescribed pulmonary medications (mean adherence rate = $44.4 \pm 26.7\%$). Depressive symptoms were correlated with adherence ($r = -.22, p < .05$), and medication beliefs ($b = -0.13, 95\% \text{ CI } [-0.24, -0.03]$) significantly mediated this relation. Higher depressive symptoms were associated with less positive medication beliefs ($b = -0.27, p < .01$), which were associated with lower medication adherence ($b = 0.49, p < .01$).

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Conclusions—Depressive symptoms are related to beliefs about and adherence to CF medications. Monitoring depressive symptoms and medication beliefs in routine CF care may help identify risks for nonadherence and facilitate interventions to reduce depression, adaptive medication beliefs, and ultimately improve adherence and CF management.

Keywords

medication beliefs; cystic fibrosis; depressive symptoms

People with chronic medical conditions are at increased risk for depression and depressive symptoms (Clarke & Currie, 2009). This poses a threat to disease management and symptom control, with evidence from a range of chronic conditions spanning pediatrics through adulthood demonstrating that elevated depressive symptoms increase the risk for nonadherence approximately two-to threefold (DiMatteo Lepper, & Croghan, 2000; Grenard et al., 2011). Specific symptoms of depression, such as negative mood, low self-esteem, feelings of ineffectiveness, deficits in memory or energy, and more perceived barriers to adherence, may detract from adherence (Katon & Ciechanowski, 2002; McGrady & Hood, 2010). Ultimately, the association between depression and poor adherence translates to increases in disease symptoms, medical costs, morbidity, and mortality (Barth, Schumacher, & Herrmann-Lingen, 2004; Katon & Ciechanowski, 2002).

The link between depressive symptoms and treatment adherence is well established, yet the mechanisms of this association are not well understood. Clarifying the processes by which depressive symptoms influence adherence would provide valuable direction for interventions to buffer the negative impact of depressive symptoms and ultimately improve health outcomes. Negative beliefs about prescribed medications (e.g., low self-efficacy to take medications, expectation of medications having null or negative outcomes, low motivation or intention to take medications) are possible mechanisms by which depressive symptoms could impede adherence. It is plausible that individuals' depressive symptoms could influence their medication beliefs to be more negative, which may reduce the likelihood of adhering to prescribed medications.

Individuals' beliefs about medications are related to medication adherence. In a recent meta-analysis, Horne and colleagues (2013) reported that higher perceived need for treatment and fewer perceived concerns about treatments are significantly associated with better adherence. This holds across many conditions: Negative beliefs about treatments or medications have demonstrated associations with poorer adherence among individuals with HIV (Barclay et al., 2007), diabetes (Gherman et al., 2011), sleep apnea (Olsen, Smith, Oei, & Douglas, 2008), hypertension (Quine, Steadman, Thompson, & Rutter, 2012), and those recovering from stroke (Robinson-Smith, Johnston, & Allen, 2000) and chronic back pain (Glattacker, Heyduck, & Meffert, 2013). Studies evaluating medication beliefs as a potential mechanism linking depression and adherence have focused almost exclusively on one specific belief, self-efficacy; results indicate that medication self-efficacy mediates the links between depression and medication adherence for hypertension (Schoenthaler, Ogedegbe, & Allegrante, 2009) and HIV (Cha, Erlen, Kim, Sereika, & Caruthers, 2008) and between

depression and glycemic control in Type 2 diabetes (Cherrington, Wallston, & Rothman, 2010).

Few studies have examined the roles that other medication beliefs aside from self-efficacy play in the link between depressive symptoms and medication adherence. One exception demonstrated that not only lower self-efficacy but also more perceived barriers to taking medications were mediators of the indirect link between depressive symptoms and self-reported adherence in adults with diabetes (Chao, Nau, Aikens, & Taylor, 2005). More research examining a broader range of medication beliefs, including motivation, perceived importance, and outcome expectancies related to taking medications, is needed to fully understand the cognitive mechanisms by which depressive symptoms relate to adherence. Understanding the role that a comprehensive set of relevant medication beliefs plays in depressive symptoms and medication adherence has the potential to inform and guide clinical interventions to reduce depressive symptoms, support adaptive health-promoting beliefs, and facilitate optimal disease management.

Cystic fibrosis (CF) is a chronic, progressive, obstructive lung disease with a complicated and demanding treatment regimen that includes multiple medications, nutritional guidelines, and chest physiotherapy, and can take several hours a day to complete (Sawicki, Sellers, & Robinson, 2009). In 1986, the median life expectancy was 27 years and less than 29% of individuals with CF were 18 years old in the United States, but with advances in drug therapies, this has changed dramatically (Cystic Fibrosis Foundation, 2013). In 2012, 49% of individuals with CF were adults and the median life expectancy was 41 years (Cystic Fibrosis Foundation, 2013). As adolescents and adults now account for over half of the CF population, there is growing attention to their health status and psychological and behavioral needs (Quon & Aitken, 2012). Depressive symptoms and medication nonadherence are emerging as significant risks for adolescents and adults with CF. Like other chronic conditions, the risk for depressive symptoms is elevated (Goldbeck, Besier, Hinz, Singer, & Quittner, 2010; Latchford & Duff, 2013; Riekert, Bartlett, Boyle, Krishnan, & Rand, 2007) and adherence to medications and other treatments is notably low (Briesacher et al., 2011; Eakin, Bilderback, Boyle, Mogayzel, & Riekert, 2011; Nasr, Chou, Villa, Chang, & Broder, 2013; Quittner et al., 2014). Despite these documented risks among people with CF and the known challenges to self-management, little is known about whether or how depressive symptoms relate to adherence to pulmonary medications for CF. One small study of adolescents with CF suggested that youths' perceptions about their illness and treatments were related to self-reported adherence rates (Bucks et al., 2009), suggesting that beliefs about medications may be related to adherence to CF treatments. However, the role that CF-related medication beliefs play in depressive symptoms and adherence has not been explored, yet is a plausible mediator, given evidence suggesting such associations in other disease groups.

No studies have examined a comprehensive set of disease-specific medication beliefs as a potential mechanism indirectly linking depressive symptoms with objectively measured medication adherence in adolescents and adults with CF or in any other chronic condition. Therefore, the aim of this study was to evaluate whether CF-related medication beliefs mediate the relationship between depressive symptoms and adherence to pulmonary

medications. It was hypothesized that lower levels of positive medication beliefs, including lower self-efficacy, motivation, and perceived importance of and less optimistic outcome expectancies related to taking medications, would mediate the association between elevated depressive symptoms and suboptimal adherence as measured by 1 year of pharmacy refill data in individuals with CF.

Method

Participants

Participants were individuals diagnosed with CF aged 16 and older enrolled in an ongoing randomized controlled trial to enhance medication adherence through motivational interviewing. All data were collected at baseline prior to randomization. Patients treated in the pediatric or adult CF center of a tertiary medical center in the Mid-Atlantic United States who were prescribed an inhaled mucolytic, inhaled antibiotic therapy, chronic macrolide therapy, and/or hypertonic saline therapy for the previous 12 months were eligible for study participation. Exclusionary criteria included previous lung transplant and diagnosis of *Burkholderia cepacia* complex isolated from the respiratory tract within the previous 2 years. Given the focus on individuals with primary responsibility for CF management, adolescents under age 16 were not eligible for the study. Of the 249 individuals who were eligible for the study, 221 were contacted before recruitment goals were met. Of those contacted, 160 (72%) consented to participate and baseline data were obtained from 128 (80%; two died, six were no longer eligible, six withdrew from the study, and 18 did not have a nonsick clinic visit during the baseline period).

Procedure

Potential participants from the hospital's pediatric and adult CF clinics were mailed an informational letter about the study with an opportunity to opt out of being contacted. Prior to their next clinic visit, patients who did not opt out were telephoned to assess interest in study participation. If eligible, informed consent/assent was obtained; authorization to collect pharmacy data was obtained at the next scheduled nonsick clinic visit. For participants younger than age 18, the study was described to both the parent and adolescent and each provided consent/assent for the adolescent to participate. Prior to the subsequent CF nonsick clinic visit, participants were asked to complete the baseline survey online at home or in clinic before the visit. All participants received a \$35 incentive for survey completion. The institutional review board approved this study.

Measures

To assess depressive symptoms, participants completed the Center for Epidemiologic Studies Depression scale (CES-D; Radloff, 1977), a commonly used measure of 20 depressive symptoms over the previous week. Possible total scores range from 0 to 60, with a cutoff score of 16 indicating the presence of elevated symptoms requiring further evaluation. The CES-D demonstrates strong psychometric properties (Radloff, 1977) and the reliability in this sample was good ($\alpha = .90$).

To measure the hypothesized mediator, medication beliefs, participants completed a questionnaire developed by the research team (Riekert, Rand-Giovannetti, Borrelli, Green, & Eakin, 2012). The medication beliefs survey has four modules measuring participants' self-efficacy (19 items), motivation (three items), and perceived importance (three items) related to CF medication adherence and outcome expectancies related to taking prescribed medications (19 items). Self-efficacy, motivation, and importance were rated on a 10-point Likert scale ranging from *not at all* to *completely* regarding participants' confidence in their ability to, motivation to, and perceived importance of taking medications as prescribed. Outcomes expectancies (19 items) were rated on a 5-point Likert scale ranging from *strongly disagree* to *strongly agree* regarding participants' expectations about positive and negative consequences of taking medications. In this sample, reliability was good to excellent (α total = .95, range = .83–.95).

To assess the primary outcome, CF medication adherence, a composite medication possession ratio (cMPR) was calculated based on participants' medication refill data. Study staff obtained records from participants' self-identified pharmacies for the previous year. A ratio was calculated for each prescribed pulmonary medication (maximum six medications: azithromycin, dornase alfa, inhaled tobramycin, hypertonic saline, colistin, and/or aztreonam lysine) using the following procedure: the sum of all days of medication supply dispensed during the previous year divided by the number of days each medication was prescribed in the same interval. Because medications dispensed during hospitalizations are not captured in pharmacy records, the number of days hospitalized during the interval was subtracted from the denominator. Values were capped at 100% and the ratios for each medication were averaged across all prescribed medications to determine a composite (cMPR) adherence score (Eakin et al., 2011). This cMPR provides an objective value representing the previous year's adherence across all prescribed pulmonary medications.

Participants self-reported demographic information, including income, insurance coverage, current employment or school status, marital status, and with whom they currently live. Clinical markers of disease severity in people with CF including body mass index (BMI) and lung function (forced expiratory volume in 1 s, FEV₁) were abstracted from the medical record to characterize the participants' health status (Simmonds, Macneill, Cullinan, & Hodson, 2010).

Data Analytic Plan

Descriptive statistics and Pearson correlations among key study variables were calculated using SAS Version 9. *t* tests and analyses of variance were also conducted to determine whether the key study variables differed by categorical demographic and clinical variables. Next, a latent variable representing medication beliefs was constructed and evaluated using confirmatory factor analysis, with the four subscales of the medication belief survey (self-efficacy, motivation, perceived importance, and outcome expectancies of taking medications) used as indicators. Because beliefs about medications are distinct yet interrelated (Chao et al., 2005), the latent variable representing medication beliefs permitted analysis of these beliefs together rather than artificially isolating each belief for the analysis

and reduced measurement error. A factor score determinacy value was calculated to quantify how well the latent variable was measured by the observed indicators.

Using the constructed latent variable, the hypothesized mediation model (depressive symptoms → medication beliefs → medication adherence; see Figure 1) was tested using structural equation modeling with MPlus software (Version 6; Muthén & Muthén, 1998–2010). The opposite direction (medication adherence → medication beliefs → depressive symptoms) was also tested and compared with the hypothesized model. Maximum likelihood procedure was used to include participants with missing data presumed to be missing at random. Bias-corrected bootstrapping was used to calculate 95% confidence intervals (CIs) to determine the significance of the indirect link between depressive symptoms and medication adherence via the medication beliefs latent variable (MacKinnon, 2008). The following empirically established indices of optimal model fit were examined to evaluate the path models' adequacy (Hu & Bentler, 1998, 1999): chi square closer to zero and $p > .05$, root mean square error of approximation (RMSEA) < 0.06 , standardized root mean square residual (SRMR) < 0.10 , Tucker–Lewis index (TLI) > 0.90 , and comparative fit index (CFI) > 0.90 . Standardized coefficients are reported to facilitate comparison across paths.

Results

Participant Characteristics

Approximately one half of the participants were male ($n = 68$, 53%), the large majority were Caucasian (93%), and the average age was 29.2 ± 11.1 years (range = 16–63 years; median = 26.0 ± 13.0 years). Nearly two thirds (63%, $n = 81$) of the sample were employed part or full time, and one quarter (24%, $n = 31$) were taking classes. Participants lived alone (7%, $n = 8$), with their spouse/partner (48%, $n = 57$), with their parents or family (35%, $n = 41$), or with other people (10%, $n = 12$), and 61% ($n = 79$) were not married. The majority (85%, $n = 109$) had private insurance. Clinical characteristics of the sample and summary depressive symptom and medication belief scores are presented in Table 1. The demographic and clinical characteristics of this sample are comparable with the overall adult CF population in the United States (Cystic Fibrosis Foundation, 2013). Nearly one half of the sample had mild lung disease (48% with $FEV_1 \geq 70\%$) and met BMI recommendations (43% of males and 42% of females had BMI ≤ 23 or 22, respectively), indicating that participants in this sample had moderate CF health status. The mean composite adherence rate was $44.4 \pm 26.7\%$, indicating that, on average, fewer than one half of prescribed doses were taken over the previous year. Approximately one quarter ($n = 30$, 23%) of participants had CES–D scores exceeding the clinical cutoff of 16, which indicates an elevated risk for major depression. Mean scores for medication beliefs were skewed toward the upper range for all four scales, representing generally positive perceptions about medications.

Descriptive Statistics

Correlations among the key study variables (i.e., total depressive symptoms, four medication belief categories, objective adherence rates) and demographic and clinical variables (i.e., age, BMI, FEV_1 , number of prescribed pulmonary medications) are presented in Table 2.

Significant bivariate correlations were evident among higher depressive symptoms, more negative medication beliefs, and lower composite adherence rates. The medication belief scales were intercorrelated. Of the demographic and clinical variables, only one was significantly correlated with more than one key study variable; more prescribed pulmonary medications were correlated with more positive medication beliefs and higher adherence rates. There were no differences in depressive symptoms, medication beliefs, or adherence rates across categories of marital status, living situation, lung function, or BMI. Thus, only the number of prescribed pulmonary medications was included in the structural equation model.

Measurement Model

To facilitate examination of a comprehensive set of medication beliefs, a latent variable was constructed using the four subscales of the medication beliefs survey as indicators. All subscale scores had significant factor loadings onto the latent variable (range = .49–.88, $p < .001$). Between 24% and 77% (R^2 range = .24–.77) of the variance for each indicator was explained by the latent factor. The resulting latent variable was labeled *medication beliefs* given that the indicators were scales from a comprehensive measure of beliefs about pulmonary medications used to treat CF. This measurement model fit the data very well ($\chi^2 = 2.02$, $p = .36$; CFI = 1.00; TLI = 1.00; RMSEA = 0.01, 90% CI [0.00, 0.18]; SRMR = 0.02) and the factor score determinacy = 0.94.

Structural Equation Mediation Model

To evaluate the whether medication beliefs mediate the association between depressive symptoms and medication adherence, a structural equation model of the hypothesized mediational associations was tested. Given the significant bivariate correlation, the number of prescribed pulmonary medications was included as a control variable in the model. All hypothesized paths were significant and in the expected direction, with the exception that the direct path between depressive symptoms and medication adherence was not significant with the inclusion of the other variables in the model. The final model fit the data very well ($\chi^2 = 16.14$, $p = .18$; CFI = 0.99; TLI = 0.98; RMSEA = 0.05, 90% CI [0.00, 0.11]; SRMR = 0.03). The final mediation model with standardized path coefficients is presented in Figure 1. Higher depressive symptoms were significantly associated with less positive medication beliefs ($B = -0.27$, $p < .01$), which were significantly associated with lower medication adherence ($B = 0.49$, $p < .01$). The indirect association between higher depressive symptoms and lower adherence through less positive medication beliefs was significant ($B = -0.13$, 95% CI [-0.24, -0.03], $p < .01$). This model explained 27.0% of the variance in adherence ($R^2 = 0.27$).

An additional structural equation model with a reversed direction of mediation (adherence $\rightarrow$ medication beliefs $\rightarrow$ depressive symptoms) was also tested. The model fit and standardized path coefficients were very similar to the hypothesized model, indicating that the models were equivalent (data not shown).

Discussion

As the median survival for people with CF has increased to 41 years (Cystic Fibrosis Foundation, 2013), the challenges of medical care and self-management during late adolescence and adulthood have become increasingly relevant (Sawyer, Drew, Yeo, & Britto, 2007; Tuchman, Schwartz, Sawicki, & Britto, 2010). Individuals with CF are at risk for suboptimal disease management and increased morbidity, and it is critical to identify potential points of intervention to reverse this trend. The goal of this study was to evaluate the role of medication beliefs in indirectly linking depressive symptoms and medication adherence to guide future adherence interventions.

Less positive medication beliefs appear to be one mechanism by which higher depressive symptoms are associated with lower medication adherence among individuals with CF. Building on previous studies reporting rates of nonadherence, this study is the first to demonstrate the importance of and interrelations among depressive symptoms, medication beliefs, and objectively measured adherence in this population. Calculation of adherence rates from pharmacy data rather than self-report reduced the impact of shared method variance on detected associations and increased credibility of the adherence data. The current sample's average medication adherence rate was below 50%, which represents a concerning level of nonadherence that is common (Briesacher et al., 2011; Eakin et al., 2011; Nasr et al., 2013; Quittner et al., 2014). Moderate elevations in depression symptoms (including nearly one quarter with clinically significant symptom levels) were likewise consistent with previously published rates (Goldbeck et al., 2010; Latchford & Duff, 2013; Riekert et al., 2007). Evidence of medication beliefs as a mediator indirectly linking depressive symptoms with adherence adds to a growing body of research across chronic conditions (Cha et al., 2008; Cherrington et al., 2010; Schoenthaler et al., 2009) and extends findings to late adolescents and adults with CF.

Results illustrate the critical role of individuals' cognitions and experiences in managing the complex and demanding CF treatment regimen. Depressive symptoms are known correlates of suboptimal disease management and control (DiMatteo et al., 2000; Grenard et al., 2011), and data from this sample of individuals with CF demonstrated that medication beliefs were of particular relevance and explained a significant portion of the association with adherence. Depressive symptoms such as depressed mood, fatigue, or irritability might impact medication beliefs by decreasing positive beliefs such as self-efficacy and motivation or distorting perceptions about medication importance and potential impact of taking all prescribed medications. Alternatively, higher levels of positive medication beliefs may buffer the risks associated with depressive symptoms and promote resilience in CF management. For example, an individual who believes that her medications will improve her lung health or is confident that she can stick with a demanding regimen despite experiencing negative affect or low energy may be protected against the deleterious effects of depressive symptoms and be more consistent in her adherence.

The finding that adherence increased with a higher number of prescribed medications is paradoxical to the common lore that greater regimen complexity is associated with lower adherence. This finding, however, is consistent with previous research in a large sample of

people with CF (Quittner et al., 2014). This may reflect the confound between regimen complexity and illness severity; as CF severity increases (i.e., more frequent pulmonary exacerbations), more medications are added to preserve lung function. Similarly, CF providers recognize the immense treatment burden and may focus on optimizing adherence to the current regimen before adding new medications. That no other demographic variable was associated with adherence is also not surprising in the context of previous findings: Quittner et al. (2014) found no differences in adherence by age, except among the youngest children, and found gender differences only for azithromycin but not for any other pulmonary medications.

The model representing the opposite direction of causality, from suboptimal adherence to elevated depressive symptoms via less positive medication beliefs, demonstrated equivalent fit, limiting the ability to determine causation. An equally plausible interpretation of these findings is that poor health and lower levels of positive medication beliefs contribute to depressive symptoms (Sacco et al., 2007). It is possible that individuals with a history of poor adherence may develop less positive beliefs about their ability to adhere to prescribed medications and the health benefits of adherence, which may generalize to more global feelings of discouragement, frustration, and depressed mood. Given the potential for fluctuations in mood, beliefs, and adherence behaviors over time, it is likely that there are bidirectional relations among these variables that could not be adequately evaluated in a cross-sectional study.

Given the growing life expectancy for people with CF and the known decline in adherence and lung function in adolescence and adulthood, this is a critically important time for CF management (Quon & Aitken, 2012; Tuchman et al., 2010). The current findings indicate an indirect association between depressive symptoms and medication adherence that is in part explained by medication beliefs, all of which may fluctuate over the life span. Yet, age was not significantly related to any of the key study variables, suggesting the possibility that associations among depressive symptoms, medication beliefs, and adherence behaviors may be relevant across adulthood. However, given the mortality rates, individuals with CF in middle to older adulthood are underrepresented in research, making conclusions about this age range difficult. Given the critical nature of medication adherence for CF management, results suggest that these issues should be addressed as a routine part of CF care.

Routine monitoring of depressive symptoms and medication beliefs may be warranted. Clinic-based screening for depression is consistent with the recommendations of the U.S. Prevention Services Task Force (2009) and may be beneficial for early identification and treatment of individuals at elevated risk not only for depressive symptoms, but also at risk for nonadherence to prescribed pulmonary medications. Compared with monitoring depressive symptoms, there has been less emphasis on engaging patients in conversations about their thoughts and feelings about their health and treatment recommendations during routine CF clinic visits. Along with depression screening, regular conversations about patients' medication beliefs likely need to occur throughout the life span to address barriers to adherence and prevent problems. In addition to alerting providers about possible nonadherence, identifying highly negative or pessimistic medication beliefs or decreases in positive medication beliefs could also be indicative of more general emotional distress that

requires further evaluation and possibly treatment. Free depressive symptoms screening measures are widely available (<http://www.cesd-r.com>; <http://www.phqscreeners.com>), and the medication beliefs measure used in this study is available on request from the authors.

This study's evidence of medication beliefs as one mechanism linking depressive symptoms and suboptimal adherence highlights medication beliefs as a potential point of intervention to promote adherence. Results suggest that to be maximally effective adherence-promotion interventions should move beyond providing illness education and problem-solving counseling to include tailored content to address individuals' beliefs and perceptions about their prescribed medications and address negative mood. Indeed, clinical interventions that target either depression (Lustman & Clouse, 2002; Safren et al., 2009) or positive beliefs about medication or health (Fumaz et al., 2012; Jacobs et al., 2004; Rawl et al., 2012) have shown promising results in terms of changing beliefs, lifting mood, increasing health behaviors, and/or improving health outcomes in other chronic illness populations. However, the potential synergy of targeting both depressive symptoms and medication beliefs together has not yet been tested. Depression treatment may impact adherence in part by influencing medication beliefs, and nonjudgmental patient-provider conversations about medication beliefs may help providers to understand and validate patients' concerns while also correcting misconceptions and promoting optimal levels of adherence. With its emphasis on empowering behavior change through patient-centered discussion of patients' experiences, goals, and beliefs, motivational interviewing is one therapeutic strategy that may be particularly well suited for this purpose (Borrelli, Riekert, Weinstein, & Cardella, 2007). Integrating motivational interviewing with established depression treatment approaches (Safren et al., 2009) has the potential to enhance the impact on health behavior by targeting both influences on adherence together.

Implications of the study should be considered in the context of methodological strengths and limitations. Measurement strategies, including the established measure of depressive symptoms and objective measure of adherence via medication refill records, lend strength to the study. In lieu of using a multimethod adherence assessment including self-report, a single objective measure was used for this study. The cMPR was selected as an objective assessment of adherence across a range of prescribed pulmonary medications because self-reported adherence has been shown to be highly inaccurate among people with CF (Daniels et al., 2011), and pharmacy-based adherence measures have been recommended for use above self-reported adherence data (McMahon et al., 2011). Furthermore, the cMPR has been found to be associated with CF health outcomes (Eakin et al., 2011) and health care utilization (Quittner et al., 2014), suggesting that it is a valid construct. Yet, it is possible that adherence rates may have over- or underestimated actual medication ingestion. Pharmacy refill data can only underestimate adherence if there is a failure to identify all refills obtained. Given that many CF medications are dispensed through specialty pharmacies and are quite expensive, accurate recall and reporting of pharmacies used in the previous year are likely. Pharmacy refill data can overestimate adherence rates because obtaining a refill does not ensure that it is ingested. However, the adherence rates seen in the current sample are similar to those obtained via electronic monitors (Daniels et al., 2011) and are much lower than self-reported rates, suggesting that they are likely not overestimates. The study focused on pulmonary medication adherence and not other aspects

of the regimen including nutrition and airway clearance. Previous CF literature shows no differences in adherence between inhaled and noninhaled medications (Eakin et al., 2011; Quittner et al., 2014). We did not have specific hypotheses about predicting adherence to particular classes of medications, but rather were interested in predicting overall adherence across a range of medications, so we averaged across all prescribed medications rather than examine different medication types. Further research is needed to evaluate whether the associations found here are replicated when looking at other regimen components.

The medication beliefs measurement builds on previous research emphasizing the importance of self-efficacy (Cha et al., 2008; Cherrington et al., 2010; Schoenthaler et al., 2009) and broadens the assessment to measure more components of Social Cognitive Theory (Bandura, 1986) including motivation and importance. The cross-sectional nature of these analyses limits the ability to draw definitive conclusions about the directionality of the relationships among variables or about causality. The sample characteristics were skewed toward those with private insurance status, employment, and education, and represent moderate CF-related health status, typical of the U.S. CF population (Cystic Fibrosis Foundation, 2013). Finally, although conclusions can be drawn only about the role of medication beliefs among individuals with CF, the concepts likely generalize to other complex chronic conditions and add to the growing body of literature in this area.

In sum, the indirect association between higher depressive symptoms and lower CF medication adherence is mediated by less positive medication beliefs including lower self-efficacy, lower motivation, less perceived importance of medications, and more negative outcome expectancies related to taking prescribed medications. Early screening for depression paired with routine discussions about medication beliefs may help providers identify at-risk individuals and promote positive beliefs and adaptive health behaviors. The overarching goal of this line of research is to guide prevention and intervention strategies that reduce burden, enhance self-management, and ultimately improve CF management and health outcomes.

Acknowledgments

This work was funded by the National Institutes of Health (National Heart, Lung and Blood Institute, Grant 5R01HL087997, PI: Kristin A. Riekert). The authors gratefully acknowledge the contributions and support of the faculty and staff of the Johns Hopkins University CF Clinic, the staff of the Johns Hopkins Adherence Research Center, and Cynthia Rand, as well as all of the study participants.

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Figure 1. Structural equation mediation model linking depressive symptoms with pulmonary medication adherence via medication beliefs, controlling for number of prescribed pulmonary medications, with standardized coefficients. $^{**}p < .01$.

Table 1

Sample Clinical and Behavioral Characteristics (N = 128)

Clinical index	Mean $\pm$ SD	n (%)
Lung function (FEV ₁)	63.7 $\pm$ 23.3%	
Mild (70%)		62 (48.4)
Moderate (40–70%)		51 (39.8)
Severe (40%)		15 (11.7)
Body mass index (BMI)	22.7 $\pm$ 3.8	
Males meeting recommended BMI (23)		29 (42.7)
Females meeting recommended BMI (22)		25 (41.7)
Number of prescribed pulmonary medications (possible range: 1–6)	3.8 $\pm$ 1.5	
cMPR	0.44 $\pm$ 0.27	
Depressive symptoms, total score (possible range: 0–60)	10.8 $\pm$ 9.2	
Exceeding clinical cutoff (16)		30 (23.4)
Medication belief scale scores (possible range)		
Self-efficacy (1–10)	6.9 $\pm$ 2.0	
Motivation (1–10)	7.3 $\pm$ 2.4	
Importance (1–10)	8.3 $\pm$ 1.9	
Outcome expectancies (1–5)	2.8 $\pm$ 0.5	

Note. FEV₁ = forced expiratory volume in 1 s, measure of lung function and cystic fibrosis (CF) severity, categories from CF Foundation guidelines (Cystic Fibrosis Foundation, 2013); BMI = body mass index, indicator of health status in CF, categories from CF Foundation (Stallings, Stark, Robinson, Feranchak, & Quinton, 2008); cMPR = composite medication possession ratio, measure of overall adherence to CF pulmonary medications. Medication belief scale scores: Higher scores indicate more positive beliefs.

Table 2

Bivariate Correlations Among Depressive Symptoms, Health Beliefs, Medication Adherence (cMPR), and Demographic and Clinical Characteristics

Variable	1	2	3	4	5	6	7	8	9
1. Depressive symptoms									
2. Self-efficacy	-.31**								
3. Motivation	-.27**	.62**							
4. Importance	-.19*	.65**	.75**						
5. Outcome expectancies	-.17	.43**	.41**	.41**					
6. cMPR	-.22*	.51**	.41**	.40**	.22*				
7. Age	.02	.04	.15	.22*	-.12	-.04			
8. BMI	.04	-.03	-.09	-.04	-.18*	-.09	.50**		
9. FEV ₁	-.01	.00	-.19*	-.17	-.09	.03	-.19*	.28**	
10. Number of medications	-.08	.31**	.37**	.33**	.15	.25**	.02	-.20*	-.40**

Note. cMPR = composite medication possession ratio; BMI = body mass index; FEV₁ = forced expiratory volume in 1 s.

* $p < 0.05$.

** $p < 0.01$.