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## SCREENING FOR SYMPTOMS OF DEPRESSION AND ANXIETY IN ADOLESCENTS AND YOUNG ADULTS WITH CYSTIC FIBROSIS

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### Summary

**Background**—Although studies have assessed symptoms of depression and anxiety in individuals with cystic fibrosis (CF), few have been conducted since the advent of new medical treatments (e.g., nebulized antibiotics, ThAIRpy Vest). Study objectives were to: 1) document symptoms of depression and anxiety for adolescents and young adults with CF and compare with normative values, 2) examine the associations among depressive/anxiety symptoms and gender, age, lung function, and body mass index, and 3) determine the relations between adolescent and caregiver symptoms of depression and anxiety.

**Methods**—Patients and caregivers completed the Hospital Anxiety and Depression Scale (HADS) anytime (e.g. beginning or end) during routine CF clinic appointments.

**Results**—Participants included 59 adolescents/young adults with CF ( $M_{age} = 15.8$  years, 54% female, 98% Caucasian,  $M_{FEV1 \% predicted} = 84.6$ ) and caregivers of 40 adolescents. Although symptom scores were in the normative range for patients with CF ( $M_{Depression} = 2.27$  and  $M_{Anxiety} = 5.59$ ), 3% and 32% exhibited clinically elevated symptoms of depression and anxiety, respectively. Symptoms of depression and anxiety were significantly associated with age ( $r = 0.28$ ,  $0.36$ ). Symptoms of depression and anxiety were also positively correlated ( $r = 0.48$ ). Females endorsed higher anxiety symptoms than males. While adolescent and caregiver anxiety scores

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were not related, higher caregiver depressive symptoms were associated with older patient age and worse lung function.

**Conclusions**—Data from the current study suggest low levels of depressive symptoms and substantial levels of anxiety symptoms in adolescents and young adults with CF. Consistent with prior literature, depressive symptoms appear higher in older patients and are significantly associated with anxiety symptoms. Caregiver symptomology appears to be more affected by an adolescent's health status, suggesting a need to screen caregivers when health begins to decline.

### Keywords

depression; anxiety; psychosocial; gender; adolescents; young adults; caregivers

## Introduction

Cystic fibrosis (CF) is a progressive, multi-system pulmonary disease, affecting approximately 30,000 individuals in the United States<sup>1</sup>. Living with CF, which requires adhering to a complex and time-consuming treatment regimen, affects health-related quality of life<sup>2-3</sup> and places patients at increased risk for depression<sup>4-5</sup>. Depression is a common psychiatric diagnosis, with lifetime prevalence rates of 10% in adolescence<sup>6</sup> and 16.6% in adults<sup>7</sup>. Prior studies, which have limitations, suggest that rates of depression in adolescents and adults with CF are significantly higher than those of the general population, ranging from 11–14.5%<sup>8-9</sup> for youth and 29%–46%<sup>8,10</sup> for adults. Furthermore, subclinical symptoms of depression (e.g. scores lower than clinical cut-offs for screening measures) have important implications and are associated with psychosocial dysfunction, functional impairment, and future episodes of major depression in the general population<sup>11</sup>. However, little is known about the continuum of symptoms of depression for individuals with CF.

A recent report by the US Preventive Services Task Force (USPSTF) recommended the routine screening of adolescents for depression within primary care settings<sup>12</sup>. Given that CF teams often see patients with CF on a quarterly basis, it seems reasonable that this type of screening could be conducted within routine CF clinical care. The early screening and identification of depressive symptoms is important because studies have shown that age of onset is decreasing. Furthermore, once a depressive episode is experienced, the likelihood of relapse is high<sup>13</sup>, placing children and adolescents at increased risk throughout their lifetime. Depression also impedes adherence to medical regimens<sup>14</sup>, thereby potentially increasing morbidity in patients with CF. Similarly, increased depressive symptoms are associated with poorer lung function in children and adults with CF<sup>2,15</sup>. Thus, routine screening of depressive symptoms during clinical encounters could result in earlier detection, further assessment, and intervention.

Given the high comorbidity between depression and anxiety<sup>16-19</sup>, assessment of anxiety symptoms is also important<sup>5</sup>. Some studies suggest normative levels of anxiety in adolescents<sup>15</sup> and adults<sup>20</sup> with CF, whereas others indicate clinical elevations<sup>8,21</sup>. Unlike depression, low/moderate levels of anxiety may serve as a protective factor for long-term health. Specifically, recent evidence suggests that adherence is higher for patients with CF exhibiting anxiety symptoms<sup>21</sup>. Given the USPSTF recommendations, one goal of the current study was to use a single screening measure to assess self-reported symptoms of depression and anxiety in patients with CF during routine clinic visits.

Limitations of prior studies of depression and anxiety in CF include use of measures/interviews that incorporated overlapping symptoms of depression and physical symptoms of CF (e.g., somatic items such as fatigue or loss of appetite)<sup>21</sup>, restricted age ranges, and assessments that occurred before the development of new CF therapies (e.g., ThAIRapy

vest, inhaled antibiotics) in the United States<sup>8-9</sup>. The latter point is especially salient because it is unclear how the additional burden of new treatments affects symptoms of depression and anxiety. For example, the initiation of inhaled antibiotics and mucolytics may increase treatment time by 20–30 minutes and decrease recreation<sup>22</sup>, which may lead to less interaction with peers. In contrast, treatment benefits could reduce physical symptoms and morbidity (e.g., pulmonary exacerbations), resulting in improved overall physical and psychological health.

Finally, mothers of children/adolescents with chronic illnesses are at increased risk for depression<sup>23</sup> with high rates in caregivers of children with CF between birth and 18 years of age (e.g., 36–44%)<sup>24</sup>. Research has demonstrated that children of depressed caregivers are at increased risk for depression compared to children of non-depressed caregivers<sup>25</sup>. In addition, caregiver depressive symptoms have been linked to poor health outcomes for adolescents with other pediatric conditions, including asthma<sup>26</sup> and diabetes<sup>27</sup>. These children are also more likely to exhibit broad psychosocial impairments in adulthood (e.g., anxiety)<sup>28</sup>. This intergenerational association of symptoms of depression and anxiety has not been studied in CF.

The objectives of this study were to: 1) document symptoms of depression and anxiety for individuals with CF (< 12 years) and compare with norms, 2) examine differences in symptoms of depression and anxiety by sex, age, and lung function, and 3) determine the association between adolescent and caregiver symptoms of depression and anxiety. Adolescents and young adults with CF were expected to report more symptoms of depression and anxiety compared to normative data. It was hypothesized that symptoms of depression and anxiety would be higher for individuals with more severe lung disease and for those who were older and female. Furthermore, a strong positive association was expected between patient- and caregiver-reported symptoms of depression and anxiety.

## Methods and Materials

### Participants and Procedure

Adolescents and young adults with CF ( $n=59$ ) receiving outpatient care at Cincinnati Children's Hospital Medical Center (CCHMC) CF Center participated in the current study. These data were part of a larger international study aimed at assessing depressive and anxious symptoms in youth and adults with CF and their caregivers ([www.Tides-CF.org](http://www.Tides-CF.org)), for which CCHMC served as a pilot site to establish feasibility of study procedures. It is important to note that CCHMC data will not be included in the larger study results. Recruitment rate for this study was 95%. Demographic and medical data are presented in Table 1. This study was approved by the CCHMC Institutional Review Board.

A convenience sample of adolescents/young adults with CF and their caregivers who attended CF clinic visits between September 2006 to November 2008 were approached for study participation. The CF Team social worker obtained adult patient/caregiver informed consent and adolescent assent. Questionnaires were then independently completed by the adolescents/young adults and, when applicable, their caregivers at any time during their clinical encounter regardless of when they received their FEV<sub>1</sub>% (forced expiratory volume in 1 second) predicted results. Caregivers completed a demographic questionnaire and depression/anxiety screening measures, while adolescents/young adults completed one depression/anxiety screening measure. Questionnaires took approximately 15 minutes to complete and were scored upon completion. If moderate to severe symptoms were endorsed, mental health referrals were provided if desired. Health status indicators (e.g., FEV<sub>1</sub>% predicted, body mass index (BMI)) were extracted from medical records.

## Measures

**Hospital Anxiety and Depression Scale**—The (HADS)<sup>29</sup> – The HADS is a 14-item instrument which assesses the cognitive symptoms of depression and anxiety. This measure is specifically used with chronic illness samples to reduce the overlap of somatic symptoms of depression/anxiety with disease-related symptoms. The HADS has excellent reliability, validity, sensitivity and specificity in individuals with and without medical conditions. Current study coefficient alphas were 0.60 and 0.79 for patient symptoms of depression and anxiety, respectively. Participants were categorized as having clinically elevated symptoms based on established clinical cut-off scores of greater than 7<sup>29</sup>. Scores between 0–7 represent normal symptom levels, 8–10 mild symptoms, 11–14 moderate symptoms, and 15–21 severe symptoms.

**Health indicators**—Forced expiratory volume predicted in one second (FEV<sub>1</sub>% predicted) was obtained from the medical chart and was based on Wang and Hankinson equations. Illness severity ratings were based on established cutoffs for FEV<sub>1</sub> % predicted values: normal ( ≥ 90%), mild (70%–89%), moderate (40%–69%), and severe ( < 39%) disease. Weight and height data were used to calculate body mass index (BMI in kg/m<sup>2</sup>).

## Statistical Analyses

Descriptive data (e.g., means, standard deviations) were calculated for adolescent/young adults and caregiver HADS scores, as well as demographic and medical variables. Z-tests were conducted to compare HADS scores of adolescents/adults with CF to normative data for a healthy population<sup>30</sup>. Controlling for pulmonary functioning, one-way analysis of variance was used to examine sex differences on patient HADS scores. Pulmonary functioning was controlled for because prior studies have demonstrated gender differences in health outcomes<sup>31–32</sup>, as well as significant associations between pulmonary functioning and symptoms of depression<sup>2</sup>. Finally, Pearson correlations were used to examine relations among patient depressive and anxious symptoms, age, pulmonary functioning, and caregiver symptoms of depression and anxiety. All analyses were conducted using SPSS 16.0.

## Results

### Descriptive Data and Normative Values

Descriptive data are presented in Table 1. Overall, means for both symptoms of depression and anxiety were within the normal range. Compared to normative data<sup>30</sup>, z-tests revealed fewer depressive symptom scores ( $z = -4.94$ ,  $p < 0.0001$ ) in individuals with CF and no significant differences in anxiety ( $z = -1.14$ ,  $p = \text{n.s.}$ ). Three percent of adolescents/young adults had clinically elevated depressive symptoms in the mild range ( $n=2$ ) while 32% exhibited clinically elevated anxiety symptoms (Mild: 25%,  $n=15$ ; Moderate: 5%,  $n=3$ ; Severe: 2%,  $n=1$ ).

Caregivers of adolescents also exhibited mean scores within the normal range for HADS depressive ( $z = -1.70$ ,  $p = \text{n.s.}$ ) and anxiety ( $z = 0.26$ ,  $p = \text{n.s.}$ ) symptom scores. However, 10% had clinically elevated HADS depressive symptoms (Mild: 8%,  $n=3$ ; Moderate: 2%,  $n=1$ ; Severe: 0%), and 35% had clinically elevated HADS anxiety symptoms (Mild: 25%,  $n=10$ ; Moderate: 8%,  $n=3$ ; Severe: 2%,  $n=1$ ).

### Relations among patient HADS scores, demographic/health status variables, and caregiver HADS scores

**Patient Depressive Symptoms**—After controlling for FEV<sub>1</sub> % predicted, no significant sex differences were found on the HADS depression scale ( $F(1, 56) = 0.49$ ,  $p = \text{n.s.}$ ;

estimated marginal means:  $M_{\text{females}} = 2.47$  vs.  $M_{\text{males}} = 2.10$ ). A significant correlation was observed between age and HADS depressive scores ( $r = 0.36$ ; See Table 2). Patient HADS depressive scores were also significantly positively correlated with HADS anxiety scores ( $r = 0.48$ , See Table 2). Patient HADS depressive symptom scores were not associated BMI or caregiver HADS scores; however, a negative trend was noted with FEV<sub>1</sub> % predicted.

**Patient Anxiety Symptoms**—Significant sex differences were found for HADS anxiety scores ( $F(1, 56) = 7.34, p = 0.009$ ; estimated marginal means:  $M_{\text{females}} = 6.92$  vs.  $M_{\text{males}} = 4.47$ ), after controlling for FEV<sub>1</sub> % predicted. Age was also significantly correlated with HADS anxiety scores ( $r = 0.28$ , See Table 2). Patient HADS anxiety symptom scores were not associated with BMI, FEV<sub>1</sub> % predicted, or caregiver HADS scores.

**Caregiver symptoms of depression and anxiety**—Caregiver HADS Depressive symptom scores were significantly associated with their adolescent's age ( $r = 0.36$ ) and pulmonary functioning ( $r = -0.52$ ). Specifically, older adolescents and those with lower pulmonary functioning had caregivers with higher depressive symptoms. A negative trend was also noted between caregiver anxiety symptoms and FEV<sub>1</sub> % predicted. A strong correlation was found between caregiver symptoms of depression and anxiety ( $r = 0.67$ ; See Table 2).

## Discussion

Results from this pilot study indicated low rates of depressive symptoms in adolescents and young adults with CF (3%). These rates are lower than previous studies and could be influenced by improved physical symptoms and psychological functioning (e.g., depressive symptoms) as a result of advances in CF treatment. The low prevalence rate of clinically elevated depressive symptoms precluded the ability to adequately examine relations with pulmonary functioning. However, the larger literature suggests a negative cumulative impact of both depressive symptoms and severe lung disease on daily functioning<sup>2</sup>. A positive trend was also noted for age, which is consistent with both the general depression<sup>6-7</sup> and CF<sup>8</sup> literature. Finally, prior studies examining depressive symptoms in CF have used measures that include somatic items that overlap with symptoms of CF, which likely contributes to prevalence discrepancies for adolescents/adults with CF. This may be a key reason that individuals in our sample reported lower HADS depressive symptoms. Furthermore, the finding that symptoms of depression were significantly lower than normative data was surprising. However we recognize that several key variables associated with symptoms of depression, were not accounted for in the current study and may help to explain this finding. For example, it is possible that our participants had high levels of social support, which could have served as a buffer for increased symptoms of depression<sup>33-34</sup>. This is an important area for future research.

In contrast to depressive symptoms, symptoms of anxiety in our sample were consistent with prior literature, with 32% reporting mild to severe symptoms. Prior literature has demonstrated there may be a healthy level of anxiety which promotes optimal adherence<sup>21</sup>, suggesting that anxiety may play an adaptive role in disease management. This needs to be further explored in adolescent and young adult populations with CF. In contrast to the potential positive impact of anxiety on adherence, there is also evidence suggesting that anxiety precedes depression and that childhood anxiety predicts the onset of later episodes of major depression<sup>35</sup>. Thus, it may be that rates of anxiety in our sample are higher than that of depression because the latter has yet to develop. To answer this question of sequential (i.e., one disorder precedes the other) and cumulative (i.e., both disorders occur during one's lifetime) comorbidity of anxiety and depression in CF, longitudinal prospective studies assessing these disorders are necessary. Regardless of the temporal relations between

depression and anxiety and consistent with prior research<sup>16-19</sup>, a significant association was found between symptoms of depression and anxiety in adolescents and young adults with CF.

Data from the extant literature suggest that depressive symptoms increase as patients with CF grow older. Although the ideal age to begin screening for depression is yet to be determined, these data suggest that screening is necessary. Screening for depression is warranted during adolescence since the prevalence increases during this developmental period when health status also typically begins to decline due to the progressive nature of the disease. This is also consistent with recent USPSTF recommendations regarding depression screening for adolescents in the general population<sup>12</sup>. Our data also revealed that females exhibit significantly higher levels of anxiety symptoms than males. This gender difference could be due to anxiety related to more frequent lung infections<sup>36</sup> and decreased life expectancy for females compared to males<sup>31</sup>. Future research focused on the CF-specific factors that result in higher levels of anxiety in females with CF seems warranted.

Finally, results indicated that caregivers of adolescents with CF exhibited clinically-elevated depressive (10%) and anxiety (35%) symptoms, with a strong association noted between symptoms. While the relation between caregiver and adolescent symptoms of depression and anxiety was non-significant, it appears that the adolescent's lung function and age were associated with caregiver depressive symptoms. Specifically, it is possible that concerns about their adolescent's progressive illness and transition to adulthood may increase caregiver symptomology. This is especially salient during the adolescent-young adulthood developmental period where increases in autonomy and independence combined with decreased parental supervision of the treatment regimen<sup>37</sup> may serve to exacerbate caregiver symptoms of depression and anxiety.

Several limitations of the current study are noteworthy. First, we did not control for the timing of questionnaire completion. It is possible that either the anticipation or awareness of current pulmonary functioning test results led to higher or lower symptom endorsement. Therefore, investigation of the impact of FEV<sub>1</sub> % predicted results on the immediate reporting of symptoms in future studies is necessary. Second, longitudinal studies are needed as the cross-sectional nature of these data prohibits conclusions about causality and the long-term impact of symptoms. Finally, it is unclear whether the use of a somatic-symptom free measure (e.g., HADS) is the most appropriate for adolescents/young adults with CF. Research has suggested that due to disease and depressive symptom overlap, somatic items should be omitted<sup>4-5</sup>. However, it is unclear whether physical symptoms of depression precede physical symptoms of CF or vice versa. Without longitudinal studies to clarify which occurs first, it remains unclear whether measures with (e.g., Beck Depression Inventory<sup>38</sup>) or without somatic items are better for assessing depression. A recent study reported that depressive symptom levels did not differ when somatic items were included compared to when they were removed using the same instrument<sup>2</sup>.

In summary, adolescents and young adults with CF in this study reported low levels of symptoms of depression and anxiety. However, a subset of individuals with CF demonstrated clinically elevated symptoms that may be in need of intervention. This subsample, as well as caregivers with elevated symptoms of anxiety and depression would benefit from recommendations, such as further assessment and treatment for symptoms of depression<sup>12</sup> and anxiety. Thus, screening for symptoms of depression and anxiety appears warranted for patients with CF and caregivers of adolescents, especially as adolescents transition into adulthood.

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## Abbreviations

<b>BMI</b>	body mass index
<b>CF</b>	cystic fibrosis
<b>FEV<sub>1</sub></b>	forced expiratory volume in 1 second
<b>HADS</b>	hospital anxiety and depression scale
<b>USPSTF</b>	US Preventive Services Task Force

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**Table 1**

## Demographic characteristics

	Mean (SD)	Percentage (n)
<b>Patient Characteristics (N = 59)</b>		
Age in years	15.77 (2.5)	
Sex		
Male		n = 32 (54%)
Female		n = 27 (46%)
Race		
Caucasian		n = 58 (98%)
African American		n = 1 (2%)
Body Mass Index	20.16 (2.7)	
FEV <sub>1</sub> % Predicted	84.56 (25.2)	
Disease Severity		
Normal ( 90)		n = 30 (50.8%)
Mild (70–89)		n = 15 (25.4%)
Moderate (40 – 69)		n = 10 (16.9%)
Severe ( 39)		n = 4 (6.8%)
Type of Visit		
Well/Routine Visit		n = 52 (88%)
Sick Visit		n = 7 (12%)
Currently taking antidepressants and or in therapy *		n = 8 (14.5%)
HADS score – Depressive Symptoms	2.27 (2.1)	
HADS score - Anxiety Symptoms	5.59 (3.6)	
<b>Caregiver Characteristics (n=40)</b>		
Age in years	43.18 (5.5)	
Caregiver Sex		
Male	10%	n = 4 (10%)
Female	90%	n = 36 (90%)
Currently taking antidepressants/in therapy **		n = 11 (28%)
HADS score – Depressive Symptoms	2.85 (3.1)	
HADS score - Anxiety Symptoms	6.30 (3.8)	

\* n=4 incomplete data;

\*\* n=1 incomplete data

**Table 2**  
Correlations between patient HAD scores, caregiver HADS scores, demographic and health status variables

Patient (n=59)	1	2	3	4	5	6	7
1. Age	---						
2. FEV <sub>1</sub> %	-0.65***	---					
3. BMI	0.19	0.07	---				
4. HADS-Depressive Symptoms	0.36**	-0.23 <sup>†</sup>	0.06	---			
5. HADS-Anxiety Symptoms	0.28*	-0.12	0.01	0.48***	---		
<b>Primary Caregiver (n=40)</b>							
6. HADS-Depressive Symptoms	0.36*	-0.52***	-0.05	0.11	0.08	---	
7. HADS-Anxiety Symptoms	0.23	-0.27 <sup>†</sup>	-0.11	-0.14	-0.09	0.67***	---

Note.

<sup>†</sup> p < .10 (trend),

\* p < .05,

\*\* p < .01,

\*\*\* p < .001.