The Social Environment and Illness Uncertainty in Chronic Obstructive Pulmonary Disease

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Abstract

Purpose—Illness uncertainty is associated with worse outcomes in patients with chronic health conditions. Research on social factors associated with uncertainty has focused on the beneficial role of social support. The goal of this study was to develop a more nuanced understanding of the social factors that are associated with uncertainty.

Methods—462 individuals with alpha-1 antitrypsin deficiency (AATD) associated chronic obstructive pulmonary disease (COPD) completed a mailed questionnaire. Measures of the social environment included general family functioning, perceived criticism from family members, whether the participant had family members with AATD or COPD, and participation in support groups. Uncertainty was measured using the Mishel Uncertainty in Illness Scale including

subscales for ambiguity (uncertainty about physical cues and symptoms) and complexity (uncertainty about treatment and the medical system). Hierarchical regression was used to identify social correlates of ambiguity and complexity while adjusting for demographic and medical characteristics and psychological distress.

Results—Perceived criticism was associated with more complexity (b=0.21, SE=0.09, p=0.015) and ambiguity (b=0.40, SE=0.12, p=0.001). Having a family member with AATD or COPD was associated with more ambiguity (b=3.28, SE=1.00, p=0.001). Participation in support groups was associated with less ambiguity. Individuals who attended three or more support groups in the prior year reported less ambiguity than individuals who had not attended any (b=−3.31, SE=1.29, p=0.010).

Conclusions—The social environment is complex and encompasses more than social support. Multiple aspects of the social environment are associated with uncertainty, including perceived criticism, having a family member with a similar illness, and participation in support groups.

Keywords

Introduction

Uncertainty about prognosis and symptoms is inherent in living with a chronic health condition. Uncertainty in Illness Theory [1, 2] describes how patients assign meaning to information about their illness. This theory defines uncertainty as a cognitive state in which a person is unable to categorize the meaning of illness-related experiences. Uncertainty has typically been treated as a unitary construct, although theory states that illness uncertainty is multifaceted. The most frequently-used measure of illness uncertainty, the Mishel Uncertainty in Illness Scale (MUIS), has been examined psychometrically with the most robust scoring method comprised of two subscales: 1) *ambiguity:* a cognitive state in which "cues about the state of the illness are vague and indistinct and tend to blur together and overlap," and 2) *complexity:* a cognitive state in which "cues about the treatment and the system of care are multiple, intricate and varied" [3](pages 8–9). Thus, ambiguity focuses on interpretation of physical cues and symptoms, while complexity focuses on the treatment system.

Given the value placed on predictability in Western culture, uncertainty is viewed as aversive because it disrupts an individual's sense of control. Research consistently indicates that greater uncertainty is associated with more symptoms of depression and anxiety and reduced quality of life in a variety of chronic illnesses [4–9]. Uncertainty has also been associated with worse physical symptoms (i.e., pain and fatigue) in cross sectional samples [4, 10]. Prospective research indicates that uncertainty is associated with worse shortness of breath over a two-year period among individuals with chronic obstructive pulmonary disease [6]. Two studies that treated uncertainty as a multifaceted construct found that ambiguity had a stronger association than complexity with a range of outcomes, including anxiety,

depression, quality of life, and physical symptoms [4, 6] suggesting that it is advisable to examine ambiguity and complexity separately.

Given that illness uncertainty is associated with worse emotional and physical symptoms, it is important to understand factors that are associated with uncertainty. Uncertainty in Illness Theory has identified social support as an important influence on uncertainty [2]. According to theory, social support helps individuals make sense of their medical situation. For example, interacting with others who have had similar experiences is thought to provide an opportunity to gather information that can increase familiarity with the illness. Consistent with theory, research has found that higher scores on measures of social support are associated with less uncertainty [11–16]. However, not all social contact is experienced as being supportive, and dissatisfaction with social interactions has been associated with greater illness uncertainty [17]. To more fully understand how the social environment is associated with uncertainty, it is necessary to include a broad range of measures that capture the quality and type of social interaction that the patient experiences.

The aim of the current study was to develop a more nuanced understanding of the association between the social environment and uncertainty. Illness uncertainty and the social environment were examined in a sample of patients with alpha-1 antitrypsin deficiency (AATD) associated chronic obstructive pulmonary disease (COPD). Our research team has previously demonstrated that illness uncertainty (specifically ambiguity) is prospectively associated with depression, anxiety, shortness of breath, and worse quality of life in this sample [6].

COPD is a progressive disease characterized by airflow limitation and associated with a combination of small airways disease, airway inflammation, and parenchymal destruction in the lung [18]. The most common symptom of COPD is shortness of breath, and patients often also experience exercise limitation, chronic cough, and sputum production. Airflow obstruction in COPD is not fully reversible necessitating a focus on treating symptoms to reduce disability and improve patients' quality of life. COPD is a leading cause of morbidity and mortality in the world [18, 19]. COPD typically has a gradually progressive course punctuated by unpredictable exacerbations. The primary behavioral risk factor for COPD is smoking [18] and the primary known genetic risk factor is alpha-1 antitrypsin deficiency (AATD), an autosomal co-dominant disorder that predisposes individuals to lung and liver disease [20]. Patients with AATDassociated COPD are clinically similar to patients with non-AATD COPD except they typically develop COPD at a younger age and a subset has the option to use augmentation therapy, which increases levels of alpha-1 antitrypsin circulating in the blood and lungs [21]. The experience of individuals with AATD-associated COPD provides a rich context in which to examine the impact of the social environment on uncertainty in chronic illness. Patients with COPD are often assumed to have restricted social contact and support due to limitations caused by COPD that result from shortness of breath and exercise limitations.

The current study measured multiple aspects of the social environment. Quality of family relationships was assessed via measures of general family functioning and perceived criticism from family members. These aspects of family relationships have been associated

with psychological distress, shortness of breath, and worse quality of life among patients with COPD [22–24]. It was hypothesized that better general family functioning would be associated with less uncertainty, while perceived criticism from family members would be associated with greater uncertainty. Exposure to other individuals with similar health problems was also examined. Given that AATD is a genetic condition, patients with AATD-associated COPD are likely to have a family member with AATD or COPD. Patients may also participate in support groups for individuals with AATD. Both types of exposure to "experientially similar others" [25] were expected to be associated with less uncertainty.

Methods

Participants and Procedures

The protocol was approved by the Institutional Review Boards at National Jewish Health and the Medical University of South Carolina. All data were collected via de-identified questionnaires that were mailed to adult members of the Alpha-1 Foundation Research Registry [26] with physician-diagnosed COPD who were residing in the US and Canada. Due to the fact that data were collected via de-identified questionnaires that posed no more than minimal risk to participants, this study was granted a waiver of documentation of informed consent. The overarching aim of the larger study was to examine social and perceptual factors that affect adjustment in AATD-associated COPD.

Questionnaires were mailed to 1727 people and were returned by 621 people (a 36% response rate). Individuals were excluded from analyses if they indicated that they did not have COPD (n = 22) or had missing data for variables used in analyses (n = 137). To be included in analyses individuals must have provided complete data for all predictors and at least one of the uncertainty subscales. Responses from 462 individuals were used in analyses.

Measures

Illness Uncertainty—Uncertainty was measured with the Mishel Uncertainty in Illness Scale for Adults (MUIS-A [3]). The MUIS-A includes subscales for ambiguity and complexity. The ambiguity subscale has 16 items that are rated on a 5-point scale from 1 (strongly disagree) to 5 (strongly agree). Scores can range from 16 to 80, and a higher score indicates more ambiguity. Items address cues about the state of the illness, such as being able to determine whether the illness is getting better or worse, the extent to which symptoms change unpredictably, and the extent to which being able to plan for the future is difficult due to unpredictability of the illness. Cronbach's alpha in the current sample was 0.88.

The complexity subscale has 12 items that are rated on a 5-point scale from 1 (strongly disagree) to 5 (strongly agree). Scores can range from 12 to 60, and a higher score indicates more complexity. Items address cues about treatment and the system of care, such as whether the purpose of treatment is clear, the effectiveness of treatment is known, results of tests are consistent, and whether providers communicate clearly and can be depended on. Cronbach's alpha in the current sample was 0.79.

Measures of the Social Environment—General family functioning was measured by the 12-item General Functioning subscale of the Family Assessment Device (FAD). The FAD has been used in studies of medical illness [27–30] including COPD [23, 24]. Questions address aspects of family relationships such as the extent to which family members express feelings with each other, feel accepted by each other, and confide in each other. Each item has four response categories, ranging from 1 (strongly agree) to 4 (strongly disagree). Reponses are averaged so scores for general family functioning can range from 1 to 4, with higher scores indicating less healthy family functioning. Cronbach's alpha was 0.90 in the current sample.

Perceived criticism from family members was measured with the criticism subscale of the Family Emotional Involvement and Criticism Scale (FEICS), which was developed to assess the respondent's overall perception of criticism by the family in primary care patients [31, 32]. The criticism subscale of the FEICS consists of 7 items that are rated on a scale from 1 (almost never) to 5 (almost always). Scores for the subscale can range from 7 to 35, with higher scores indicating more criticism. Items assess critical behaviors such as trying to get the respondent to change and complaining about what the respondent does for fun. Cronbach's alpha was 0.73 in the current sample.

Two measures of exposure to experientially similar others were calculated: whether any family members had been diagnosed with AATD or COPD, and participation in support groups. Respondents indicated whether any of their family members had been diagnosed with AATD or COPD. Responses were coded to indicate no exposure to experientially similar others in the family (i.e., no family members had been diagnosed with AATD or COPD) versus any exposure to experientially similar others in the family (i.e., at least one family member had been diagnosed with AATD and/or COPD). With regard to participation in support groups, respondents reported the number of times in the past 12 months they had attended alpha-1 support groups or educational meetings. Responses were coded to indicate participation in zero groups/meetings, 1–2 groups/meetings, or 3 or more groups/meetings in the past 12 months.

Covariates—The questionnaire included items to assess age, gender, and highest level of education completed. These variables were included as covariates in analyses to adjust for basic patient characteristics. In addition, variables that measure behavioral (i.e., lifetime tobacco exposure) and genetic (i.e., AATD genotype) risk for COPD were included as covariates in analyses. Lifetime tobacco exposure in pack years was calculated as average number of cigarette packs smoked per day times number of years smoked. With regard to genotype, individuals with an AATD genotype comprised of two severely deficient alleles are considered "severely deficient," and individuals with a genotype comprised of only one severely deficient allele are considered "not severely deficient" and are often referred to as "carriers." Genotype was categorized as severely deficient (ZZ, SZ, FZ, P-Null, Z-Null, ZPlowell, ZMmalton, and ZMheerlen), not severely deficient (MZ, MS, M-Null, and SS), or unknown.

Respondents reported the number of years since they were diagnosed with COPD, whether they were currently using oxygen for their COPD, and whether they had ever used

augmentation therapy. Three questions were used to assess exacerbations in the prior year. These questions assessed the number of times in the prior year the respondent had experienced an increase in symptoms of COPD that resulted in: 1) a prescription for antibiotics, 2) a prescription for oral steroids, and 3) a hospital admission. A single variable was created to indicate whether each respondent reported a zero for all three variables (i.e., no exacerbations), at least one exacerbation that resulted in antibiotics and/or steroids but no hospitalization, or at least one exacerbation that resulted in a hospitalization.

Depression and anxiety were included in the regression models as covariates because they are likely to confound the association of the predictors of interest (i.e., social environment) with uncertainty. Depression and anxiety have consistently been associated with uncertainty [4–9], with depression and anxiety typically considered to be outcomes of higher uncertainty. Depression and anxiety are likely also associated with measures of the social environment. Symptoms of depression and anxiety were measured by the Hospital Anxiety and Depression Scale [33]. The HADS was designed for use with medical patients; as such, items focus on mood disturbance rather than physical symptoms that could be attributed to chronic illness. The HADS subscales for depression and anxiety each have 7 items that are answered on a 4-point scale, and subscale scores range from 0 to 21, with higher scores indicating more symptoms of depression and anxiety. Cronbach's alpha was 0.82 for depression and 0.86 for anxiety in the current sample.

Data Analysis

Data were analyzed using SPSS Version 21. Characteristics of the sample were summarized using means and standard deviations for continuous variables and number and percentage of participants for categorical variables. Correlation analysis was performed to examine associations between depression, anxiety, measures of the social environment, and uncertainty. Two hierarchical linear regression models were used to examine the association between the social environment and uncertainty: one model for ambiguity, and one for complexity. In both models, demographic and medical characteristics were entered as a first step (i.e., age, gender, education, lifetime tobacco exposure, genotype, number of years since COPD diagnosis, oxygen use, augmentation therapy use, and exacerbations in the prior year). Symptoms of depression and anxiety were entered as a second step. The measures of the social environment were added as a third step to examine the extent to which the social environment is associated with uncertainty after adjusting for: 1) demographic and medical characteristics and 2) depression and anxiety. Significance tests were two-sided with a significance level of 0.05.

Results

Characteristics of Participants

Individuals with COPD who were removed from the sample due to missing data were compared to individuals who were included in analyses. The two groups were compared on every independent variable included in the regression models, as well as on ambiguity and complexity. The two groups did not differ with regard to any of these variables (p > 0.05) with the exception of age and AATD genotype. Individuals who were removed from the

sample were older ($t_{(df = 597)}$ = 2.12, p = 0.035, M (SD) = 61.4 (9.8) years old if removed from the sample and 59.3 (9.9) years old if included in analyses). The percentage of individuals who did not know their genotype was higher in the group that was removed from the sample ($\chi^2_{(df = 2)}$ = 6.83, p = 0.033, 15.3% if removed from the sample versus 9.1% if included in analyses).

Characteristics of the sample are in Table 1. Nearly half of the sample was female and the mean age was just under 60. Almost one third of the sample (30.1%) had never smoked and the vast majority of the sample (83.5%) had a severely deficient genotype. The average length of time since diagnosis was 12 years; as such, this sample largely reflects the experiences of individuals who have been living with COPD for more than a decade. Nearly three quarters of the sample (71.9%) had a family member who also had AATD or COPD. Nearly two thirds of the sample (64.3%) had not participated in any support groups or educational meetings in the prior year.

The mean score for ambiguity was 36.2 and the mean score for complexity was 25.6. Compared to a sample of hospitalized COPD patients using the same measure [34] the degree of perceived complexity was similar but the degree of perceived ambiguity was slightly less in the current outpatient sample.

Correlations

Table 2 presents results of the bivariate correlations. General family functioning and perceived criticism were significantly correlated with depression and anxiety. In addition, people who participated in fewer support groups or educational meetings in the prior year were more likely to report higher levels of depression. The measures of the social environment consistently had significant correlations with uncertainty. Uncertainty was also correlated with depression and anxiety, with correlation coefficients that indicate that depression and anxiety have a stronger association with uncertainty than do the measures of the social environment. The correlation between ambiguity and complexity was 0.68, which indicates that the percent of shared variance is 46%. As such, the two components of uncertainty are related to but distinct from each other.

Results of Hierarchical Linear Regression Models

Ambiguity—Table 3 presents results of the hierarchical linear regression model for ambiguity. The change in R^2 was statistically significant at all three steps. This indicates that depression and anxiety make a significant contribution to the model for ambiguity after adjusting for demographic and medical characteristics, and the measures of the social environment make a significant contribution after adjusting for depression and anxiety in addition to the demographic and medical characteristics. The overall model at Step 3 was statistically significant ($F_{(20, 429)}$ = 10.43, p < .001). The adjusted R^2 at Step 3 was .30, indicating that the model accounts for 30% of the variance in ambiguity. Three of the four measures of the social environment had a statistically significant association with ambiguity. Individuals reported more ambiguity if they reported more perceived criticism from family members (b = 0.40, SE = 0.12, p = 0.001). Individuals also reported more ambiguity if they had a family member who had been diagnosed with AATD or COPD (b = 3.28, SE = 1.00, p

= 0.001). Participation in support groups and educational meetings was associated with less ambiguity. Compared to individuals who had not participated in any support groups or educational meetings in the prior year, individuals who had participated in three or more had an ambiguity score that was 3.31 points lower on average (b = −3.31, SE = 1.29, p = 0.010).

Complexity—Table 4 presents results of the hierarchical linear regression model for complexity. The change in R^2 was statistically significant at all three steps. This indicates that depression and anxiety make a significant contribution to the model for complexity after adjusting for demographic and medical characteristics, and the measures of the social environment make a significant contribution after adjusting for depression and anxiety in addition to the demographic and medical characteristics. The overall model at Step 3 was statistically significant ($F_{(20, 434)}$ = 4.92, p < .001). The adjusted R^2 at Step 3 was .15, indicating that the model accounts for 15% of the variance in complexity. Consistent with the findings for ambiguity, perceived criticism was associated with complexity. Individuals reported more complexity if they reported more perceived criticism from family members (b = 0.21, SE = 0.09, p = 0.015).

Discussion

The primary goal of the current study was to develop a more nuanced understanding of the association between the social environment and uncertainty among a sample of patients with AATD-associated COPD. Perceived criticism from family members was associated with more ambiguity (i.e., uncertainty about physical cues and symptoms) and complexity (i.e., uncertainty about treatment and the medical system). This finding is consistent with a prior study that found an association between dissatisfaction with social interactions and greater uncertainty among individuals with systemic sclerosis [17]. Unsupportive interactions (such as criticism) may lead patients to feel that members of their social system are not available to provide support, or worse, may indicate that members of their social system are more a source of stress than support. This may make it difficult for patients to interpret and manage fluctuations in their symptoms and navigate the medical system. Future research should attempt to elucidate how unsupportive social interactions contribute to high illness uncertainty.

Having a family member with AATD or COPD was associated with greater ambiguity, while participation in support groups/educational meetings was associated with less ambiguity. Leaders of support groups and educational meetings may guide interactions in the group to ensure that accurate medical information is clearly conveyed, which serves to decrease ambiguity for participants. In contrast, family members with the same illness may share inaccurate or conflicting medical information, have a difficult time supporting other patients in their family, or discuss personal experiences that serve to increase ambiguity. Future research should examine the quality of support and information provided by family members and support groups to better understand the current findings.

Ambiguity and complexity are related but distinct components of uncertainty. Research suggests that ambiguity has a stronger association than complexity with outcomes such as quality of life, psychological distress, and physical symptoms [4, 6]. The current study

suggests that different factors drive the experience of each component of uncertainty. While perceived criticism was associated with both ambiguity and complexity, participation in support groups and having a family member with AATD or COPD were associated with ambiguity but not complexity. A greater percentage of the variance in ambiguity was accounted for in the regression models (30% for ambiguity versus 15% for complexity). Less than half of the variance in either component of uncertainty was accounted for in the current study. While perceived criticism has a statistically significant association with ambiguity and complexity after accounting for depression, anxiety, and other covariates, further research is needed to learn about the clinical significance of this association. This study identified novel aspects of the social environment that are associated with uncertainty, however, additional correlates of uncertainty remain to be identified. Quality of relationships with medical providers, type and quality of information provided by medical staff, and aspects of the medical system may be particularly salient for complexity [1] and should be the focus of additional research. There is a growing body of literature, in populations other than COPD, that documents the negative impact of loneliness on health, including morbidity and mortality [35–38]. Future studies would benefit from including measures of social isolation and loneliness.

Illness uncertainty is a cognitive state that is associated with worse outcomes in patients with a variety of chronic health conditions. This cognitive state is potentially modifiable. In fact, interventions have been developed to help patients with various medical conditions learn strategies for managing illness uncertainty [39–41]. Research that focuses on understanding the role of the social environment in illness uncertainty is highly relevant to these interventions. For example, individuals with unsupportive social networks may have the greatest need for these interventions. In addition, these interventions may be more effective at reducing illness uncertainty if they address aspects of the social environment that contribute to high uncertainty. Future research should examine how the social environment moderates and mediates the effectiveness of interventions to help patients manage illness uncertainty.

This study has several limitations. Objective measures of COPD severity were not included because all data were collected via self-report questionnaires. Oxygen use was included in the regression models as a proxy for disease severity, but airflow limitation was not objectively quantified. There was a 36% initial response rate, and some individuals who returned the questionnaire were excluded from analyses due to missing data. A comparison of individuals who were included to those who were excluded indicated that the two groups differed with regard to only 2 of the 17 variables used in these analyses. The percentage of individuals who did not know their genotype was higher in the group that was removed from the sample due to missing data. This may reflect an underlying lack of commitment, both to knowing their genotype and to completing a questionnaire focused on their health condition.

An important limitation is the cross-sectional nature of the study, which makes it impossible to rule out the alternative direction of association. For example, it is possible that people with greater uncertainty avoided support groups/educational meetings. The cross-sectional design also precludes an examination of the extent to which the social environment, psychological distress (i.e., depression and anxiety), and uncertainty influence each other.

The social environment is correlated with psychological distress, and both the social environment and psychological distress are correlated with uncertainty. Longitudinal research is needed to disentangle the likely complex and bidirectional nature of the relations among these variables.

A primary strength of this study is that it provides a more nuanced focus on the social context than previous research. Results indicate that perceived criticism, participation in support groups, and the presence of a family member with a similar illness are associated with the degree of uncertainty that patients experience. Findings are based on a large, geographically diverse sample of patients who have been diagnosed with the third leading cause of death in the US. Given that patients had, on average, been diagnosed more than a decade prior to participating in this study, results contribute to understanding factors associated with uncertainty among patients who have lived with their chronic illness for many years.

Acknowledgements

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Table 1

Characteristics of the Sample (N=462)

Variable	Mean (SD)	N (%)
Age (years)	59.3 (9.9)	
Gender (male)		237 (51.3)
Highest Level of Education Completed		
Grade 12 or less		133 (28.8)
College 1 to 3 years		176 (38.1)
College graduate or more		153 (33.1)
Race/ethnicity		
Caucasian non-Hispanic		453 (98.7)
Black non-Hispanic		2 (0.4)
Hispanic		3 (0.7)
Other		1 (0.2)
Lifetime Tobacco Exposure		
Never smoked		139 (30.1)
1 to 20 pack years		166 (35.9)
More than 20 pack years		157 (34.0)
Genotype		
Severely deficient		386 (83.5)
Not severely deficient		34 (7.4)
Unknown		42 (9.1)
Number of Years since COPD Diagnosis		12.0 (7.6)
Oxygen Use		247 (53.5)
Augmentation Therapy Use		364 (78.8)
Exacerbations in Prior Year		
None		92 (19.9)
Medications but no hospitalizations		298 (64.5)
Exacerbation requiring hospitalization		72 (15.6)
Symptoms of Depression	5.5 (3.6)	
Symptoms of Anxiety	6.6 (4.1)	
General Family Functioning	1.7 (0.6)	
Perceived Criticism	10.1 (4.1)	
Family Member with AATD and/or COPD		332 (71.9)
Participation in Prior Year		
None		297 (64.3)
1–2 support groups/meetings		86 (18.6)
3 or more support groups/meetings		79 (17.1)
Ambiguity Score	36.2 (11.0)	
Complexity Score	25.6 (7.0)	

Table 2

Bivariate Correlations between Psychosocial Variables[†]

	1	2	3	4	5	6	7	8
1 Symptoms of Depression	—	.62[**]	.27[**]	.20[**]	-.03	-.15[**]	.42[**]	.27[**]
2 Symptoms of Anxiety		—	.30[**]	.30[**]	.05	-.05	.43[**]	.25[**]
3 General Family Functioning			—	.45[**]	.11[*]	-.01	.23[**]	.18[**]
4 Perceived Criticism				—	.05	.02	.27[**]	.21[**]
5 Family with AATD and/or COPD					—	.07	.14[**]	.10[*]
6 Participation in Prior Year						—	-.13[**]	-.10[*]
7 Ambiguity							—	.68[**]
8 Complexity								—

[†]
Pearson correlation coefficient is reported for the association between two interval variables

Point-biserial correlation coefficient is reported for the association between a dichotomous and an interval variable

Spearman's rho correlation coefficient is reported for the association between an ordinal and an interval variable

Rank-biserial correlation coefficient is reported for the association between a dichotomous and an ordinal variable

[*]
Correlation is significant at the p 0.05 level (2-tailed)

[**]
Correlation is significant at the p 0.01 level (2-tailed)

Table 3

Results of Hierarchical Linear Regression Model to Predict Ambiguity

Predictors	Step 1: b (SE), p	Step 2: b (SE), p	Step 3: b (SE), p
Age (year)	0.003 (0.06), 0.954	0.12 (0.05), 0.034	0.16 (0.05), 0.004
Gender			
Male	Reference	Reference	Reference
Female	−1.07 (1.04), 0.304	−1.88 (0.95), 0.049	−1.56 (0.93), 0.096
Education			
Grade 12 or less	5.52 (1.33), < 0.001	4.10 (1.21), 0.001	3.77 (1.18), 0.002
College 1 to 3 years	3.05 (1.23), 0.014	2.58 (1.11), 0.021	2.48 (1.08), 0.023
College grad or more	Reference	Reference	Reference
Lifetime Tobacco Exposure			
Never smoked	Reference	Reference	Reference
1 to 20 pack years	−0.63 (1.36), 0.645	−1.47 (1.23), 0.231	−1.29 (1.20), 0.280
More than 20 pack years	−1.89 (1.36), 0.167	−2.31 (1.23), 0.060	−1.92 (1.20), 0.111
Genotype			
Severely deficient	Reference	Reference	Reference
Not severely deficient	4.63 (2.29), 0.044	2.18 (2.07), 0.293	1.80 (2.03), 0.375
Unknown	0.68 (1.80), 0.707	−1.02 (1.63), 0.530	−1.48 (1.61), 0.362
Number of Years since COPD Diagnosis	−0.15 (0.07), 0.041	−0.16 (0.07), 0.014	−0.17 (0.06), 0.010
Oxygen Use			
No	Reference	Reference	Reference
Yes	2.28 (1.13), 0.044	0.97 (1.05), 0.357	0.95 (1.04), 0.364
Augmentation Therapy Use			
No	Reference	Reference	Reference
Yes	−1.10 (1.49), 0.462	−1.44 (1.35), 0.287	−0.33 (1.35), 0.810
Exacerbations in Prior Year			
None	Reference	Reference	Reference
Meds but no hospitalizations	2.78 (1.31), 0.034	0.73 (1.19), 0.539	1.23 (1.18), 0.297
Exacerbation requiring hospitalization	5.04 (1.75), 0.004	1.62 (1.61), 0.314	1.87 (1.59), 0.239
Symptoms of Depression		0.55 (0.17), 0.001	0.52 (0.17), 0.002
Symptoms of Anxiety		0.87 (0.15), < 0.001	0.72 (0.15), < 0.001
General Family Functioning			0.65 (0.91), 0.472
Perceived Criticism			0.40 (0.12), 0.001
Family with AATD and/or COPD			
No			Reference
Yes			3.28 (1.00), 0.001
Participation in Prior Year			
None			Reference
1–2 support groups/meetings			−0.29 (1.22), 0.810
3 or more support groups/meetings			−3.31 (1.29), 0.010

Predictors	Step 1: b (SE), p	Step 2: b (SE), p	Step 3: b (SE), p
Change Statistics			
R^2	0.11	0.28	0.33
Change in R^2	0.11	0.17	0.05
Significance of Change in R^2	< 0.001	< 0.001	< 0.001
Adjusted R^2	0.08	0.26	0.30

Table 4

Results of Hierarchical Linear Regression Model to Predict Complexity

Predictors	Step 1: b (SE), p	Step 2: b (SE), p	Step 3: b (SE), p
Age (year)	0.02 (0.04), 0.643	0.06 (0.04), 0.090	0.08 (0.04), 0.035
Gender			
Male	Reference	Reference	Reference
Female	−0.10 (0.67), 0.887	−0.38 (0.65), 0.561	−0.21 (0.65), 0.753
Education			
Grade 12 or less	2.28 (0.85), 0.008	1.65 (0.82), 0.046	1.53 (0.82), 0.062
College 1 to 3 years	1.73 (0.79), 0.030	1.48 (0.76), 0.053	1.47 (0.75), 0.052
College grad or more	Reference	Reference	Reference
Lifetime Tobacco Exposure			
Never smoked	Reference	Reference	Reference
1 to 20 pack years	−0.42 (0.87), 0.626	−0.75 (0.83), 0.372	−0.80 (0.83), 0.336
More than 20 pack years	−1.15 (0.87), 0.188	−1.38 (0.84), 0.101	−1.32 (0.84), 0.113
Genotype			
Severely deficient	Reference	Reference	Reference
Not severely deficient	0.37 (1.45), 0.800	−0.33 (1.39), 0.812	−0.52 (1.39), 0.710
Unknown	0.48 (1.16), 0.678	−0.16 (1.12), 0.890	−0.20 (1.13), 0.856
Number of Years since COPD Diagnosis	−0.07 (0.05), 0.146	−0.08 (0.05), 0.097	−0.08 (0.05), 0.093
Oxygen Use			
No	Reference	Reference	Reference
Yes	0.05 (0.72), 0.944	−0.72 (0.72), 0.320	−0.67 (0.73), 0.358
Augmentation Therapy Use			
No	Reference	Reference	Reference
Yes	−3.09 (0.93), 0.001	−3.13 (0.90), 0.001	−2.71 (0.92), 0.003
Exacerbations in Prior Year			
None	Reference	Reference	Reference
Meds but no hospitalizations	0.37 (0.83), 0.653	−0.45 (0.81), 0.578	−0.16 (0.81), 0.839
Exacerbation requiring hospitalization	2.36 (1.12), 0.036	0.86 (1.10), 0.435	1.01 (1.11), 0.364
Symptoms of Depression		0.34 (0.12), 0.004	0.32 (0.12), 0.007
Symptoms of Anxiety		0.29 (0.10), 0.004	0.21 (0.10), 0.048
General Family Functioning			0.73 (0.63), 0.245
Perceived Criticism			0.21 (0.09), 0.015
Family with AATD and/or COPD			
No			Reference
Yes			1.04 (0.70), 0.138
Participation in Prior Year			
None			Reference
1–2 support groups/meetings			−0.16 (0.85), 0.848
3 or more support groups/meetings			−1.03 (0.89), 0.251

Predictors	Step 1: b (SE), p	Step 2: b (SE), p	Step 3: b (SE), p
Change Statistics			
R^2	0.08	0.16	0.19
Change in R^2	0.08	0.08	0.03
Significance of Change in R^2	< 0.001	< 0.001	0.017
Adjusted R^2	0.05	0.13	0.15