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The Impact of Age on Outcomes in Chronic Obstructive Pulmonary Disease Differs by Relationship Status

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Abstract

Alpha-1 antitrypsin deficiency (AATD) is a genetic condition that can lead to early-onset chronic obstructive pulmonary disease (COPD). The objective of this study was to examine the impact of age on psychological and clinical outcomes among individuals with AATD-associated COPD. 468 individuals with AATD-associated COPD (age 32 to 84 at baseline) completed questionnaires at baseline, 1- and 2-year follow-up. Age was examined as a predictor of depression, anxiety, health-related quality of life, and breathlessness at all three time points using linear mixed models. Age was associated with anxiety ($b = -0.09$, $SE = 0.02$, $p < 0.001$) and health-related quality of life ($b = -0.29$, $SE = 0.09$, $p < 0.001$). Age also had a statistically significant interaction with relationship status when predicting depression, health-related quality of life, and breathlessness. Among individuals who were single, younger age was associated with more symptoms of depression ($b = -0.08$, $SE = 0.03$, $p < 0.01$), worse health-related quality of life ($b = -0.61$, $SE = 0.16$, $p < 0.001$), and more breathlessness ($b = -0.023$, $SE = 0.009$, $p < 0.01$) throughout the two-year study. Age was not associated with these three outcomes among individuals who were married/part of an unmarried couple. Results suggest that individuals who develop a chronic illness at a young age, particularly those who are single, may be more likely to have worse psychological and clinical outcomes.

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Keywords

Age; Relationship Status; Chronic Obstructive Pulmonary Disease; Depression; Anxiety; Clinical Outcomes

Introduction

Timing of illness is a central component of the experience of living with a chronic illness. Older individuals are more likely than younger individuals to expect illness as a normative part of aging (Lazarus & DeLongis, 1983). The diagnosis of a chronic illness before or during middle age can be described as “off-time” with regard to the anticipated life cycle (Neugarten, 1976, 1979), and can be extremely disruptive to pursuing a career and raising a family. As such, age is likely to be associated with adjustment to chronic illness, with younger individuals having more difficulty adjusting to illness than older individuals.

Individuals with alpha-1 antitrypsin deficiency (AATD) associated chronic obstructive pulmonary disease (COPD) are an ideal population in which to study the impact of illness timing. AATD is a genetic cause of COPD, and individuals with severe AATD are at risk for developing early-onset COPD. COPD is commonly diagnosed after the age of 45, and is usually considered a disease of the elderly. Individuals with AATD can develop COPD of similar severity at younger ages. The primary risk factor among individuals with severe AATD is personal smoking (Mayer et al., 2006). Smokers with severe AATD can develop COPD as early as their 20s, but individuals with a less severely deficient AATD genotype who have minimal exposure to risk factors will develop COPD in their 60s or 70s, if at all (Ioachimescu & Stoller, 2005; Silverman & Sandhaus, 2009). Individuals who develop COPD at the younger end of the age spectrum are likely to experience challenges related to pursuing careers and raising families. In one survey of individuals with AATD, 15.8% of respondents with a severely deficient genotype reported losing a job, 19.1% reported changing to a physically easier job, and 44.4% reported retiring early due to AATD. The mean age of these individuals was less than 50 years (Stoller et al., 1994).

COPD is the third leading cause of death in the United States (Kochanek et al., 2011). It is an incurable disease that typically has a gradually progressive course. The primary symptom is breathlessness. Because COPD is incurable, treatment focuses on reducing breathlessness and maintaining quality of life. Patients with AATD-associated COPD are clinically similar to patients with non-AATD COPD except that they are likely to be younger when they are diagnosed with COPD and a subset has an additional treatment option available (i.e., augmentation therapy—a treatment to increase levels of alpha-1 antitrypsin). AATD is a genetic condition that increases the risk of lung disease (Sandhaus, 2004). Although a minority of individuals with AATD-associated COPD is aware of their genetic risk prior to diagnosis of COPD, most individuals learn about their AATD during the process of diagnosis and treatment for COPD. In a recent study of more than 3000 individuals with COPD who did not have prior knowledge of their AATD status, 0.63% were found to have a severely deficient AATD genotype and 10.88% had a mildly deficient or carrier AATD genotype (Rahaghi et al., 2012).

Several studies have reported that younger patients with COPD report more symptoms of depression and anxiety (Al-shair et al., 2009; Cleland et al., 2007; Felker et al., 2001; van Manen et al., 2001) and worse quality of life than older patients with COPD (Campos, Alazemi, Zhang, Salathe, et al., 2009; Mangueira et al., 2009; Moy et al., 2009). This is consistent with research in a variety of chronic illnesses that indicates that younger age is associated with more psychological distress (Cassileth et al., 1984; Hinz et al., 2011; Hughson et al., 1988; Jamison et al., 1978; Schrag et al., 2003; Starkstein et al., 1989; Vinokur et al., 1989) and worse quality of life (Ganz et al., 1992; Schrag et al., 2003). Most studies have been cross-sectional and have not focused on the association of age with patient report of physical symptoms such as breathlessness. Further, the impact of age on patient outcomes may differ based on educational and social resources. It is likely that the impact of age is greatest among individuals with fewer resources. Psychosocial interventions can target the individuals who are most in need if we can identify characteristics of individuals for whom young age poses a greater risk for negative outcomes.

The current study examines the impact of age on psychological and clinical outcomes over a two-year period in a sample of more than 450 individuals with AATD-associated COPD. Data were collected through the Alpha-1 Foundation Research Registry, which provided an opportunity to gather data from a large sample of individuals with a broad range of experience related to illness timing (i.e., age at COPD diagnosis ranged from 25 to 80 in this sample). The study had two objectives. The primary objective was to determine the association of age with symptoms of depression and anxiety, quality of life, and breathlessness. We hypothesized that being younger is associated with worse outcomes. The secondary objective was to determine whether the impact of age differs based on educational and social resources. We hypothesized that the impact of age is stronger among individuals with fewer educational and social resources. This study extends prior research by examining the impact of age on four patient-centered outcomes, including the primary physical symptom experienced by individuals with COPD (i.e., breathlessness). In addition, this study moves beyond prior cross-sectional research by prospectively measuring patient outcomes over a two-year period. Finally, this study is the first to try to identify subgroups of individuals with AATD-associated COPD for which age may be particularly important.

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 (Alpha-1 Foundation, 2012) with physician-diagnosed COPD who were residing in the United States and Canada. Due to the fact that data were collected via de-identified questionnaires, this study was granted a waiver of informed consent. The overarching aim of the study was to examine social and perceptual factors that affect adjustment in AATD-associated COPD.

Baseline questionnaires were mailed to 1727 people and were returned by 621 people. Follow-up data were collected each year for the subsequent two years by mailing

questionnaires to all 621 individuals who had returned the baseline questionnaire. Individuals were excluded from analyses for the following reasons: indicating that they did not have COPD (n=22), death during the course of the study (n=27), lung transplant during the course of the study (n=7), returning only the baseline questionnaire (n=68), and missing data for variables used in analyses (n=29). To be included in analyses, individuals need to have provided complete data for all predictors used in the linear mixed models, and data at a minimum of two time points for at least one of the dependent variables. Responses from 468 individuals were used in analyses.

Measures

Demographic and Health Characteristics—Collected demographic information at baseline included age, number of years since COPD was diagnosed, gender, relationship status, education, income, race, and ethnicity. Relationship status was categorized as single (divorced/separated, widowed, or never married) versus coupled (married or member of an unmarried couple). Lifetime tobacco exposure in pack years was calculated as average number of cigarette packs smoked per day times number of years smoked. AATD 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. Participants reported whether they were currently using oxygen for their COPD and whether they had ever undergone augmentation therapy (a treatment to increase levels of alpha-1 antitrypsin circulating in the blood and lungs). Participants also indicated their age at AATD diagnosis, which was used to determine whether AATD was diagnosed prior to COPD.

Psychological Outcomes of COPD—*Symptoms of depression and anxiety* were measured at baseline and in both follow-up questionnaires by the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). 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 can range from 0 to 21. Higher scores indicate more symptoms of depression and anxiety. Cronbach's alpha in the current sample for the depression subscale was .79, .79, and .81 for the three time points. Cronbach's alpha for the anxiety subscale was .84, .86, and .86 for the three time points.

Clinical Outcomes of COPD—*Health-related quality of life* was measured at baseline and in both follow-up questionnaires by the Saint George's Respiratory Questionnaire (SGRQ), a 50-item scale designed for use in patients with airflow limitation (Barr et al., 2000; Jones et al., 1992). Items are summed and weighted to create a total score that can range from 0 to 100, with a higher score indicating worse health-related quality of life. Cronbach's alpha in the current sample was .93, .94, and .94 for the three time points.

Breathlessness was measured at baseline and in both follow-up questionnaires by the Modified Medical Research Council Dyspnea Scale (MMRC) (Fletcher et al., 1959), a 5-point grading scale to measure shortness of breath that is predictive of 5-year survival among patients with COPD (Nishimura et al., 2002). The score can range from 1 to 5, with a higher score indicating more breathlessness.

Data Analysis

Data were analyzed using SAS 9.3. Baseline demographic and health characteristics of the sample were summarized using means and standard deviations for continuous variables and number and percentage of participants for categorical variables. Linear mixed models (PROC MIXED) were used to address the primary and secondary objectives. These models account for the correlation within participants over time and also permit inclusion of participants with partially missing outcome data. Participants needed to have valid data for an outcome at a minimum of two time points to be included in analyses for that outcome. On average, 68% of the 468 participants who were included in analyses provided valid data at all three time points for the outcomes. Several combinations of random effects for subjects and error covariance structures were examined and compared using the Akaike Information Criterion, a goodness-of-fit statistic that can be used to compare models to determine which model has a better fit. The best overall fit was an unstructured error covariance structure without a random intercept or random time effect, and thus was used for all reported analyses. An unstructured error covariance structure allows the variance at each wave of data collection and the covariance between waves of data collection to be different. Models were fit using restricted maximum likelihood estimation. For all analyses, significance tests were two-sided with a significance level of 0.05.

For the primary objective of determining the association of age with psychological and clinical outcomes, four linear mixed models were fit: one to predict symptoms of depression, one for symptoms of anxiety, one for health-related quality of life, and one for breathlessness. Age at baseline was the predictor of interest, and all models adjusted for the following covariates measured at baseline: number of years since COPD was diagnosed, gender, relationship status, highest level of education completed, lifetime tobacco exposure, genotype, oxygen use, and augmentation therapy use. All models also included a fixed effect for time (treated as a categorical variable). All covariates were chosen *a priori* based on patient characteristics that are likely to be associated with the psychological and clinical outcomes. These models test the effect of age after accounting for the effect of all covariates.

The secondary objective was to determine whether the impact of age differs based on educational and social resources. For each dependent variable, two additional models were fit that included an interaction term (for a total of 8 additional linear mixed models). All of these models included all predictors used when testing the primary objective, with the addition of interactions for: 1) age with highest level of education completed (using the same three categories as in Table 1), and 2) age with relationship status (using the same two categories as in Table 1).

Results

Characteristics of Participants

Individuals with COPD who were removed from the sample due to death, lung transplant, returning only the baseline questionnaire, and missing data were compared to individuals who were included in analyses. The two groups did not differ with regard to age at baseline,

number of years since COPD was diagnosed, gender, relationship status, highest level of education completed, lifetime tobacco exposure, or whether they had ever undergone augmentation therapy ($p > 0.05$). However, the percentage of individuals on oxygen at baseline (which is a proxy for severity of COPD) was higher in the group that was removed from the sample ($\chi^2_{(df=1)} = 10.71$, $p = 0.001$, 64.3% if removed from the sample versus 48.1% if included in analyses). When the two groups were compared on each outcome at baseline using t-tests, individuals who were removed from the sample reported more depression ($t_{(df=173)} = 3.76$, $p < 0.001$, M (SD) = 6.8 (4.2) if removed from the sample and 5.2 (3.5) if included in analyses), anxiety ($t_{(df=176)} = 4.05$, $p < 0.001$, M (SD) = 8.0 (4.7) if removed from the sample and 6.2 (3.9) if included in analyses), impairment in health-related quality of life ($t_{(df=578)} = 4.13$, $p < 0.001$, M (SD) = 54.9 (20.8) if removed from the sample and 46.9 (18.6) if included in analyses), and breathlessness ($t_{(df=183)} = 3.88$, $p < 0.001$, M (SD) = 3.3 (1.3) if removed from the sample and 2.8 (1.1) if included in analyses). Overall, these comparisons indicate that individuals with more severe COPD and worse outcomes were more likely to be removed from the sample.

Demographic and health characteristics of the sample at baseline are in Table 1. Mean age at baseline was 60. As expected, the age range was very broad—from 32 to 84. Participants had been diagnosed with COPD an average of 12 years prior to baseline. Slightly more than three-quarters of the sample was either married or a member of an unmarried couple. Nearly half of the sample was using oxygen for their COPD. Among the individuals who were using oxygen, the mean length of time they had been using oxygen was 6.5 years and half were prescribed oxygen 24 hours per day. Approximately one quarter of the sample was aware of their genetic risk prior to developing COPD.

Description of Outcomes

The sample means for all outcomes were quite stable over time (see Table 2). With regard to psychological outcomes, the mean depression score was just above 5.0 at all three time points and the mean anxiety score ranged from 5.8 to 6.2. This indicates that, on average, the individuals in this sample reported a low level of depression and anxiety. With regard to clinical outcomes, mean scores for health-related quality life life and breathlessness were both slightly below the midpoint of possible scores on their respective instruments at all three time points. The mean scores for health-related quality life life were consistent with two prior studies that have used the same instrument to examine health-related quality of life among individuals with AATD-associated COPD in other cohorts (Campos, Alazemi, Zhang, Wanner, Salathe, et al., 2009; Campos, Alazemi, Zhang, Wanner, & Sandhaus, 2009).

Results of Linear Mixed Models

Primary Objective—As seen in Table 3, age at baseline was prospectively associated with anxiety ($b = -0.09$, $SE = 0.02$, $p < 0.001$) and health-related quality of life ($b = -0.29$, $SE = 0.09$, $p < 0.001$). Younger age was associated with more symptoms of anxiety and worse health-related quality of life throughout the two-year study. Results can be interpreted as follows: in the model for anxiety, on average a one-year increase in age at baseline is associated with a 0.09-point decrease on the anxiety scale after adjusting for all covariates.

Secondary Objective—The association between age and outcomes may be stronger among individuals with fewer educational and social resources. In all four models that tested whether the impact of age differs based on highest level of education completed, the interaction term that allowed the effect of age to differ based on education was not significant ($p > 0.05$). This indicates that the impact of age on depression, anxiety, health-related quality of life, and breathlessness does not differ based on highest level of education completed.

In three of the four models that tested whether the impact of age differs based on relationship status, the interaction term was significant (see Table 4). When predicting depression, health-related quality of life, and breathlessness, age was associated with the outcome among individuals who were single, but was not associated with the outcome among individuals who were part of a couple. For example, in the model for depression, on average a one-year increase in age at baseline is associated with a 0.08-point decrease on the depression scale among individuals who are single. This association between age and depression among single participants is significant at $p < 0.01$. Among individuals who are in a couple relationship, on average a one-year increase in age at baseline is associated with only a 0.01-point decrease on the depression scale. This association between age and depression among participants in a couple relationship is not significant ($p = 0.67$). The interaction of age with relationship status was not significant in the model for anxiety ($p = 0.59$). Individuals who were younger reported more symptoms of anxiety, regardless of whether they were single or in a couple relationship. These analyses indicate that, with the exception of anxiety, age is associated with worse outcomes among individuals who are single but not among individuals who are in a couple relationship.

Post-Hoc Analyses—Given that relationship status moderates the effect of age for three of the four outcomes, post-hoc analyses were conducted to better understand the association between age and relationship status. A t-test that examined the association between age and relationship status indicated that individuals who were single did not differ from individuals who were in a couple relationship with regard to age ($t_{(df=466)} = 0.24$, $p = 0.81$, M (SD) = 59.7 (10.6) if single and 60.0 (9.4) if in a couple relationship). However, the association of age with relationship status differed by gender. Single men were younger, on average, than men who were in a couple relationship ($t_{(df=230)} = 3.12$, $p < 0.01$, M (SD) = 56.2 (9.9) if single and 61.3 (9.0) if in a couple relationship). In contrast, single women were older, on average, than women who were in a couple relationship ($t_{(df=234)} = 2.27$, $p = 0.02$, M (SD) = 61.8 (10.4) if single and 58.5 (9.6) if in a couple relationship). In addition, a chi-squared test indicated that gender is associated with relationship status ($\chi^2_{(df=1)} = 8.49$, $p < 0.01$). Among individuals who are single, there is a higher percentage of women (63.1%) than men (36.9%).

Gender is associated with relationship status, and the association of age with relationship status differs by gender. Gender may also influence the interaction of age with relationship status—for example, age may be associated with worse outcomes only among women (or men) who are single. To examine this possibility, the three-way interaction of gender, age, and relationship status was investigated by fitting four additional linear mixed models: one for each dependent variable. All of these models included all predictors used when testing

the secondary objective, with the addition of interaction terms that should be included when testing the interaction of gender, age, and relationship status (i.e., these models added terms for the interaction of gender with age, gender with relationship status, and gender with age with relationship status). In all four models, all new interaction terms were not significant, including the interaction of gender with age with relationship status ($p > .05$).

Awareness of genetic risk may confound the effect of age on psychological and clinical outcomes. To test this possibility, the eight original models that tested interactions were recalculated (i.e., the four models testing an interaction of age with education and the four models testing an interaction of age with relationship status). These new models included all of the predictors used in the original analyses, and added a variable that indicated whether the individual was aware of their genetic risk prior to developing COPD. The variable for awareness of genetic risk was not statistically significant in any model. All of the interactions that were not statistically significant in the original analyses remained not significant. All of the interactions that were statistically significant in the original analyses remained significant with the following exception: the interaction of age with relationship status was originally significant at $p = 0.02$ when predicting health-related quality of life and became marginally significant at $p = .06$ when awareness of genetic risk was included in the model. Among individuals who were single, there was still a highly significant effect of age: in the original model $b = -0.61$ ($SE = 0.16$, $p < 0.001$) and in the model that includes genetic risk $b = -0.55$ ($SE = 0.17$, $p < 0.001$). Among individuals who were part of a couple, the effect of age became significant: in the original model $b = -0.18$ ($SE = 0.10$, $p = 0.07$) and in the model that includes genetic risk $b = -0.19$ ($SE = 0.10$, $p = 0.05$).

Discussion

This is the first study to examine the impact of age on psychological and clinical outcomes in a large sample of individuals with AATD-associated COPD. Results indicate that younger individuals report more symptoms of anxiety over a two-year period, regardless of relationship status. In contrast, younger individuals report more symptoms of depression, worse health-related quality of life, and more breathlessness only if they are single. Age was not associated with depression, health-related quality of life, or breathlessness among individuals who were in a couple relationship. These results suggest that being in a relationship is an important social resource for younger individuals with AATD-associated COPD and are consistent with prior research from a variety of contexts that indicates that being married positively influences outcomes ranging from psychological distress (Goldzweig et al., 2009) to mortality (Berkman & Syme, 1979; House et al., 1988; Rogers, 1995). Additional social resources may also be important, including the quality of relationships with family members and the strength of friendship networks.

Breathlessness is an important clinical outcome in COPD. It is the primary physical symptom experienced by individuals with COPD, and a fundamental goal of treatment is to reduce breathlessness. However, breathlessness is a subjective symptom that is heavily influenced by factors other than effectiveness of medications and underlying lung function. In fact, at the most, 50% of the variance in breathlessness is accounted for by measures of lung function (Eakin et al., 1993). The present study indicates that, among people who are

single, younger individuals perceive themselves as having more breathlessness than older individuals with AATD-associated COPD. This is consistent with a study of men with various types of cancer in which younger patients reported more pain and nausea than older patients (Ganz et al., 1985).

There are multiple avenues for future research. One avenue is to examine the extent to which social comparison accounts for the association between younger age and worse psychological and clinical outcomes. The association of younger age with worse outcomes may reflect that younger individuals do not expect to have chronic symptoms and physical limitations, which older individuals are more likely to expect due to their age. Younger individuals with AATD-associated COPD may be more likely to perceive a greater discrepancy between their health and the health of their peers, who are unlikely to need oxygen therapy or have their work and family lives compromised by a chronic disease. In addition, age is a proxy that does not fully represent beliefs about illness timing. At any given age, some individuals may consider themselves to have developed COPD “off-time” while other individuals may think that they have developed COPD “on time.” Future research should explicitly examine individual beliefs about illness timing.

Research should also examine the extent to which findings from this sample of individuals with AATD-associated COPD generalize to the COPD population more broadly. Among individuals who do not have AATD, there is still a broad range of ages at which COPD is diagnosed (i.e., individuals who do not have AATD can still develop COPD at a relatively young age). In addition, AATD may have an effect on psychological and clinical outcomes that is independent of COPD.

Finally, research should focus on identifying the unique concerns and needs of young individuals with a chronic illness, particularly those who are single. A qualitative study of young women with breast cancer has identified some difficulties that are unique to younger individuals (Siegel et al., 1999), although it did not focus on individuals who are single. In this study, young women with breast cancer indicated that they felt isolated because they did not know other women their age with breast cancer. They even felt isolated when participating in patient support groups because the other participants were so much older and therefore had very different life circumstances (Siegel et al., 1999). Findings of this qualitative study suggest that younger individuals may need their own support groups, developed exclusively for their needs and attended only by young individuals with chronic illness.

Findings of this study should be interpreted in light of a few limitations. One limitation is that objective measures of COPD severity were not included because all data were collected via self-report questionnaires. Oxygen use at baseline was included in all models as a proxy for disease severity, and severity of AATD genotype was also included in all models. In addition, the sample was reduced both from non-response to the original questionnaire and from individuals being removed from analyses due to death, lung transplant, failure to complete a follow-up questionnaire, and missing data. Individuals who responded to the original questionnaire may not represent the entire population of individuals with AATD-associated COPD, and comparison of individuals who were removed from the sample to

individuals who were included in analyses indicates that individuals with more severe COPD and worse outcomes were more likely to be removed from the sample. This limited analyses to an investigation of the impact of age on outcomes among more healthy individuals with AATD-associated COPD.

The strengths of the current study include the large sample size and the fact that participants were recruited from a nation-wide disease registry. Use of the Alpha-1 Foundation Research Registry provided access to an ideal sample in which to study illness timing, since it yielded a sample with a broad age range. A further strength of this study is the use of four different outcome measures, which permitted an examination of a comprehensive set of patient-centered outcomes, including the primary symptom of COPD (i.e., breathlessness). Finally, the prospective study design provided measurement of outcomes at three time points over a two-year period.

In summary, the current study examined the impact of age on psychological and clinical outcomes over a two-year period among individuals with AATD-associated COPD. Younger individuals reported more symptoms of anxiety throughout this two-year period, regardless of relationship status. Younger individuals reported more symptoms of depression, worse health-related quality of life, and more breathlessness only if they were single. Results suggest that younger individuals with AATD-associated COPD, particularly those who are single, have unique needs due to their young age at onset of a serious chronic disease. Further research is needed to identify the specific concerns of younger patients with AATD-associated COPD who are single. Further research is also needed to determine the extent to which these results are consistent across illness populations versus unique to AATD-associated COPD.

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Table 1

Characteristics of the Sample at Baseline (N=468)

Variable	Mean (SD)	Minimum	Maximum
Age (years)	59.9 (9.6)	32	84
Length of Time since COPD was Diagnosed (years)	12.0 (7.6)	0	40

Variable	N (%)
Gender (% male)	232 (49.6)
Relationship Status	
Single	103 (22.0)
Coupled	365 (78.0)
Highest Level of Education Completed	
Grade 12 or less	138 (29.5)
College 1 to 3 years	165 (35.3)
College graduate or more	165 (35.3)
Annual Household Income	
$35,000 or less	129 (28.8)
Between $35,001 and $75,000	160 (35.7)
$75,001 or more	159 (35.5)
Race/ethnicity	
Caucasian non-Hispanic	459 (98.7)
Black non-Hispanic	2 (0.4)
Hispanic	2 (0.4)
Other	2 (0.4)
Lifetime Tobacco Exposure	
Never smoked	155 (33.1)
1 to 20 pack years	170 (36.3)
More than 20 pack years	143 (30.6)
Genotype	
Severely deficient	386 (82.5)
Not severely deficient	41 (8.8)
Unknown	41 (8.8)
Currently Using Oxygen (O_2) for COPD	225 (48.1)
If using O_2, M (SD) number of years of O_2 use	6.5 (4.5)
If using O_2, N (%) prescribed O_2 24 hours per day	112 (50.5)
Has Undergone Augmentation Therapy	359 (76.7)
Aware of Genetic Risk Prior to Developing COPD	
Yes—AATD was diagnosed prior to COPD	117 (26.1)
No—AATD was not diagnosed prior to COPD	331 (73.9)

Table 2

Psychological and Clinical Outcomes

	Mean (SD), Range		
Outcome	**Baseline**	**Year 1**	**Year 2**
Hospital Anxiety and Depression Scale (HADS)			
Depresion	5.2 (3.5), 0–19	5.2 (3.4), 0–16	5.3 (3.5), 0–19
Anxiety	6.2 (3.9), 0–21	6.1 (4.0), 0–19	5.8 (4.0), 0–21
St. George's Respiratory Questionnaire (SGRQ)			
Health-related quality of life	46.9 (18.6), 0–93.5	45.6 (19.2), 0–94.4	45.7 (19.8), 0–88.0
Modified Medical Research Council Dyspnea Scale (MMRC)			
Breathlessness	2.8 (1.1), 1–5	2.8 (1.2), 1–5	2.8 (1.2), 1–5

Table 3

Results of Linear Mixed Models for Age at Baseline Predicting Psychological and Clinical Outcomes of COPD

	Outcomes			
Predictors	**Depression b (SE), p**	**Anxiety b (SE), p**	**Health-Related Quality of Life b (SE), p**	**Breathlessness b (SE), p**
Age at Baseline	−0.03 (0.02), 0.10	−0.09 (0.02), < 0.001	−0.29 (0.09), < 0.001	−0.003 (0.005), 0.56
Years Since COPD was Diagnosed	0.01 (0.02), 0.54	0.01 (0.02), 0.61	0.36 (0.11), < 0.001	0.023 (0.006), < 0.001
Gender				
Male	Reference	Reference	Reference	Reference
Female	−0.001 (0.29), 0.998	0.93 (0.33), < 0.01	2.14 (1.55), 0.17	0.077 (0.085), 0.36
Relationship Status				
Single	Reference	Reference	Reference	Reference
Coupled	−0.25 (0.34), 0.46	−0.53 (0.38), 0.17	−4.83 (1.81), < 0.01	−0.119 (0.099), 0.23
Education	Overall p < 0.001	Overall p = 0.07	Overall p < 0.001	Overall p < 0.01
Grade 12 or less	1.36 (0.35), < 0.001	0.94 (0.40), 0.02	7.98 (1.90), < 0.001	0.358 (0.104), < 0.001
College 1 to 3 years	0.69 (0.33), 0.04	0.48 (0.38), 0.21	5.04 (1.81), < 0.01	0.224 (0.099), 0.02
College graduate or more	Reference	Reference	Reference	Reference
Lifetime Tobacco Exposure	Overall p = 0.68	Overall p = 0.70	Overall p = 0.93	Overall p = 0.72
Never smoked	Reference	Reference	Reference	Reference
1 to 20 pack years	0.20 (0.36), 0.58	0.04 (0.41), 0.93	−0.20 (1.93), 0.92	0.044 (0.106), 0.68
More than 20 pack years	0.32 (0.37), 0.38	0.31 (0.42), 0.46	0.50 (2.00), 0.80	0.089 (0.109), 0.42
Genotype	Overall p < 0.01	Overall p = 0.11	Overall p < 0.01	Overall p = 0.04
Severely deficient	Reference	Reference	Reference	Reference
Not severely deficient	1.38 (0.57), 0.02	1.10 (0.65), 0.09	8.48 (3.08), < 0.01	−0.154 (0.168), 0.36
Unknown	1.19 (0.50), 0.02	0.92 (0.57), 0.11	8.30 (2.77), < 0.01	0.328 (0.150), 0.03
Oxygen Use				
No	Reference	Reference	Reference	Reference
Yes	1.63 (0.29), < 0.001	0.39 (0.33), 0.24	13.50 (1.57), < 0.001	0.973 (0.086), < 0.001
Augmentation Therapy Use				
No	Reference	Reference	Reference	Reference
Yes	−0.48 (0.39), 0.22	0.37 (0.44), 0.41	2.06 (2.11), 0.33	−0.129 (0.116), 0.27
Time	Overall p = 0.75	Overall p = 0.07	Overall p = 0.26	Overall p = 0.34

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Predictors	Outcomes			
	Depression b (SE), p	**Anxiety b (SE), p**	**Health-Related Quality of Life b (SE), p**	**Breathlessness b (SE), p**
Baseline	−0.11 (0.14), 0.45	0.34 (0.16), 0.03	0.63 (0.61), 0.30	−0.025 (0.043), 0.56
1-year follow-up	−0.05 (0.13), 0.70	0.29 (0.16), 0.07	−0.29 (0.50), 0.56	−0.066 (0.045), 0.15
2-year follow-up	Reference	Reference	Reference	Reference

Table 4

Results of Linear Mixed Models with Interaction of Age at Baseline with Relationship Status

	Outcomes			
	Depression b (SE), p	**Anxiety b (SE), p**	**Health-Related Quality of Life b (SE), p**	**Breathlessness b (SE), p**
Interaction Age x Relationship Status	Overall p = 0.03	Overall p = 0.59	Overall p = 0.02	Overall p < 0.01
Effect of Age if Single	−0.08 (0.03), < 0.01	−0.08 (0.03), 0.02	−0.61 (0.16), < 0.001	−0.023 (0.009), < 0.01
Effect of Age if Coupled	−0.01 (0.02), 0.67	−0.10 (0.02), < 0.001	−0.18 (0.10), 0.07	0.005 (0.005), 0.39
Age at Baseline[a]	−0.04 (0.02), 0.01	−0.09 (0.02), < 0.001	−0.39 (0.10), < 0.001	−0.009 (0.005), 0.07
Years Since COPD was Diagnosed	0.01 (0.02), 0.53	0.01 (0.02), 0.61	0.37 (0.11), < 0.001	0.023 (0.006), < 0.001
Gender				
Male	Reference	Reference	Reference	Reference
Female	0.12 (0.29), 0.67	0.89 (0.34), < 0.01	2.88 (1.57), 0.07	0.124 (0.086), 0.15
Relationship Status[b]				
Single	Reference	Reference	Reference	Reference
Coupled	−0.25 (0.34), 0.47	−0.53 (0.38), 0.17	−4.66 (1.80), < 0.01	−0.108 (0.098), 0.27
Education	Overall < 0.01	Overall p = 0.06	Overall p < 0.001	Overall p < 0.01
Grade 12 or less	1.24 (0.35), < 0.001	0.97 (0.41), 0.02	7.21 (1.91), < 0.001	0.310 (0.104), < 0.01
College 1 to 3 years	0.66 (0.33), 0.05	0.49 (0.38), 0.20	4.87 (1.80), < 0.01	0.218 (0.098), 0.03
College graduate or more	Reference	Reference	Reference	Reference
Lifetime Tobacco Exposure	Overall p = 0.61	Overall p = 0.71	Overall p = 0.91	Overall p = 0.65
Never smoked	Reference	Reference	Reference	Reference
1 to 20 pack years	0.24 (0.36), 0.49	0.02 (0.41), 0.95	0.01 (1.92), 0.995	0.060 (0.105), 0.57
More than 20 pack years	0.36 (0.37), 0.33	0.30 (0.42), 0.48	0.73 (1.99), 0.71	0.100 (0.109), 0.36
Genotype	Overall p < 0.01	Overall p = 0.12	Overall p < 0.001	Overall p = 0.03
Severely deficient	Reference	Reference	Reference	Reference
Not severely deficient	1.45 (0.57), 0.01	1.08 (0.65), 0.10	8.81 (3.07), < 0.01	−0.131 (0.167), 0.43
Unknown	1.25 (0.50), 0.01	0.90 (0.58), 0.12	8.79 (2.77), < 0.01	0.353 (0.149), 0.02
Oxygen Use				
No	Reference	Reference	Reference	Reference
Yes	1.65 (0.29), < 0.001	0.39 (0.34), 0.24	13.56 (1.56), < 0.001	0.978 (0.086), < 0.001
Augmentation Therapy Use				

	Outcomes			
	Depression b (SE), p	**Anxiety b (SE), p**	**Health-Related Quality of Life b (SE), p**	**Breathlessness b (SE), p**
No	Reference	Reference	Reference	Reference
Yes	−0.42 (0.39), 0.27	0.35 (0.44), 0.43	2.42 (2.10), 0.25	−0.101 (0.115), 0.38
Time	Overall p = 0.74	Overall p = 0.07	Overall p = 0.26	Overall p = 0.34
Baseline	−0.11 (0.14), 0.44	0.34 (0.16), 0.03	0.63 (0.61), 0.30	−0.025 (0.043), 0.56
1-year follow-up	−0.05 (0.13), 0.70	0.29 (0.16), 0.07	−0.29 (0.50), 0.56	−0.065 (0.045), 0.15
2-year follow-up	Reference	Reference	Reference	Reference

[a] Effect of age, unweighted average over both relationship statuses

[b] Effect of relationship status for the average age