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Differences in Adjustment between Individuals with Alpha-1 Antitrypsin Deficiency (AATD) Associated COPD and Non-AATD COPD

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Abstract

Smokers who have severe alpha-1 antitrypsin deficiency (AATD) are at risk for developing COPD earlier in life than smokers without AATD, and are likely to experience challenges adjusting to their illness because they are in a highly productive life stage when they are diagnosed with COPD. This study examined whether individuals with AATD-associated COPD differ from individuals with non-AATD COPD with regard to depression, anxiety, dyspnea, and health-related quality of life (HRQL). Cross-sectional data were collected via self-report questionnaires completed by 480 individuals with non-AATD COPD and 578 individuals with AATD-associated COPD under protocols with IRB approval. Multiple linear regression models were used to test whether individuals with non-AATD COPD differed from individuals with AATD-associated COPD with regard to depression, anxiety, dyspnea, and HRQL. All models adjusted for demographic and health characteristics. Individuals with AATD-associated COPD did not report more symptoms of depression or anxiety; however, they did report more dyspnea ($B = 0.31$, 95% CI = 0.16 to 0.47, $p < 0.001$) and impairment in HRQL ($B = 4.75$, 95% CI = 2.10 to 7.41, $p < 0.001$) than other individuals with COPD. Individuals with AATD-associated COPD were more likely to be a member of a couple (rather than single) and had a higher level of education when compared to individuals with non-AATD COPD. Resources available to persons with AATD-associated COPD, such as being in a serious relationship and having higher education, may offset the effect of age when considering symptoms of depression and anxiety in patients with COPD.

Keywords

Alpha-1 Antitrypsin Deficiency; Anxiety; Depression; Dyspnea; Health Status; Psychological Adjustment

Introduction

Alpha-1 antitrypsin deficiency (AATD) is one genetic cause of early-onset COPD, most commonly emphysema [1, 2], and smokers who have severe AATD are at risk for developing COPD earlier in life than smokers without AATD. The early age at onset of a debilitating and incurable disease comes at a time in their lives when patients are pursuing careers and raising families. Their peers are unlikely to have COPD or require oxygen therapy and are unlikely to have their work and family lives compromised by a chronic disease. For these reasons, individuals with AATD-associated COPD may be at increased risk for depression and anxiety, but no research to date has reported on mood symptoms in this group of COPD patients.

In other chronic conditions, an inverse association between age and symptoms of depression and anxiety has been demonstrated. Breast cancer patients diagnosed at a younger age report more depression and anxiety than women diagnosed later in life [3–5]. A study of 758 patients with one of six different chronic illnesses found that, across diseases, younger patients reported worse mental health than older patients [6]. Similarly, several studies have reported that younger patients with COPD report more symptoms of depression and anxiety than older patients with COPD [7–9].

The primary aim of this study was to test the hypothesis that individuals with AATD-associated COPD report more symptoms of depression and anxiety than individuals with non-AATD COPD. The secondary aim of this study was to examine whether individuals with AATD-associated COPD differ from individuals with non-AATD COPD with regard to dyspnea and health-related quality of life (HRQL). This is the first study to provide a description of symptoms of depression and anxiety in a large sample of patients with AATD-associated COPD and test the hypothesis that having an identified genetic subtype of COPD is associated with symptoms of depression and anxiety.

Methods

Sample and Procedures

Data collection was approved by the Institutional Review Boards at National Jewish Health and the Medical University of South Carolina, and the Colorado Multiple Institutional Review Board. Anonymized, cross-sectional data were collected via questionnaires mailed to two groups of individuals with physician-diagnosed COPD: 1) individuals with non-AATD COPD and 2) individuals with AATD-associated COPD. All participants with non-AATD COPD had been assessed or treated for COPD at a tertiary-care respiratory hospital or a university-affiliated public hospital in Denver. At the tertiary-care hospital, questionnaires were mailed to patients who had registered with the clinical research unit and clinic patients who had consented to be contacted for research studies. At the university-affiliated hospital, questionnaires were mailed to all patients with ICD-9 codes indicative of COPD at three internal medicine clinics associated with the hospital. All participants with AATD-associated COPD were adult members of the Alpha-1 Foundation Research Registry residing in the US and Canada who had physician-diagnosed COPD [10].

Several individuals who returned the questionnaire were excluded because they indicated that they did not have COPD. These respondents did not agree with their physician's diagnosis and were excluded because many of the items on the questionnaire only pertain to individuals who self-identify as having COPD. Listwise deletion was used to handle missing data in the regression analyses, which resulted in the exclusion of additional respondents. Figure 1 delineates the number of returned surveys excluded from analyses for each reason. Responses from a total of 1058 individuals with COPD were used in analyses.

Measures

Demographic and Health Characteristics—Collected demographic information included gender, relationship status, age, 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 by multiplying the average number of cigarette packs smoked per day by the number of years the participant smoked. Participants also indicated whether they were using oxygen for their COPD. Individuals who were recruited via the Alpha-1 Foundation Research Registry reported their genotype.

Measures of Adjustment—Symptoms of depression and anxiety were measured by the Hospital Anxiety and Depression Scale (HADS). The HADS was designed to measure depression and anxiety in medical outpatients [11] and has frequently been used in studies of COPD [7, 12–14]. The HADS subscales for depression and anxiety have scores that can range from 0 to 21. Scoring bands are the same for both subscales: a score of 0 to 7 is considered normal, 8 to 10 is mild, 11 to 14 is moderate, and 15 to 21 is severe.

Dyspnea was measured by the Modified Medical Research Council Dyspnea Scale (MMRC), a 5-point grading scale to measure shortness of breath [15] that is predictive of 5-year survival among patients with COPD [16]. The score can range from 1 to 5, with a higher score indicating more dyspnea.

Health-related quality of life (HRQL) was measured by the Saint George's Respiratory Questionnaire (SGRQ), a 50-item scale designed for use in patients with airflow limitation [17]. The SGRQ Total Score was used. This score can range from 0 to 100, with a higher score indicating more impairment in HRQL.

Data Analysis

SPSS Statistics Version 19 was used for all analyses, with a two-sided significance level of 0.05.

Characteristics of Participants—All demographic and health characteristics were treated as categorical variables. These characteristics were summarized using number and percentage of participants in each category. Chi-square tests were used to examine whether the two samples differed with regard to each individual variable that was planned for inclusion in the multivariate regression models.

Primary Analyses—To test whether the two samples differed with regard to depression, anxiety, dyspnea, and HRQL without adjusting for any covariates, t-tests and chi-square tests were used. To test whether the two samples differed while adjusting for demographic and health characteristics, four multiple linear regression models were generated using continuous scores for each dependent variable. The same set of independent variables was used for all four models and included: type of COPD (AATD versus non-AATD), gender, relationship status, age, highest level of education completed, lifetime tobacco exposure, and whether the respondent used oxygen for COPD. All of the independent variables were entered simultaneously. Regression coefficients and significance tests for each independent variable reflect the effect of that variable after accounting for the effect of all other independent variables in the model.

Secondary Analyses—Secondary analyses were conducted to determine whether results differ from results of the primary analyses if: 1) depression and anxiety were treated as categorical rather than continuous variables, and 2) individuals with a genotype that does not

result in severe AATD and individuals who did not know their genotype were excluded from the sample. This second set of secondary analyses focuses on comparing individuals with non-AATD COPD to individuals with AATD-associated COPD who have a genotype resulting in severe AATD. Genotype may be relevant because individuals with severe AATD have lower levels of circulating alpha-1 antitrypsin enzyme and are thus more vulnerable to lung damage caused by tobacco smoke and infection compared to individuals with genotypes that result in less severe AATD.

For the analyses in which depression and anxiety were treated as categorical variables, the scoring bands on the HADS were used. Mild, moderate, and severe symptoms were combined into a single group that indicates symptoms in the clinical range. Two simultaneous multiple logistic regression models were calculated, one for depression and one for anxiety. The dependent variable in each logistic regression model denotes symptoms in the normal range versus symptoms in the clinical range. The same predictors were used in the logistic regression models as in the linear regression models conducted for the primary analyses; the only difference was that symptoms of depression and anxiety were considered as categorical rather than continuous dependent variables in the secondary analyses.

Given that there is a wide range in AAT deficiency based on genotype, additional analyses were conducted to examine whether results differed when only individuals with a severely deficient genotype were included in the sample used in analyses. For these analyses, individuals with a severely deficient genotype were compared to individuals with non-AATD COPD in regressions with depression, anxiety, dyspnea, and HRQL as dependent variables. Individuals with a genotype that is not severely deficient and individuals who did not know their genotype were excluded from the sample used to calculate the regression models. The predictors were the same as used in the primary analyses; the only difference was that a subset of individuals with AATD-associated COPD was used in these models.

Results

Characteristics of Participants

Demographic and health characteristics of participants are presented in Table 1. With regard to genotype of the individuals with AATD-associated COPD, 81.7% had a severely deficient genotype (ZZ, SZ, FZ, P-Null, Z-Null, ZPlowell, ZMmalton, and ZMheerlen), 8.5% had a genotype that was not severely deficient (MZ, MS, M-Null, and SS), and 9.9% did not know their genotype. Individuals with AATD-associated COPD differed from individuals with non-AATD COPD with regard to all demographic and health characteristics except for gender (see Table 1). As expected, individuals with AATD-associated COPD were younger than individuals with non-AATD COPD. Individuals with AATD-associated COPD were also more highly educated and more likely to be a member of a couple (rather than single).

Individuals who were removed from the sample due to missing data ($n=70$) did not differ from individuals with complete data with regard to gender, age, lifetime tobacco exposure, oxygen use for COPD, depression, anxiety, dyspnea, or HRQL. Individuals who were removed from the sample due to missing data did differ with regard to relationship status (less likely to be married or in a relationship, $\chi^2_{(df=1)} = 7.47$, $p = 0.006$) and education. The percentage of individuals with a high school education or less was higher among the group that was removed from the sample due to missing data than among the group that had complete data ($\chi^2_{(df=2)} = 10.75$, $p = 0.005$). In addition, individuals with non-AATD COPD were more likely to be removed from the sample due to missing data ($\chi^2_{(df=1)} = 15.96$, $p < 0.001$).

Primary Analyses

Depression and Anxiety—On average, individuals with AATD-associated COPD reported symptoms of depression and anxiety that were in the non-clinical range (i.e., a score below 8 on the HADS). The mean score for symptoms of depression among this group was 5.5 and the mean score for symptoms of anxiety was 6.5. Twenty-five percent of individuals with AATD-associated COPD reported depressive symptoms in the clinical range (14.5% mild, 8.8% moderate, and 2.1% severe). Thirty-six percent of individuals with AATD-associated COPD reported symptoms of anxiety in the clinical range (20.5% mild, 10.9% moderate, and 4.4% severe).

T-tests were used to compare individuals with AATD-associated COPD to individuals with non-AATD COPD when depression and anxiety were treated as continuous variables. Chi-square was used to compare the two groups when using the scoring bands to quantify symptoms of depression and anxiety. Results (see Table 2) indicate that individuals with AATD-associated COPD reported fewer symptoms of depression than individuals with non-AATD COPD, both when depression is treated as a continuous variable ($t_{(df=1029)} = 2.32, p = 0.020$) and a categorical variable ($\chi^2_{df=3} = 8.74, p = 0.033$). The two groups did not differ with regard to anxiety, regardless of whether anxiety was treated as a continuous or a categorical variable.

The two groups differed with regard to many demographic and health characteristics, and multiple linear regression models were used to adjust for these differences. These models utilized continuous measures rather than scoring bands for symptoms of depression and anxiety. Type of COPD was not a statistically significant predictor of symptoms of depression ($p = 0.511$) or anxiety ($p = 0.137$). Several of the demographic covariates were significant predictors of symptoms of depression and anxiety, including relationship status, age, and education (see Table 3). Individuals who were a member of a couple reported less depression and anxiety than individuals who were single. Younger age and less education were associated with more symptoms of depression and anxiety. In addition, oxygen use was associated with more symptoms of depression.

Dyspnea and HRQL—Bivariate analyses did not show differences between individuals with AATD-associated COPD and individuals with non-AATD COPD with regard to dyspnea or HRQL (see Table 2). However, regression models that adjust for demographic and health differences indicate that the two groups differed with regard to both dyspnea and HRQL (see Table 3). Type of COPD was a statistically significant predictor of dyspnea ($B = 0.31, 95\% \text{ CI} = 0.16 \text{ to } 0.47, p < 0.001$), with individuals with AATD-associated COPD reporting more dyspnea than individuals with non-AATD COPD. Type of COPD was also a statistically significant predictor of HRQL ($B = 4.75, 95\% \text{ CI} = 2.10 \text{ to } 7.41, p < 0.001$). On average, individuals with AATD-associated COPD had an SGRQ total score that is 4.75 points higher (indicating worse quality of life) than individuals with non-AATD COPD when demographic and health characteristics are adjusted for. A difference of at least 4 points in the SGRQ total score is considered clinically significant [18, 19]. Consistent with the models for depression and anxiety, individuals who were in a couple relationship reported less dyspnea and less impairment in HRQL than individuals who were single. Individuals who had less education reported more dyspnea and impairment in HRQL. In addition, oxygen use was associated with more dyspnea and impairment in HRQL.

Secondary Analyses

Treating Depression and Anxiety as Categorical Variables—When depression and anxiety were treated as categorical variables, the results did not differ from when they are treated as continuous variables. Consistent with the primary analyses, type of COPD was not

a statistically significant predictor of symptoms of depression ($p = 0.311$) or anxiety ($p = 0.336$). In both logistic regression models, all covariates that were statistically significant in the linear regression models remained statistically significant, and all covariates that were not significant in the linear regression models remained non-significant.

Focusing on a Subsample of the Group with AATD-Associated COPD—The four linear regression models used for the primary analyses were calculated again, this time comparing individuals with a severely deficient genotype to individuals with non-AATD COPD (excluding individuals with a genotype that is not severely deficient and individuals who do not know their genotype from the sample). Results were largely the same as results of the primary analyses. Consistent with the primary findings, the two groups did not differ with regard to depression ($p = 0.084$) or anxiety ($p = 0.053$), and they did differ with regard to dyspnea ($B = 0.30$, 95% CI = 0.13 to 0.46, $p < 0.001$) and HRQL ($B = 3.11$, 95% CI = 0.29 to 5.93, $p = 0.031$). In all four models, all covariates that were not significant in the primary analyses remained non-significant. All covariates that were statistically significant in the primary analyses remained statistically significant, with the exception that college 1 to 3 years became non-significant in the model for depression ($p = 0.051$).

Discussion

This study is the first to focus on symptoms of depression and anxiety in a large sample of individuals with AATD-associated COPD. Based on prior research in COPD [7–9] and other illnesses such as breast cancer [3–5] and Parkinson's disease [20] we hypothesized that individuals with AATD-associated COPD would report more symptoms of depression and anxiety than individuals with non-AATD COPD due to their younger age at onset of a serious chronic disease. Our hypothesis was not supported. Individuals with AATD-associated COPD did not report more symptoms of depression or anxiety, even though they were younger than individuals with non-AATD COPD. In our regression models type of COPD was not a significant predictor of depression or anxiety, regardless of whether depression and anxiety were treated as continuous or categorical variables.

Individuals with AATD-associated COPD appear to have additional resources that counterbalance the risk associated with their younger age. In our sample, individuals with AATD-associated COPD were more likely to be coupled (rather than single) than individuals with non-AATD COPD. Being part of a couple was associated with better outcomes in our regression models for depression, anxiety, dyspnea, and impairment in HRQL. Our findings are consistent with prior research in COPD that has demonstrated that being single is associated with more symptoms of depression [21, 22] and are congruent with reports from a variety of contexts showing that being married positively influences patient-centered outcomes ranging from psychological distress [23] to mortality [24–26].

Education is an additional resource that individuals with AATD-associated COPD were more likely to have than individuals with non-AATD COPD. Compared to individuals with at least a college degree, individuals with less education reported more depression, anxiety, dyspnea, and impairment in HRQL. This is consistent with research that indicates that higher socioeconomic status is associated with a variety of better health outcomes [27–29]. Among individuals with COPD, an inverse association of education [9, 22] and other measures of socioeconomic status [21, 30] with symptoms of depression has been reported. Low education has also been associated with more impairment in quality of life among individuals with COPD [31].

Overall, our results are consistent with prior research demonstrating that higher education and being a member of a couple are associated with less distress among individuals with

COPD and other populations. In our sample, education and relationship status were associated with all four outcomes, even after statistically adjusting for type of COPD. As such, while these resources were associated with positive outcomes across our sample, the individuals with AATD-associated COPD in our sample were more likely to possess (and therefore benefit from) these resources. In addition, some resources are available exclusively to individuals with AATD-associated COPD. For example, individuals with AATD-associated COPD can access support groups for educational materials and shared experiences, and disease management programs that are specific to AATD. Access to these resources may be protective for depression and anxiety.

This study also provides information about impairment in HRQL among individuals with AATD-associated COPD. In our study, the mean SGRQ Total Score for the AATD-associated COPD sample was 48.5, which is consistent with two prior studies that have used the SGRQ to examine HRQL among individuals with AATD-associated COPD [32, 33]. Also consistent with Campos et al. [34], we found that our youngest age group reported more impairment in HRQL than our oldest age group. Individuals with AATD-associated COPD had an SGRQ total score that is almost 5 points higher than individuals with non-AATD COPD when demographic and health characteristics are adjusted for. The significant findings for age and type of COPD may reflect that individuals with AATD-associated COPD do not expect to have chronic symptoms and physical limitations, which individuals with non-AATD COPD may be more likely to expect due to their age. Individuals with AATD-associated COPD are more likely to experience a greater discrepancy in HRQL in comparison to their peers than are individuals with non-AATD COPD.

Results of this study should be interpreted in light of certain limitations. A primary limitation is that spirometry was not available for characterizing the severity of COPD because all data were collected via self-report questionnaires. Second, individuals with AATD-associated COPD were recruited from a much broader geographic area than were individuals with non-AATD COPD. The Alpha-1 Research Registry encompasses the United States and Canada, while individuals with non-AATD COPD were recruited from medical centers in Denver, Colorado. The altitude of Denver could affect oxygen prescribing, and oxygen use was higher in the non-AATD population. This difference in oxygen use was adjusted for in all regression models. Third, the response rate differed between the two groups: 52% of individuals with non-AATD COPD returned the questionnaire, while 36% of individuals with AATD-associated COPD returned the questionnaire. We suspect that individuals who are having more difficulty adjusting to their COPD are less likely to return the questionnaire. As such, this difference in response rates would make it more difficult to identify differences in adjustment between individuals with non-AATD COPD and AATD-associated COPD. Fourth, it is possible that some of the individuals in the non-AATD COPD sample actually have AATD-associated COPD, which would also make it more difficult to identify differences in adjustment between the two groups. Fifth, age and years of education were treated as categorical variables in our analyses as this was how these variables were measured in the questionnaires. Statistical power to examine the effect of these covariates would have been higher if they had been treated as continuous variables. Finally, some individuals who returned the questionnaire were excluded from analyses due to missing data. However, a comparison of individuals with complete data to individuals with missing data indicated that the two groups differed with regard to only three of the eleven variables used in these analyses.

Strengths of this study include the carefully planned use of the same measures in two different groups of individuals with COPD. Use of the same measures made it possible to test for differences in depression, anxiety, dyspnea, and HRQL by type of COPD. A further strength of this study is the use of four different measures of adjustment, which allowed us

to examine a comprehensive set of patient-centered outcomes with valid and reliable measures. In addition, this is the first study to describe symptoms of depression and anxiety among individuals with AATD-associated COPD, and to compare these symptoms to individuals with non-AATD COPD. Finally, the large sample size made it possible to test for differences between individuals with AATD-associated COPD and non-AATD COPD, even while using multiple regression to adjust for demographic and health characteristics that differed between the two groups.

A quarter of the individuals with AATD-associated COPD reported symptoms of depression in the clinical range and 36% reported symptoms of anxiety in the clinical range. These findings indicate that patients with AATD-associated COPD, like those with non-AATD COPD, should be routinely evaluated for symptoms of both depression and anxiety to better identify mental health symptoms and needs for intervention.

Conclusions

COPD is a heterogeneous disease, and AATD-associated COPD is a unique subtype in which individuals frequently develop COPD at a young age. This is the first study to describe symptoms of depression and anxiety in a large sample of patients with AATD-associated COPD and test the hypothesis that having an identified genetic subtype of COPD is associated with symptoms of depression and anxiety. Results of this study suggest that, despite their younger age, individuals with AATD-associated COPD are not at increased risk for depression and anxiety compared to individuals with non-AATD COPD, perhaps because individuals with AATD-associated COPD were more likely to have resources such as education and being part of a committed couple. Despite having these resources, a quarter of the individuals with AATD-associated COPD reported symptoms of depression in the clinical range and an even higher percentage reported elevated symptoms of anxiety. These patients, like those with non-AATD COPD, should be routinely evaluated for symptoms of both depression and anxiety.

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Declaration of Interest

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References

1. Ioachimescu OC, Stoller JK. A review of alpha-1 antitrypsin deficiency. COPD: journal of chronic obstructive pulmonary disease. 2005; 2(2):263–275.
2. Molino NA. Genetics of COPD. Chest. 2004; 125(5):1929–1940. [PubMed: 15136409]
3. Mor V. QOL measurement scales for cancer patients: differentiating effects of age from effects of illness. Oncology (Williston Park). 1992; 6(2 Suppl):146–152. [PubMed: 1532730]
4. Vinokur AD, Threath BA, Caplan RD, Zimmerman BL. Physical and psychosocial functioning and adjustment to breast cancer. Long-term follow-up of a screening population. Cancer. 1989; 63(2): 394–405. [PubMed: 2910447]
5. Hughson AV, Cooper AF, McArdle CS, Smith DC. Psychosocial consequences of mastectomy: levels of morbidity and associated factors. J Psychosom Res. 1988; 32(4–5):383–391. [PubMed: 3236266]
6. Cassileth BR, Lusk EJ, Strouse TB, Miller DS, Brown LL, Cross PA, Tenaglia AN. Psychosocial status in chronic illness. A comparative analysis of six diagnostic groups. N Engl J Med. 1984; 311(8):506–511. [PubMed: 6749208]
7. Cleland JA, Lee AJ, Hall S. Associations of depression and anxiety with gender, age, health-related quality of life and symptoms in primary care COPD patients. Fam Pract. 2007; 24(3):217–223. [PubMed: 17504776]
8. Al-shair K, Dockry R, Mallia-Milanes B, Kolsum U, Singh D, Vestbo J. Depression and its relationship with poor exercise capacity, BODE index and muscle wasting in COPD. Respir Med. 2009; 103(10):1572–1579. [PubMed: 19560330]
9. Felker B, Katon W, Hedrick SC, Rasmussen J, McKnight K, McDonnell MB, Fihn SD. The association between depressive symptoms and health status in patients with chronic pulmonary disease. Gen Hosp Psychiatry. 2001; 23(2):56–61. [PubMed: 11313071]
10. Alpha-1 research program. [<http://www.musc.edu/alphaoneregistry/>]
11. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983; 67(6):361–370. [PubMed: 6880820]
12. Bosley CM, Corden ZM, Rees PJ, Cochrane GM. Psychological factors associated with use of home nebulized therapy for COPD. Eur Respir J. 1996; 9(11):2346–2350. [PubMed: 8947083]
13. Dahlen I, Janson C. Anxiety and depression are related to the outcome of emergency treatment in patients with obstructive pulmonary disease. Chest. 2002; 122(5):1633–1637. [PubMed: 12426264]
14. Hajiro T, Nishimura K, Tsukino M, Ikeda A, Oga T. Stages of disease severity and factors that affect the health status of patients with chronic obstructive pulmonary disease. Respir Med. 2000; 94(9):841–846. [PubMed: 11001074]
15. Fletcher CM, Elmes PC, Fairbairn AS, Wood CH. The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. Br Med J. 1959; No 5147:257–266. [PubMed: 13823475]
16. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. Chest. 2002; 121(5):1434–1440. [PubMed: 12006425]
17. Barr JT, Schumacher GE, Freeman S, LeMoine M, Bakst AW, Jones PW. American translation, modification, and validation of the St. George's Respiratory Questionnaire. Clin Ther. 2000; 22(9): 1121–1145. [PubMed: 11048909]
18. Jones PW. Interpreting thresholds for a clinically significant change in health status in asthma and COPD. Eur Respir J. 2002; 19(3):398–404. [PubMed: 11936514]
19. Jones PW. St. George's Respiratory Questionnaire: MCID. COPD. 2005; 2(1):75–79. [PubMed: 17136966]
20. Schrag A, Hovris A, Morley D, Quinn N, Jahanshahi M. Young- versus older-onset Parkinson's disease: impact of disease and psychosocial consequences. Mov Disord. 2003; 18(11):1250–1256. [PubMed: 14639664]
21. Ng TP, Niti M, Tan WC, Cao Z, Ong KC, Eng P. Depressive symptoms and chronic obstructive pulmonary disease: effect on mortality, hospital readmission, symptom burden, functional status, and quality of life. Arch Intern Med. 2007; 167(1):60–67. [PubMed: 17210879]

22. Xu W, Collet JP, Shapiro S, Lin Y, Yang T, Platt RW, Wang C, Bourbeau J. Independent effect of depression and anxiety on chronic obstructive pulmonary disease exacerbations and hospitalizations. *Am J Respir Crit Care Med*. 2008; 178(9):913–920. [PubMed: 18755925]
23. Goldzweig G, Andritsch E, Hubert A, Walach N, Perry S, Brenner B, Baider L. How relevant is marital status and gender variables in coping with colorectal cancer? A sample of middle-aged and older cancer survivors. *Psychooncology*. 2009; 18(8):866–874. [PubMed: 19061195]
24. Rogers RG. Marriage sex, and mortality. *Journal of Marriage and the Family*. 1995; 57:515–526.
25. Berkman LF, Syme SL. Social networks, host resistance, and mortality: a nine-year follow-up study of Alameda County residents. *Am J Epidemiol*. 1979; 109(2):186–204. [PubMed: 425958]
26. House JS, Landis KR, Umberson D. Social relationships and health. *Science*. 1988; 241(4865):540–545. [PubMed: 3399889]
27. Adler NE, Boyce T, Chesney MA, Cohen S, Folkman S, Kahn RL, Syme SL. Socioeconomic status and health. The challenge of the gradient. *Am Psychol*. 1994; 49(1):15–24. [PubMed: 8122813]
28. Adler NE, Boyce WT, Chesney MA, Folkman S, Syme SL. Socioeconomic inequalities in health. No easy solution. *Jama*. 1993; 269(24):3140–3145. [PubMed: 8505817]
29. Schnittker J. Education and the changing shape of the income gradient in health. *J Health Soc Behav*. 2004; 45(3):286–305. [PubMed: 15595508]
30. Yohannes AM, Baldwin RC, Connolly MJ. Depression and anxiety in elderly outpatients with chronic obstructive pulmonary disease: prevalence, and validation of the BASDEC screening questionnaire. *Int J Geriatr Psychiatry*. 2000; 15(12):1090–1096. [PubMed: 11180464]
31. Prigatano GP, Wright EC, Levin D. Quality of life and its predictors in patients with mild hypoxemia and chronic obstructive pulmonary disease. *Arch Intern Med*. 1984; 144(8):1613–1619. [PubMed: 6380440]
32. Campos MA, Alazemi S, Zhang G, Wanner A, Salathe M, Baier H, Sandhaus RA. Exacerbations in subjects with alpha-1 antitrypsin deficiency receiving augmentation therapy. *Respir Med*. 2009; 103(10):1532–1539. [PubMed: 19464158]
33. Campos MA, Alazemi S, Zhang G, Wanner A, Sandhaus RA. Effects of a disease management program in individuals with alpha-1 antitrypsin deficiency. *COPD*. 2009; 6(1):31–40. [PubMed: 19229706]
34. Campos MA, Alazemi S, Zhang G, Salathe M, Wanner A, Sandhaus RA, Baier H. Clinical characteristics of subjects with symptoms of alpha1-antitrypsin deficiency older than 60 years. *Chest*. 2009; 135(3):600–608. [PubMed: 19017884]

Figure 1.
Recruitment Flow Diagram

Table 1

Demographic and Health Characteristics of the Sample

Variable	Combined Sample (n = 1058)	Non-AATD COPD (n = 480)	AATD COPD (n = 578)	p value for Comparison
Gender	N (%)	N (%)	N (%)	0.597
Male	535 (50.6)	247 (51.5)	288 (49.8)	
Female	523 (49.4)	233 (48.5)	290 (50.2)	
Relationship Status				<0.001
Single	351 (33.2)	219 (45.6)	132 (22.8)	
Coupled	707 (66.8)	261 (54.4)	446 (77.2)	
Age				<0.001
59 or younger	387 (36.6)	103 (21.5)	284 (49.1)	
60 to 69	399 (37.7)	201 (41.9)	198 (34.3)	
70 or older	272 (25.7)	176 (36.7)	96 (16.6)	
Highest Level of Education				<0.001
Grade 12 or less	346 (32.7)	178 (37.1)	168 (29.1)	
College 1 to 3 years	406 (38.4)	192 (40.0)	214 (37.0)	
College graduate or more	306 (28.9)	110 (22.9)	196 (33.9)	
Income				<0.001
Less than \$15,000	188 (18.5)	149 (32.1)	39 (7.1)	
Between \$15,001 and \$35,000	268 (26.4)	135 (29.1)	133 (24.1)	
Between \$35,001 and \$75,000	312 (30.7)	117 (25.2)	195 (35.3)	
\$75,001 or more	248 (24.4)	63 (13.6)	185 (33.5)	
Race/ethnicity				<0.001
Caucasian non-Hispanic	976 (92.6)	410 (85.4)	566 (98.6)	
Black non-Hispanic	28 (2.7)	26 (5.4)	2 (0.3)	
Hispanic	40 (3.8)	36 (7.5)	4 (0.7)	
Other	10 (0.9)	8 (1.7)	2 (0.3)	
Tobacco Exposure				<0.001
Never smoked	198 (18.7)	15 (3.1)	183 (31.7)	
1 to 49 pack years	574 (54.3)	220 (45.8)	354 (61.2)	
50 or more pack years	286 (27.0)	245 (51.0)	41 (7.1)	
Oxygen Use for COPD				<0.001
No	452 (42.7)	171 (35.6)	281 (48.6)	
Yes	606 (57.3)	309 (64.4)	297 (51.4)	

Table 2

Depression, Anxiety, Dyspnea, and Health-Related Quality of Life

	Combined Sample (n = 1058)	Non-AATD COPD (n = 480)	AATD COPD (n = 578)	p value for Comparison
Variable	M (SD)	M (SD)	M (SD)	
Depression (Continuous)	5.8 (3.7)	6.1 (3.8)	5.5 (3.7)	0.020
Anxiety (Continuous)	6.7 (4.2)	7.0 (4.4)	6.5 (4.1)	0.107
Dyspnea	2.9 (1.1)	2.9 (1.1)	2.9 (1.2)	0.802
Impairment in HRQL	47.9 (19.4)	47.3 (19.4)	48.5 (19.4)	0.310
Variable	N (%)	N (%)	N (%)	
Depression (Using Scoring Bands)				0.033
Normal	730 (70.8)	313 (66.3)	417 (74.6)	
Mild	174 (16.9)	93 (19.7)	81 (14.5)	
Moderate	100 (9.7)	51 (10.8)	49 (8.8)	
Severe	27 (2.6)	15 (3.2)	12 (2.1)	
Anxiety (Using Scoring Bands)				0.119
Normal	635 (61.7)	274 (58.7)	361 (64.2)	
Mild	219 (21.3)	104 (22.3)	115 (20.5)	
Moderate	115 (11.2)	54 (11.6)	61 (10.9)	
Severe	60 (5.8)	35 (7.5)	25 (4.4)	

Table 3

Simultaneous Multiple Linear Regression Models for Primary Analyses

	Depression (adj R² = .11) Unstand B (95% CI), p	Anxiety (adj R² = .11) Unstand B (95% CI), p	Dyspnea (adj R² = .23) Unstand B (95% CI), p	HRQL (adj R² = .22) Unstand B (95% CI), p
Type of COPD				
Non-AATD COPD	Reference	Reference	Reference	Reference
AATD COPD	-0.18 (-.73 to .36), 0.511	-0.47 (-1.09 to .15), 0.137	0.31 (.16 to .47), <0.001	4.75 (2.10 to 7.41), <0.001
Gender				
Male	Reference	Reference	Reference	Reference
Female	-0.22 (-.67 to .23), 0.345	0.78 (.27 to 1.29), 0.003	-0.04 (-.17 to .08), 0.497	-0.50 (-2.69 to 1.69), 0.654
Relationship Status				
Single	Reference	Reference	Reference	Reference
Coupled	-0.78 (-1.27 to -.29), 0.002	-0.82 (-1.38 to -.26), 0.004	-0.17 (-.31 to -.04), 0.013	-3.24 (-5.63 to -.86), 0.008
Age				
59 or younger	1.58 (.97 to 2.18), <0.001	2.35 (1.66 to 3.04), <0.001	-0.01 (-.18 to .16), 0.892	6.31 (3.32 to 9.29), <0.001
60 to 69	0.32 (-.24 to .88), 0.267	0.69 (.05 to 1.33), 0.036	-0.10 (-.25 to .07), 0.243	1.87 (-.90 to 4.64), 0.186
70 or older	Reference	Reference	Reference	Reference
Highest Level of Educ.				
Grade 12 or less	1.37 (.80 to 1.94), <0.001	1.63 (.97 to 2.28), <0.001	0.53 (.37 to .69), <0.001	10.16 (7.38 to 12.95), <0.001
College 1 to 3 yrs	0.60 (.06 to 1.15), 0.031	0.94 (.32 to 1.57), 0.003	0.28 (.12 to .43), 0.001	5.99 (3.32 to 8.66), <0.001
College grad or more	Reference	Reference	Reference	Reference
Tobacco Exposure				
Never smoked	Reference	Reference	Reference	Reference
1 to 49 pack yrs	0.10 (-.53 to .72), 0.764	0.32 (-.40 to 1.04), 0.380	0.10 (-.08 to .28), 0.269	0.13 (-2.94 to 3.21), 0.932
50 or more pack yrs	0.60 (-.19 to 1.39), 0.135	0.58 (-.32 to 1.48), 0.205	0.22 (-.01 to .44), 0.057	3.43 (-.44 to 7.29), 0.082
Oxygen Use for COPD				
No	Reference	Reference	Reference	Reference
Yes	1.61 (1.16 to 2.06), <0.001	0.24 (-.27 to .75), 0.361	0.98 (.85 to 1.11), <0.001	15.02 (12.83 to 17.21), <0.001