Original Investigation

Depression, Anxiety, and COPD: The Unexamined Role of Nicotine Dependence

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Abstract

Introduction: Previous studies have shown links between anxiety and depression and chronic obstructive pulmonary disease (COPD), but little is known about possible mechanisms of this association. The current study examined whether the observed relationship between anxiety and depression and COPD is explained by confounding due to cigarette smoking and lifetime nicotine dependence.

Methods: Data were drawn from the National Comorbidity Survey Replication, a community-based representative sample of adults in the United States.

Results: Analyses suggest that the association between anxiety disorders and COPD appears to be largely explained by confounding by former cigarette smoking and lifetime nicotine dependence. The association between mood disorders and COPD appears to be largely explained by confounding by lifetime nicotine dependence.

Conclusions: These findings provide initial evidence suggesting that the association between anxiety, depression, and COPD may be at least partly attributable to confounding by cigarette smoking and nicotine dependence. Efforts toward prevention of chronic lung disease may be more effective if treatment and prevention efforts aimed at smoking cessation address mental health problems.

Introduction

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of mortality in the United States (Hurd, 2000). In

1996, 6.0% of the United States population was estimated to have COPD (Mannino, 2002). The economic burden of COPD in the United States is calculated at greater than \$14 billion and in 1998, was responsible for 14.2 million ambulatory visits to hospitals or physician offices (Mannino, 2002). However, this figure is likely to be higher now, as the prevalence of COPD in the United States has been increasing (Hurd, 2000; Mannino, Homa, Akinbami, Ford, & Redd, 2002). Understanding the key preventable risk factors for COPD is therefore essential to reducing the impact of this disease on the community. Cigarette smoking is known to be the single most important preventable risk factor for COPD (Mannino, 2002; Mannino et al., 2002).

In recent years, there has been growing interest in the relationship between mental disorders and COPD among adults. Several epidemiologic and clinical studies have found high rates of mood and anxiety disorders among adults with COPD (Di Marco et al., 2006; Goodwin, Chuang, Simuro, Davies, & Pine, 2007; Janson, Bjornsson, Hetta, & Boman, 1994; Karajgi, Rifkin, Doddi, & Kolli, 1990; Light, Merrill, Despars, Gordon, & Mutalipassi, 1985; van Manen et al., 2002; Yellowlees, Alpers, Bowden, Bryant, & Ruffin, 1987; Yohannes, Baldwin, & Connolly, 2000). Specifically, clinical studies have found elevated rates of depressive and anxious symptomatology (Eisner et al., 2010; Giardino et al., 2010; Karajgi et al., 1990; Light et al., 1985; Ottenheim, Giltay, Zitman, van der Mast, & de Craen, 2010; Yohannes et al., 2000) and mood and anxiety disorders (Kunik et al., 2005; Laurin et al., 2007) among patients with COPD, and population-based studies have found links between COPD and mood and anxiety disorders among adults in the community (Moody, McCormick, & Williams, 1990).

The mechanism(s) of the association between COPD and anxiety/mood disorders are not known. It could be that having COPD

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leads to the onset of anxiety/mood disorders-related possibly to discomfort, functional limitations, and/or the knowledge that one has a serious and often irreversible illness. It is also conceivable that anxiety/mood disorders lead—either directly or through some mediating factor—to the onset of COPD. Finally, it is possible that the co-occurrence of COPD and anxiety/mood disorders arises from exposure to common antecedent risk factors for both.

In a parallel line of research, there has been mounting evidence of strong links between cigarette smoking/nicotine dependence and mood and anxiety disorders among adults in the community (Breslau, 1995; Breslau, Kilbey, & Andreski, 1991; Nelson & Wittchen, 1998; Substance Abuse and Mental Health Services Administration, 1996a, 1996b; Sullivan & Kendler, 1998). A recent study indicated that over 70% of cigarettes are consumed by adults with at least one mental disorder (Grant, Hasin, Chou, Stinson, & Dawson, 2004; Mykletun, Overland, Aaro, Liabo, & Stewart, 2008). There is also evidence of a dose-response relationship between cigarette smoking and anxiety/mood disorders (Cardenas et al., 2002; Lasser et al., 2000). Cigarette smoking is the strongest risk factor for COPD (Global Initiative for Chronic Obstructive Lung Disease, 2005). Yet, to our knowledge, studies to date have not fully examined the potential role of cigarette smoking in the relationship between anxiety/mood disorders and COPD. As cigarette smoking is associated with both mood/anxiety disorders and COPD, it is possible that the link between anxiety/mood disorder and COPD is due to confounding or mediation by cigarette smoking. Previous studies that have examined the role of smoking in the relationship between anxiety/depression and COPD have adjusted only for current smoking. This is limited because cumulative smoking across one's lifetime is the exposure that is thought to contribute to COPD—not simply smoking in the past 12 months. To our knowledge, no studies to date have examined the potential confounding and/or mediating role of former smoking on the relationship between anxiety and depressive disorders and COPD.

Approximately half of adults who smoke cigarettes develop nicotine dependence (DiFranza et al., 2000; McNeill, 1991). Nicotine dependence is a diagnosable mental disorder (Diagnostic and Statistical Manual of Mental Disorders, 1994) according to *DSM-IV*, as are mood and anxiety disorders, yet there are few available data on the relationships between mental disorders and COPD that have included an examination of the association between nicotine dependence and COPD. This is likely attributable to measurement issues of several types, including the lack of measurement of nicotine dependence in studies that gather information on cigarette use and COPD and lack of information on COPD in studies that gather information on nicotine dependence. Nicotine dependence is also highly comorbid with anxiety/mood disorders (John, Meyer, Rumpf, & Hapke, 2004; Strong et al., 2007; Zimmerman, Chelminski, & McDermut, 2002). Therefore, examining the potentially confounding role of nicotine dependence in the relationship between anxiety/mood disorders and COPD may also be informative in better understanding this link.

In light of this literature, the goal of the current study was to begin to address these important gaps in existing research. First, this study examined the relationship between nicotine dependence and COPD among adults in the United States. Second, this study examined the relationship between anxiety and mood disorders and COPD in this population. Third, this study

investigated current and former cigarette smoking and lifetime nicotine dependence as separate potential confounders in the relationship between anxiety and depression and COPD among adults. We hypothesized that former cigarette smoking and nicotine dependence would act as confounders in the relationship between anxiety and depressive disorders and COPD, as both are hypothesized to be independent risk factors for anxiety and depressive disorders (Berlin & Singleton, 2008; Dube et al., 2009; Grant et al., 2005; Mykletun et al., 2008) as well as COPD.

Methods

Study Sample

Data on individuals aged 18 years and older who completed Parts I and II of the National Comorbidity Survey Replication (NCS-R) were used in this study. The NCS-R is a nationally representative sample ($N = 9,882$) of English-speaking individuals aged 18 years and older living in U.S. households between February 2001 and December 2004 (Breslau, 1995). Part I of the NCS-R survey, which comprised core diagnostic assessment, was administered to all respondents, Part II was administered to only those individuals who met lifetime criteria for a Part I disorder and a probability sample of other respondents (Breslau, Kilbey, & Andreski, 1993). Assessment of COPD, the primary outcome of interest, was a component of Part I, but mental disorders, the exposure of interest, was assessed in Part II. As such, analyses were carried out on the sample that completed both Parts I and II (i.e., $N = 5,692$). The data were weighted to adjust for the sampling scheme of the NCS-R including the oversampling of those individuals who met lifetime criteria for Part I disorders. The NCS-R received human subjects consent approval from Harvard Medical School and the University of Michigan.

Outcome of Interest

The main dependent outcome was a history of COPD, which was ascertained by a single question, "Did a doctor or other health professional ever tell you that you had any other chronic lung disease, like COPD or emphysema?" This question followed questions about asthma and tuberculosis. Individuals who responded affirmatively were classified as having COPD, and those who did not were classified as not having COPD.

Independent Variables

Age, sex, marital status (never married, married/cohabitating, separated/divorced/widowed), and race/ethnicity (non-Hispanic Whites, Blacks, Hispanics, and other) were the demographic factors examined as covariates. Lifetime depressive and anxiety disorders as well as nicotine dependence were examined as potential predictors based on previous findings of their significant associations with COPD (Breslau et al., 1991; Di Marco et al., 2006; Goodwin et al., 2007; Halpern, Stanford, & Borker, 2003; Janson et al., 1994; Jemal, Ward, Hao, & Thun, 2005; Karajgi et al., 1990; Light et al., 1985; Mannino, 2002; National Institutes of Health, 2004; Sullivan & Kendler, 1998; van Manen et al., 2002; Yellowlees et al., 1987; Yohannes et al., 2000). These mental disorders were assessed in the NCS-R using the disorder-specific components of the Composite International Diagnostic Interview (CIDI) and examined as dichotomous variables (yes, no) in these analyses.

DSM-IV Mental Disorders

Anxiety and mood disorders and nicotine dependence were assessed using the World Health Organization CIDI Version 3.0. The CIDI is a structured diagnostic interview, which is administered by lay interviewers who are specifically trained in CIDI administration (Kessler & Ustun, 2004). The anxiety disorders assessed by the CIDI included panic disorder, generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), specific phobia, social phobia, agoraphobia, and separation anxiety disorder and the mood disorders assessed included major depression, dysthymia, and bipolar I disorder. Clinical reappraisal studies have shown good concordance between CIDI diagnoses and diagnoses made with the research version of the Structured Clinical Interview for *DSM-IV* (First, Spitzer, Gibbon, & Williams, 2002; Haro et al., 2006). Due to low cell counts, we did not include bipolar disorder, panic disorder, separation anxiety disorder, agoraphobia, or dysthymia in our tables.

Nicotine Dependence

Assessment of nicotine dependence was based on the unique characteristics of nicotine dependence as distinct from other substances. To that end, the AUDADIS-IV used an extensive list of over 40 questions to assess nicotine dependence and obtains extensive information on time frames of nicotine use and dependence. Diagnoses were made according to the *DSM-IV* criteria (Diagnostic and Statistical Manual of Mental Disorders, 1994). Criteria for nicotine dependence include 3/7 of the following: (a) the need for more nicotine to achieve desired effect, (b) the subject meets the criteria for nicotine withdrawal syndromes, (c) the use of tobacco by the subject more than the subject intended, (d) the persistent desire or unsuccessful efforts to cut down on nicotine use, (e) a great deal of time spent using tobacco (e.g., chain smoking), (f) the necessity to give up activities in favor of nicotine use, and (g) continued use despite recurrent physical or psychological problems likely to have been caused by nicotine use. Nicotine withdrawal was assessed as a syndrome as described by the *DSM-IV* based on four symptoms: (a) the use of nicotine upon waking, (b) the use of nicotine after being in a situation in which nicotine was restricted, (c) the use of nicotine to relieve or avoid withdrawal symptoms, and (d) the need to wake up in the middle of the night to use nicotine.

The reliability and validity of the nicotine dependence diagnosis was assessed via random subsample of 347 respondents who were reinterviewed with the nicotine dependence module up to 10 weeks after initial appraisal (Grant, Moore, & Kaplan, 2003). The reliability of the previous 12-month (i.e., current) diagnosis was good ($k = .63$). Furthermore, a series of linear regression analyses were used to validate the diagnoses by examining the association between nicotine dependence and Short-Form-12v2 (an often used measure of generic quality of life which generates 10 component and profile scores assessing various dimensions of physical and mental disability; Ware, Kosinski, Turner-Bowker, & Gandek, 2002) physical disability scores. Lifetime nicotine dependence (vs. no lifetime nicotine dependence) was measured as a binary variable.

Smoking

Smoking was measured with two binary variables: current smoking (vs. never smoking) and former smoking (lifetime, but not current smoking vs. never smoking).

Demographic Variables

Age, sex, marital status (never married, married/cohabitating, separated/divorced/widowed), and race/ethnicity (non-Hispanic Whites, Blacks, Hispanics, and other) were the demographic factors examined as covariates.

Data Analysis

Statistical Package for Social Sciences (SPSS) Version 14.0 for Windows was used for all analyses (Nelson & Wittchen, 1998). Frequency distributions and measures of central tendency were conducted to characterize the study sample. Chi-square analyses were conducted to compare individuals with and without COPD on demographic characteristics and mental disorders. Logistic regression analyses were used to examine the relationships between current smoking, former smoking, and nicotine dependence and COPD, adjusting for differences in demographics. The same procedure was then used to examine the relationship between COPD and depressive and anxiety disorders, adjusting for sociodemographic factors and current smoking. Analyses were then adjusted for former smoking, and subsequently lifetime nicotine dependence was added to the model. All analyses were evaluated using the two-tailed 0.05 level of statistical significance.

Results

COPD, Mental Disorders, and Demographics

As shown in Table 1, 36.0% of those with COPD had lifetime nicotine dependence, 17.7% had GAD, and 24.8% had major depressive disorder. Adults with COPD were significantly older (59.7 [16.2%] vs. 44.7 [17.8%], $p < .0001$), more likely to be female (62.1% vs. 37.9%, $p = .045$), less likely to be married/cohabitating (46.4% vs. 53.6%, $p < .0001$), and more likely to be Caucasian (70.4% vs. 29.6%, $p < .0001$) compared with those who did not have COPD.

Smoking, Nicotine Dependence, and COPD

Current smoking (past 12-months) was associated with significantly increased odds of COPD (see Table 2). This association persisted after adjusting for differences in demographic characteristics and nicotine dependence, though the strength of the relationship was attenuated. Former smoking was also significantly associated with COPD, though the strength of the link was not as strong as current smoking. Almost 1 in 10 individuals with nicotine dependence had COPD; the odds of COPD among those with nicotine dependence were significantly elevated compared with those without nicotine dependence, even after adjusting for demographic differences (see Table 3). The odds of COPD associated with nicotine dependence were significantly greater than that associated with cigarette smoking (after adjusting for nicotine dependence).

Mental Disorders and COPD

Any anxiety disorder, GAD, social phobia, and PTSD were associated with significantly increased odds of COPD compared with those without anxiety disorders (see Table 4). These associations remained statistically significant after adjusting for

Table 1. Characteristics According to COPD Status, Weighted *n* (%)

	No COPD, <i>n</i> = 5,572	COPD, <i>n</i> = 147	
Age (mean, <i>SD</i>)	44.7 (17.8)	59.7 (16.2)	87.1, <i>p</i> < .0001
Female	2941 (52.8)	147 (62.1)	4.2, <i>p</i> = .04
Race/ethnicity			20.9, <i>p</i> < .0001
Hispanic	622 (11.2)	8 (6.4)	
Black	689 (12.4)	15 (12.0)	
Other	203 (3.6)	14 (11.2)	
White	4,052 (72.8)	88 (70.4)	
Marital status			41.9, <i>p</i> < .0001
Married/cohabitating	3,125 (56.1)	58 (46.4)	
Separated/divorced/widowed	1,131 (20.3)	54 (43.2)	
Never married	1,310 (23.5)	13 (10.4)	
Education			47.9, <i>p</i> < .0001
0–11 years	906 (16.3)	48 (38.4)	
12 years	1,810 (32.5)	41 (32.8)	
13–15 years	1,546 (27.8)	21 (16.8)	
16+ years	1,304 (23.4)	15 (12.0)	
Mental health status (lifetime)			
Nicotine dependence	424 (7.6)	45 (36.0)	130.2, <i>p</i> < .0001
Generalized anxiety disorder	421 (7.6)	22 (17.7)	17.5, <i>p</i> < .0001
Major depressive disorder	914 (16.4)	31 (24.8)	6.2, <i>p</i> = .01
Posttraumatic stress disorder	371 (6.7)	18 (14.4)	11.8, <i>p</i> = .001
Social phobia	668 (12.0)	26 (20.8)	8.8, <i>p</i> = .003
Specific phobia	702 (12.6)	18 (14.8)	NS

Note. COPD = chronic obstructive pulmonary disease; NS = not significant.

demographic differences and current smoking. After adjusting for former smoking, the associations between any anxiety disorder and PTSD and COPD were no longer statistically significant. After adjusting for former smoking and nicotine dependence, only the relationship between social phobia and COPD remained statistically significant.

Any mood disorder and major depression were associated with significantly increased odds of COPD compared with those without mood disorders (see Table 4). These associations remained significant and even increased slightly in strength after adjusting for differences in demographics and current cigarette smoking. After adjusting for former smoking, these associations were no longer statistically significant, and their strength was attenuated even further after adjusting for nicotine dependence.

Table 2. Association of Current Smoking, Former Smoking, and Odds of COPD

	COPD, weighted, <i>n</i> (%)	OR (95% CI)	AOR ^a (95% CI)
Never smoker	25 (1.00)	Ref	Ref
Current smoker	72 (4.38)	4.53 (2.86–7.20)	2.80 (1.60–4.80)
Former smoker	49 (3.47)	2.74 (1.70–4.60)	1.97 (1.10–3.44)

Note. AOR = adjusted odds ratio; COPD = chronic obstructive pulmonary disease; OR = odds ratio. Bold values represent *p* < .05.

^aAdjusted for age, sex, education, marital status, race, household income and lifetime nicotine dependence.

Discussion

There are three main findings of this study. First, the observed relationship between cigarette smoking and COPD appears to be confounded by *DSM-IV* nicotine dependence, as nicotine dependence is strongly associated with both an increased odds of cigarette smoking and COPD. Second, the association between all anxiety disorders and COPD appears to be largely explained by confounding by former cigarette smoking and nicotine dependence, with the exception of the relationship between COPD and social phobia. Specifically, the links between any anxiety disorder and COPD and PTSD and COPD appears to be explained by confounding with former cigarette smoking, and the link between COPD and GAD appears to be explained by confounding with nicotine dependence. Third, the association between mood disorders and COPD appears to be largely explained by nicotine dependence. The consistency of these findings with previous results as well as the clinical and public health implications will be discussed below.

Table 3. Association of Lifetime Nicotine Dependence and Odds of COPD

	COPD, weighted, <i>n</i> (%)	AOR ^a (95% CI)
No nicotine dependence	89 (1.75)	Ref
Nicotine dependence	58 (9.3)	6.10 (4.30–8.77)

Note. AOR = adjusted odds ratio; COPD = chronic obstructive pulmonary disease. Bold values represent *p* < .05.

^aAdjusted for age, sex, education, marital status, race, and household income.

Table 4. Association of Mental Disorders^a and Odds of COPD

Lifetime mental disorders	Weighted, n (%)		OR (95% CI)	AOR ^b (95% CI)	AOR ^c (95% CI)	AOR ^d (95% CI)	AOR ^e (95% CI)
	No COPD n = 5,572	COPD n = 147					
Any anxiety	2,557 (45.89)	80 (54.42)	1.41 (1.01–1.96)	1.73 (1.23–2.44)	1.78 (1.17–2.72)	1.52 (0.94–2.44)	1.39 (0.86–2.24)
Generalized disorder	714 (12.81)	38 (25.85)	2.37 (1.63–3.46)	2.54 (1.72–3.77)	2.33 (1.46–3.72)	1.91 (1.08–3.39)	1.79 (1.00–3.18)
Specific phobia	1,122 (20.14)	33 (22.45)	1.15 (0.78–1.70)	1.23 (0.82–1.84)	1.33 (0.83–2.13)	1.26 (0.70–2.26)	1.21 (0.67–2.18)
Social phobia	1,072 (19.24)	44 (29.93)	1.79 (1.25–2.57)	2.12 (1.46–3.08)	2.33 (1.51–3.60)	2.12 (1.26–3.56)	2.01 (1.20–3.39)
Posttraumatic stress disorder	573 (10.28)	29 (19.73)	2.14 (1.42–3.25)	2.49 (1.61–3.86)	2.54 (1.54–4.18)	1.86 (0.94–3.67)	1.79 (0.91–3.54)
Any mood disorder	1,686 (30.26)	56 (38.10)	1.42 (1.01–1.99)	1.74 (1.22–2.48)	1.64 (1.08–2.49)	1.47 (0.90–2.42)	1.38 (0.84–2.27)
Major depressive disorder	1,507 (27.03)	51 (34.69)	1.43 (1.02–2.02)	1.76 (1.23–2.52)	1.66 (1.09–2.54)	1.48 (0.89–2.45)	1.40 (0.84–2.32)

Note. AOR = adjusted odds ratio; COPD = chronic obstructive pulmonary disease; OR = odds ratio. Bold values represent $p < .05$.

^aReference group for each category is the absence of the specified mental disorder.

^bAdjusted for age, sex, race, education, marital status, and household income.

^cAdjusted for age, sex, race, education, marital status, household income, and current smoking.

^dAdjusted for age, sex, race, education, marital status, household income, and former smoking.

^eAdjusted for age, sex, race, education, marital status, household income, former smoking, and lifetime nicotine dependence.

The first objective of this paper was to examine the role of nicotine dependence in the relationship between cigarette smoking and COPD. We found that confounding by nicotine dependence partially explained the link between cigarette smoking and COPD. While number of cigarettes is likely to be the mechanism of this link, this finding has important and underexamined public health implications. Specifically, the Healthy People 2010 goal of reducing cigarette smoking to 12% of the population has not been met (Levy, Nikolayev, Mumford, & Compton, 2005). The intractability of nicotine dependence is considered similar to an addiction to alcohol and/or drug use disorders. Yet, treatments for illicit drug use disorders are more widely available and reimbursable by insurance and Medicaid, and many more resources are put toward clinical interventions with these populations. For instance, New York State Medicaid offers two courses of smoking cessation therapy per year at a maximum, and if one course is not completed, it cannot be replaced (State of New York Department of Health, 2007). A greater emphasis on treating nicotine dependence among cigarette smokers will yield the most productive outcomes in terms of reducing smoking-related COPD. Not surprisingly, we also found that lifetime nicotine dependence is even more strongly associated with COPD than either current or former cigarette smoking. While this may seem obvious, what is important in documenting this finding is that nicotine dependence is a mental disorder, as defined by the *DSM-IV*. Therefore, these data suggest that a mental disorder (i.e., nicotine dependence) appears to account for a substantial percentage of COPD, a leading cause of premature mortality among adults. This highlights the potential cost and life-saving benefit of devoting more resources toward improving access to smoking cessation programs that address nicotine dependence, either through behavioral or pharmacologic therapies. These programs are more costly—but show much greater effectiveness than those without such components—in successful quit rates (Crain & Bhat, 2010).

Our second finding suggests that the previously observed link between anxiety disorders and COPD appears to be largely due to confounding by smoking and nicotine dependence. Specifically, the links between any anxiety disorders and COPD and PTSD and COPD are no longer significant after adjusting for former smoking. As both anxiety disorders and COPD are

strongly related to cigarette smoking, these results are not surprising. But these results do call into question whether, and to what degree, the link can be attributed to anxiety over having COPD and instead suggests that common risk factors for both COPD and anxiety disorders may explain this association. Finally, the relationship between GAD and COPD appears to be attributable to confounding by nicotine dependence. Previous studies have suggested that cigarette smoking may lead to GAD (Johnson et al., 2000), and strong associations have been found between nicotine dependence and GAD (Grant et al., 2004).

Third, we found that the relationship between mood disorders and COPD appears to be explained by confounding with nicotine dependence. Specifically, the association between mood disorders and COPD is no longer statistically significant after adjusting for nicotine dependence. This is consistent with our hypothesis that the link between COPD and mood disorders may be explained by exposure to a common risk factor for both, rather than a causal link between the two. As these data are cross sectional, we are only able to test for possible confounding but not for mediation. A recent study found that depressive symptoms remained associated with COPD after adjusting for smoking (Ng, Niti, Fones, Yap, & Tan, 2009). Our findings are not necessarily inconsistent with this in that we also found that the link between major depression and COPD remained after adjusting for smoking, but only that it was no longer significant after adjusting for nicotine dependence. To our knowledge, this is the first study that has examined the role of nicotine dependence in this link.

Limitations of this study should be considered when interpreting these results. First, we relied upon self-reports of COPD, which leave our results vulnerable to self-report bias. However, cases of COPD would more likely be underreported rather than overreported as many people with less severe COPD do not realize that they have the disease (Rennard & Vestbo, 2006). In addition, underreporting of COPD would unlikely be influenced by whether or not a person has a mental disorder. This type of potential nondifferential misclassification of disease would lead to an underestimate of the strength of the relationships between anxiety and mood disorders and COPD, and thus, our findings are likely to be conservative. Also, the question about COPD or

emphysema was somewhat vague, so it is possible that those with rare lung disease such as primary pulmonary hypertension or sarcoidosis are included here, though this is likely to be a very small number since these diseases are rare. Future studies that can obtain physician-diagnosed specific diseases on large population samples would be useful in confirming these results and in determining whether they apply to specific diseases and not others. Also, longitudinal studies will be needed in order to prospectively examine the nature of these relationships to gain a better understanding of these associations and whether there is evidence of mediation. In addition, we are limited in the range of mental disorders we could examine to those measured in the NCS-R. Future studies that can examine the role of smoking and nicotine dependence in the relationship between severe and persistence mental disorders (e.g., some forms of schizophrenia) are needed as rates of COPD are high among persons with these conditions (Carney, Jones, & Woolson, 2006).

Despite these limitations, this study also has a number of important strengths. These include a large representative sample of the U.S. population; the use of a valid and reliable interview measure for a wide range of anxiety disorders, mood disorders, and nicotine dependence; and being the first study to assess nicotine dependence in addition to smoking status in relation to COPD.

In conclusion, our results suggest that much of the observed relationship between COPD and anxiety and depressive disorders may be attributable to confounding due to cigarette smoking and lifetime nicotine dependence, rather than a direct causal link between the two. This highlights the important role of poor health behaviors in the link between psychiatric comorbidity and COPD and points to the need for smoking cessation interventions that simultaneously address nicotine dependence and anxiety and depressive disorders.

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Declaration of Interests

None Declared.

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RDG conceived of the study, planned original analyses, and wrote the first draft of the manuscript; KLL, ESB, DAF, and ARL contributed to writing the manuscript and each made important contributions to the study design and interpretation of results; EJ analyzed the data.

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