

# Chronic Bronchitis, Cigarette Smoking, and the Subsequent Onset of Depression and Anxiety: Results From a Prospective Population-Based Cohort Study

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**Objective:** The authors used data from a prospective, population-based cohort study to examine: (a) whether the presence of chronic bronchitis predicts the subsequent onset of depression or anxiety, and (b) if the incidence of depressed or anxious cases was different for smokers compared with nonsmokers. **Materials and Methods:** For studying the relation between chronic bronchitis and anxiety or depression, we used data from respectively 4468 and 4520 respondents. **Results:** The number of incident anxious (19.1%,  $n = 17$ ) and depressed (14.0%,  $n = 13$ ) cases was highest in employees with chronic bronchitis compared with employees without respiratory complaints (4.3%,  $n = 189$  and 3.3%,  $n = 145$ , respectively). The presence of chronic bronchitis was associated with a significant increase in anxious and depressed cases (odds ratio (OR) for anxiety = 5.09, 95% confidence interval (CI) 2.91, 8.89; OR for depression = 4.38, 95% CI 2.35, 8.16). The incidence of anxiety as well as depression was strongest in the smokers group (OR for anxiety = 8.94, 95% CI 4.08, 19.59; OR for depression = 7.56, 95% CI 3.37, 16.96). **Conclusions:** This prospective study shows significantly higher levels of anxiety as well as depression in employees with chronic bronchitis. Results also seem to indicate that smoking cigarettes modifies this association, resulting in an increased risk of depression and anxiety in employees with chronic bronchitis who smoke. **Key words:** chronic bronchitis; depression; anxiety; cigarette smoking; prospective cohort.

**COPD** = chronic obstructive pulmonary disease; **HADS** = Hospital Anxiety and Depression Scale; **HADS-A** = HADS anxiety subscale; **HADS-D** = HADS depression subscale.

## INTRODUCTION

Patients with chronic bronchitis or emphysema (i.e., chronic obstructive pulmonary disease (COPD)) have repeatedly been characterized as being at increased risk of developing psychiatric disorders such as depression and anxiety. However, until recently, the empirical evidence for a significant risk of depression in patients with COPD remained inconclusive (1). Based on their systematic review, Van Ede et al. (1) concluded that most studies were of poor methodological quality, did not use a (healthy) control group, and used small sample sizes. Since the publication of the review conducted by Van Ede et al. (1), the number of studies addressing the relation between psychiatric morbidity and COPD has increased. Patients with COPD not only seem to be at increased risk of depression (e.g., 2–6), the prevalence of anxiety disorders, particularly generalized anxiety disorder and panic disorder, also seems to be higher in patients with COPD compared with that in the general public (see Brenes (7) for an overview and Wagena et al. (5,6)).

To our knowledge, all studies addressing the relation between psychiatric disorders and COPD have been of cross-sectional design (e.g., 2–4,8–14). However, this design is known to be prone to bias because cause and effect cannot be separated. Therefore, in the present study we used data from a prospective, population-based cohort study to extend the in-

vestigation of the psychiatric consequences of COPD. Because most studies on this topic used cross-sectional data, we wanted to examine whether the presence of COPD predicts the subsequent onset of depression or anxiety. Furthermore, because recent research has shown that associations between smoking cigarettes and psychiatric disorders are attributable, at least in part, to the role of smoking in predicting the onset of psychiatric disorders (15,16), we examined whether the incidence of depressed or anxious cases was different in subjects with COPD compared with that in healthy subjects, stratified by smoking status.

## MATERIALS AND METHODS

### Sample

Because COPD is defined as a disease state characterized by airflow limitation that is not fully reversible and usually progressive (especially if a person continues to smoke) (17), and we wanted to investigate the psychiatric consequences mainly in subjects with mild or moderate COPD, we used data from a cohort study among employees. This study, the Maastricht Cohort Study was set up as a prospective population-based cohort study among Dutch employees and is described in detail by Kant et al. (18). Although this cohort was established in 1999 the first data on COPD were available from January 2001. In January 2001 we sent a questionnaire on respiratory complaints, depression, anxiety, and smoking to 8070 employees. In total, 7483 employees completed and returned the questionnaire (92.7%). All employees who returned this questionnaire received a second questionnaire in June 2002, containing the same set of variables. Five thousand five hundred and forty-two employees completed and returned the second questionnaire (74.1%). When we studied the relation between chronic bronchitis and anxiety, we excluded the data from respondents who fulfilled the criteria for anxiety caseness and doubtful caseness at the first assessment (i.e., anxiety score  $>7$ ), respondents who had a missing value on the anxiety scale of the Hospital Anxiety and Depression Scale (HADS) on one or both assessments, respondents who were classified differently on both assessments with regard to chronic bronchitis, and those respondents who could not be classified as having chronic bronchitis or not. This resulted in a sample size of 4468. When we studied the relation between chronic bronchitis and depression, we excluded the data from respondents who fulfilled the criteria for depression caseness and doubtful caseness at the first assessment (i.e., depression score  $>7$ ), respondents who had a missing value on the depression scale of the HADS on one or both assessments, respondents who were classified differently on both assessments with regard to chronic bronchitis, and those

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respondents who could not be classified as having chronic bronchitis or not. This resulted in using data from 4520 respondents.

## Assessment of Chronic Bronchitis

In clinical terms, chronic bronchitis is usually defined by the presence of chronic or recurrent increases in bronchial secretions sufficient to cause expectoration and cough (19). In this study, the chronic bronchitis definition conforms with the definition and classification of chronic bronchitis for clinical and epidemiological purposes, as proposed by the Medical Research Council: "the presence of cough and sputum production on most days for a minimum of 3 months per year, in the previous 2 successive years, and cannot be attributed to other pulmonary or cardiac causes" (20,21). This procedure has been used in several other epidemiological studies (22,23). The diagnoses were described in a way that was easy to understand for all respondents.

## Assessment of Depression and Anxiety

We used the validated Dutch version of the HADS (24,25). The HADS was developed by Zigmond and Snaith (26) originally to identify caseness (possible and probable) of anxiety and depression among patients in nonpsychiatric hospital clinics. Spinhoven et al. (24) found that the Dutch version of the HADS was stable across different age groups from the general population and in different clinical samples. It is divided in an anxiety subscale (HADS-A) and a depression subscale (HADS-D) both containing seven items. Each question is rated 0 to 3, giving a possible maximum score for anxiety as well as depression of 21. Subjects scoring  $\geq 11$  on the depression subscale were classified as being depressed and subjects scoring  $\geq 11$  on the anxiety subscale were classified as being anxious. Subjects who scored between 7 and 11 were classified as doubtful case.

## Assessment of Smoking Status

Questions regarding the smoking habits of employees refer only to cigarette smoking. To assess the smoking status of respondents, we asked them if they smoked cigarettes on a daily basis and if they used to smoke every day in the past. We defined respondents as never smokers if they answered "no" to both questions. "Past smokers" were defined as giving an affirmative response only to the second question, and "current smokers" if they gave an affirmative response to the question "Do you smoke every day?" We also assessed how many cigarettes they (used to) smoke on average per day.

## Statistical Procedures

First, *t* test for two independent samples and  $\chi^2$  test were used to test the differences in demographic and smoking characteristics between employees with chronic bronchitis and healthy employees. Next, multivariate logistic regression analyses were performed to calculate for sex, age, educational

level, and smoking status adjusted odds ratio ((ORs) with 95% confidence intervals (CI) for the association between chronic bronchitis (assessed in January 2001), and the subsequent onset of psychiatric disorders (assessed in June 2002). The analyses were conducted separately for anxiety and depression. Third, the multivariate logistic regression analyses were repeated but now stratified for smoking status. The statistical analyses were carried out using SAS release 8.02 (SAS Institute Inc., Cary, NC).

## RESULTS

Tables 1 and 2 show the demographic and smoking characteristics of the samples used to study the relation between chronic bronchitis and anxiety, and chronic bronchitis and depression, respectively. Both samples (as well as the groups of employees with chronic bronchitis and those without respiratory complaints) consisted mainly of men (approximately 70%). In both samples, the percentage of smokers in the group of employees with chronic bronchitis was significantly higher ( $p < .001$ ). In addition, the percentage of smokers who smoke more than 10 cigarettes per day is higher in the group of employees with chronic bronchitis compared with employees without respiratory complaints. At the first assessment, 634 respondents were classified as anxious (score  $\geq 11$  on the anxiety subscale; 8.5%), and 504 as depressed (score  $\geq 11$  on the depression subscale; 6.7%).

Tables 3 and 4 show that the number of incident anxious (19.1%,  $n = 17$ ) and depressed (14.0%,  $n = 13$ ) cases is highest in employees with chronic bronchitis compared with employees without respiratory complaints (4.3%,  $n = 189$  and 3.3%,  $n = 145$ , respectively). The presence of chronic bronchitis was associated with a significant increase in anxious and depressed cases during the 18 month follow-up period (adjusted ORs for anxiety = 5.09, 95% CI 2.91, 8.89; adjusted OR for depression = 4.38, 95% CI 2.35, 8.16). Furthermore, although in nonsmoking employees with chronic bronchitis, the risk of developing anxiety or depression is also increased (OR for anxiety in nonsmokers = 2.93, 95% CI 1.22, 7.03; OR for depression in nonsmokers = 2.01, 95% CI 0.61, 6.57), this risk is highest in smokers (OR for anxiety in smokers = 8.94, 95% CI 4.08, 19.59; OR for depression in smokers =

TABLE 1. Characteristics of Employees With Chronic Bronchitis and Healthy Individuals at First Assessment (Anxiety)

	Employees with Chronic Bronchitis (N = 89)	Employees without Respiratory Complaints (N = 4379)	Statistics
Mean (SD) age (years)	42.5 (8.6)	41.7 (8.3)	$t = -0.087, df = 4466, p = .38$
Men (%)	59 (66.3%)	3237 (73.9)	$\chi^2 = 2.6, df = 1, p = .11$
Smoking status			
No. of smokers (%)	40 (44.9)	861 (19.7)	$\chi^2 = 34.5, df = 1, p < .001$
No. of non-smokers (%)	49 (55.1)	3510 (80.3) <sup>a</sup>	
Cigarettes per day			
1 to 10 cigarettes (%)	17 (19.8)	1005 (23.4)	$\chi^2 = 5.3, df = 2, p = .07$
11 to 20 cigarettes (%)	31 (36.1)	922 (21.5)	
More than 20 cigarettes (%)	10 (11.6)	422 (9.8)	
Education			
Low education (%)	32 (36.4)	1152 (26.8)	$\chi^2 = 5.2, df = 2, p = .07$
Medium education (%)	29 (33.0)	1387 (32.2)	
High education (%)	27 (30.7) <sup>c</sup>	1764 (41.0) <sup>b</sup>	

<sup>a</sup> 8 missing values, <sup>b</sup> 76 missing values, <sup>c</sup> 1 missing value.

TABLE 2. Characteristics of Employees With Chronic Bronchitis and Healthy Individuals at First Assessment (Depression)

	Employees with Chronic Bronchitis (N = 93)	Employees without Respiratory Complaints (N = 4427)	Statistics
Mean (SD) age (years)	42.7 (8.5)	41.7 (8.3)	$t = -1.09, df = 4518, p = .27$
Men (%)	65 (69.9)	3243 (73.3)	$\chi^2 = 0.52, df=1, p = .47$
Smoking status			
No. of smokers (%)	43 (46.2)	884 (20.0)	$\chi^2 = 38.4, df = 1, p < .001$
No. of non-smokers (%)	50 (53.8)	3536 (80.0) <sup>a</sup>	
Cigarettes per day			
1 to 10 cigarettes (%)	18 (20.2)	1025 (23.6)	$\chi^2 = 5.6, df = 2, p = .06$
11 to 20 cigarettes (%)	32 (36.0)	939 (21.6)	
More than 20 cigarettes (%)	14 (15.7)	427 (9.8)	
Education			
Low education (%)	36 (39.6)	1167 (26.9)	$\chi^2 = 8.0, df = 2, p = .02$
Medium education (%)	28 (30.8)	1397 (32.2)	
High education (%)	27 (29.7) <sup>c</sup>	1770 (40.8) <sup>b</sup>	

<sup>a</sup> 7 missing values, <sup>b</sup> 93 missing values, <sup>c</sup> 2 missing values.

TABLE 3. Incident Anxious Cases and Odds Ratios for the Association Between Chronic Bronchitis and Psychiatric Morbidity in Dutch Employees Stratified for Smoking Status

	n	Anxious Cases, n (%)	Adjusted Odds Ratio, (95% CI)
Total group			
Chronic bronchitis	89	17 (19.1)	5.09 (2.91,8.89) <sup>a</sup>
Healthy controls	4379	189 (4.3)	1.00
Smokers			
Chronic bronchitis	40	11 (27.5)	8.94 (4.08,19.59) <sup>b</sup>
Healthy controls	861	36 (4.2)	1.00
Non-smokers			
Chronic bronchitis	49	6 (12.2)	2.93 (1.22,7.03) <sup>b</sup>
Healthy controls	3510	152 (4.3)	1.00

<sup>a</sup> Odds ratios adjusted for sex, age, educational level and smoking status.

<sup>b</sup> Odds ratios adjusted for sex, age, educational level.

TABLE 4. Incident Depressed Cases and Odds Ratios for the Association Between Chronic Bronchitis and Psychiatric Morbidity in Dutch Employees Stratified for Smoking Status

	n	Depressed Cases, n (%)	Adjusted Odds Ratio, (95% CI)
Total group			
Chronic bronchitis	93	13 (14.0)	4.38 (2.35,8.16) <sup>a</sup>
Healthy controls	4427	145 (3.3)	1.00
Smokers			
Chronic bronchitis	43	10 (23.3)	7.56 (3.37,16.96) <sup>b</sup>
Healthy controls	884	37 (4.2)	1.00
Non-smokers			
Chronic bronchitis	50	3 (6.0)	2.01 (0.61,6.57) <sup>b</sup>
Healthy controls	3536	107 (3.0)	1.00

<sup>a</sup> Odds ratios adjusted for sex, age, educational level and smoking status.

<sup>b</sup> Odds ratios adjusted for sex, age, educational level.

7.56, 95% CI 3.37, 16.96). When controlling for age, gender, education, and the presence of chronic bronchitis, smoking status does not seem to be significantly related to the devel-

opment of anxiety (OR = 1.01, 95% CI 0.71, 1.44), although the risk of developing depression is slightly increased in smokers (OR = 1.44, 95% CI 1.00, 2.08). The number of employees who picked up smoking as well as those who quit during follow-up was too low to assess whether these employees were at increased risk for developing anxiety and/or depression.

## DISCUSSION

Results from this population-based sample revealed that the presence of chronic bronchitis was associated with an increased risk of developing anxiety as well as depression compared with employees without respiratory complaints. Results also seem to indicate that smoking cigarettes modifies this association, resulting in an increased risk of depression and anxiety in smoking employees with chronic bronchitis.

As we already stated in the introduction, all studies addressing the relation between chronic bronchitis and psychiatric morbidity have been of cross-sectional design, and as a result are more likely to be prone to bias compared with prospective studies. The present study is therefore an important extension of the existing knowledge on psychiatric morbidity in patients with COPD. However, one limitation of this study needs to be mentioned. To determine the presence of chronic bronchitis, all participants were asked to complete a questionnaire on respiratory complaints and diagnoses. The assessment of chronic bronchitis was thus self-reported. We could not evaluate the presence of chronic bronchitis by using spirometry. As a result, we may have systematically over- or underestimated the presence of chronic bronchitis. Misclassification of cases may therefore have occurred. However, if it occurred, it is expected to be nondifferential.

Several mechanisms may be responsible for the observed association between chronic bronchitis and depression or anxiety. The physical illness itself is often considered to be reason enough for patients to feel anxious or depressed. The presence of these psychiatric complaints is therefore in many cases regarded as a complication of the physical complaints (27).

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Conforming to earlier studies (5,6,9,28), the results found in this study could be explained by a difference in severity of the respiratory complaints. Patients with chronic bronchitis might feel more depressed and/or anxious when thinking about their health status and the future. However, because the sample consisted mainly of middle-aged employees (a generally healthy sample), it is unlikely that the group of employees with chronic bronchitis consisted of patients with severe complaints. Furthermore, the follow-up time of 18 months is rather short for someone's lung function to decrease significantly. However, mild or moderate complaints might also cause these subjects to feel anxious or depressed, because in an earlier study we failed to find a significant increase in psychiatric complaints in patients with severe or very severe COPD compared with patients with mild or moderate COPD (6). Our finding that smokers are at increased risk for developing psychiatric complaints like anxiety and depression is not surprising. The complexity of nicotine addiction is often accompanied by comorbid depression or depressive symptoms (29–31). Contending explanations include a causal influence of smoking on psychiatric complaints based on the possible effects of long-term nicotine exposure on neurobiological systems implicated in the etiology of these complaints (32), and the effects of shared environmental or genetic factors that predispose to both smoking and depression (32). In smokers, the risk of psychiatric morbidity might be increased compared with nonsmokers because of a negative self-evaluation when they compare themselves with peers regarding sports and activities of daily living.

In conclusion, this prospective study shows a significantly higher incidence of anxiety as well as depression in employees with chronic bronchitis. We also found that smoking cigarettes seems to modify this association, resulting in an increased risk for depression and anxiety in smoking employees with chronic bronchitis. As depression and anxiety remain easily undiagnosed because of under presentation and because the symptoms are not very specific, it is important to consider the presence of these disorders in primary and secondary care settings. Furthermore, because we could not assess the severity of chronic bronchitis, future research should assess whether smokers with severe chronic bronchitis are at increased risk for becoming anxious or depressed compared with smokers with less severe chronic bronchitis.

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