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Impact and factors associated with nighttime and early morning symptoms among patients with chronic obstructive pulmonary disease

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Judith J Stephenson[1]
Qian Cai[1]
Michelle Mocarski[2]
Hiangkiat Tan[1]
Jalpa A Doshi[3]
Sean D Sullivan[4]

[1]HealthCore, Inc., Wilmington, DE, USA; [2]Forest Research Institute, Inc., an affiliate of Actavis, Inc., Jersey City, NJ, USA; [3]University of Pennsylvania, Philadelphia, PA, USA; [4]University of Washington, Seattle, WA, USA

Abstract: Patients with chronic obstructive pulmonary disease (COPD) exhibit poor sleep quality and consider morning as the worst time of day for their symptoms. While work has been done to characterize nighttime (NT) and early morning (EM) symptoms in various populations, the impact and factors associated with NT/EM symptoms among patients with COPD in the United States is not well understood. Commercially insured patients aged ≥40 years with one or more medical claim for COPD and one or more pharmacy claim for COPD maintenance medication were identified from the HealthCore Integrated Research Database between September 1, 2010 and August 31, 2011. Consenting respondents were asked whether they had COPD symptoms on at least three nights or at least three mornings during the past week. Respondents were then either assigned to one of three symptom groups to complete the survey or excluded if their predefined group quota limit had been met. Survey completers completed the survey with questions about COPD symptoms and other commonly used patient-reported outcome measures. Respondents with NT/EM symptoms were asked about the frequency, severity, and impact of the symptoms on sleep, morning activities, and anxiety levels. Among respondents with symptoms, 73.1% of respondents with NT symptoms (N=376) and 83% of respondents with EM symptoms (N=506) experienced at least three distinct types of symptoms over the past week, with cough being the most frequently reported symptom. Approximately half of respondents with NT or EM symptoms perceived their symptoms as moderate to very severe, with a majority reporting their symptoms affected their NT sleep and morning activities, and more than half felt anxious due to their symptoms. Multinomial logistic regression showed COPD patients with both or either NT/EM symptoms were associated with poorer health status compared to those without. Improved disease management may reduce NT/EM symptoms and improve health status in patients with COPD.

Keywords: chronic airflow obstruction, chronic limitation of activity, quality of life, sleep

Introduction

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable pulmonary condition characterized by persistent airflow limitation that is not fully reversible.[1] In the United States, approximately 24 million American adults may have airflow limitations consistent with COPD,[2] with about half being undiagnosed.[3,4] COPD has risen to the third leading cause of death in the US, accounting for approximately 138,000 deaths in 2010.[5,6] COPD has also risen to the third cause of death worldwide from 1990 to 2010, although the change in numbers of deaths declined by 7%.[7]

The most common symptoms of COPD include dyspnea, chronic cough, sputum production, wheezing, and chest tightness.[8] COPD symptoms are particularly disruptive during the nighttime (NT) and/or early morning (EM), contributing to sleep

Correspondence: Judith J Stephenson
HealthCore, Inc., 800 Delaware Avenue, 5th Floor, Wilmington, DE 19801, USA
Tel +1 302 230 2142
Email jstephenson@healthcore.com

disturbance, limited morning activities, and poor health status.[9–13] Epidemiological data indicate that more than 75% of patients with COPD may experience nocturnal symptoms.[9] NT symptoms are often underreported, are not considered in the clinical management of COPD, and are likely to negatively impact sleep quality and impair health status.[9] Similar to effects of NT symptoms, Kessler et al[10] found that morning symptoms were also a burden to patients with COPD, with the majority reporting troublesome phlegm and cough upon waking or in the EM. Moreover, the morning has been reported as the worst time of a day by COPD patients, especially among those with severe COPD, as COPD symptoms in the morning have been shown to limit patients' ability to perform morning activities.[10,11,13] Patients with COPD expect their treatment to provide fast symptom relief, greater mobility, and improvement in morning activities;[13] however, such patient expectations have not been emphasized in clinical management guidelines.[14] In an effort to improve COPD management, the present study determined the type, frequency, severity, and duration of NT/EM symptoms; assessed the impact of these symptoms on sleep, morning activities, and anxiety levels; and investigated factors associated with the presence of these symptoms among commercially insured COPD patients in the US.

Methods

Study design

The study consisted of a cross-sectional survey of patients with COPD. The patient sample was identified using medical and pharmacy claims from the HealthCore Integrated Research Database, a large administrative claims database with claims from 14 geographically dispersed US health plans.

Patients were included if they met the following criteria at the time the patient sample list was determined: 1) at least one medical claim with an *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) diagnosis code for COPD (ICD-9-CM 491.xx, 492.xx, or 496.xx) and at least one pharmacy claim for a COPD maintenance medication (ie, inhaled corticosteroids, short acting β_2 adrenergic agonist, long acting β_2 adrenergic agonist, short acting anticholinergics, methylxanthines, phosphodiesterase-4 inhibitors) between September 1, 2010 and August 31, 2011; 2) at least 40 years of age; 3) continuous health plan eligibility between September 1, 2010 and August 31, 2011; 4) commercially insured, active health plan member; and 5) satisfied all other HealthCore survey eligibility criteria (eg, no missing contact information, and not on any do-not-call lists). Patients with medical claims for other lung diseases (eg, lung cancer, cystic fibrosis, active tuberculosis, interstitial lung disease, α1-antitrypsin deficiency) or HIV were excluded.

Survey recruitment

Eligible patients were invited to participate in the study via a prenotification letter, which included telephone numbers that patients could call to proactively opt into or opt out of the study. Patients who did not respond to the prenotification letter were contacted by telephone, and those patients who gave verbal consent were asked whether they had COPD symptoms on at least three nights (ie, between the time of going to bed and the time of getting up to start a day) or at least three mornings (ie, between the time of getting out of bed and approximately 11 am) during the past week. Based on their responses, patients were either assigned to one of three symptom groups (both NT and EM symptoms; NT symptoms only or EM symptoms only; or no symptoms) and completed the full survey, or excluded if their predefined group quota limit had been met. The targeted number of completed surveys was 750. Survey completers were administered a 30-minute survey with questions about COPD symptoms, clinical and demographic information, and other commonly used patient-reported outcome measures. The survey recruitment began in February 2012 and ended in April 2012.

A central Institutional Review Board reviewed and approved all survey-related materials (survey protocol, prenotification letter, telephone recruiting script, and patient survey) and all patients provided verbal consent before responding to questions. Patient-level data were handled in compliance with the Health Insurance Portability and Accountability Act regulations. Any information that could uniquely identify individual patients was removed from the survey data prior to analysis and reporting.

Survey measures

Assessment of NT and EM symptoms

Respondents with NT and/or EM symptoms were asked about the specific symptoms they experienced at night or in the EM, respectively. Respondents with symptoms were further asked about the number of nights/mornings during the past week that they had experienced these symptoms, the severity of their symptoms, and the impact of their symptoms on their sleep or EM activities. Finally, respondents were asked how long they had experienced their symptoms.

Demographic and clinical characteristics

Demographic and patient-reported clinical information was collected from all respondents. Clinical information included

age at COPD diagnosis; duration of COPD; current smoking status; height and body weight; the use of home oxygen, oral steroids, and/or sleep medications during the week prior to the survey; and the number of COPD exacerbations in the past 12 months.

Patient-reported outcome measures

The modified Medical Research Council (mMRC) dyspnea scale consists of a single question describing the degree of breathlessness associated with various physical activities, such as walking or dressing,[15] and was used as a proxy measure of COPD severity, with higher grades indicating more-severe dyspnea.[16] The COPD Assessment Test is an eight-item scale used to assess the impact of COPD on health status,[17] with higher scores indicating a greater impact of COPD on health status. The Morisky Medication Adherence Scale consists of eight items and assessed adherence in respondents currently taking COPD medications, with scores less than 6 indicating low adherence, scores of 6 to <8 indicating moderate adherence, and scores of 8 indicating high adherence.[18]

Statistical analyses

Descriptive statistics were used to summarize the data, including frequencies and percentages for categorical variables and means and standard deviations for continuous variables. Demographic and clinical characteristics were analyzed using chi-square or Fisher's exact test for categorical variables, and analysis of variance for continuous variables. Multinomial logistic regression was used to identify factors associated with NT and/or EM symptoms using patients without symptoms as the reference group. A conventional alpha of 0.05 and two-tailed level of significance was used. All analyses were conducted using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

Patient disposition

Of the 6,818 patients who were contacted, 496 were excluded because they no longer met the study inclusion criteria (Figure 1). Of the remaining 6,322 patients, 1,239 gave verbal consent to participate and 5,083 patients refused. The cooperation rate (the rate of participation agreement among patients who met the inclusion criteria) was 19.6%.

Patients who agreed to participate (n=1,239) were 8.2% more likely to be female ($P<0.01$), nearly 1 year younger ($P=0.01$), and 13.4% more likely to belong to health plans in the Midwest and Southern regions of the US ($P<0.01$) than those who refused to participate.

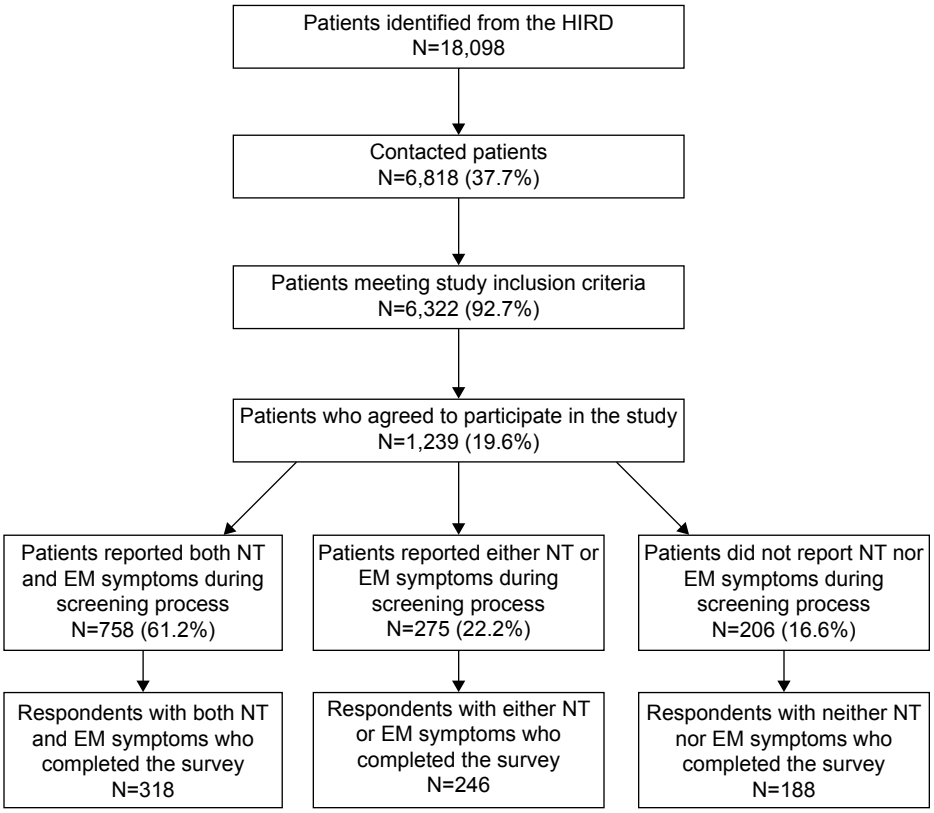

Figure 1 Flow chart of survey respondents.
Abbreviations: EM, early morning; HIRD, HealthCore Integrated Research Database; NT, nighttime.

Presence of symptoms

NT and EM symptoms were common among consenting respondents (n=1,239), with 758 (61.2%) patients reporting having both NT and EM symptoms on at least three nights and three mornings during the week prior to the survey. A total of 216 (17.4%) experienced only EM symptoms and 59 (4.8%) experienced only NT symptoms, meaning that the remaining 206 (16.6%) patients did not report experiencing NT or EM symptoms on more than three nights or three mornings during the prior week.

Demographic characteristics

Of the 1,239 consenting respondents, 752 respondents completed the survey (Figure 1). The mean (standard deviation) age was 60.2 (8.0) years, and the average duration of COPD was 6.5 (6.3) years (Table 1). The majority of respondents were female (60.5%), white (91.6%), with at least some college education (58.1%), current or former smokers (87.1%), and overweight or obese (69.7%).

Pattern and impact of NT symptoms

Respondents who reported having NT symptoms in the week prior to the survey (n=376) reported that, on average, they had experienced these symptoms for at least 5 years, and 73.1% experienced at least three symptoms over the past week (Table 2). The most frequently reported symptoms were coughing (72.9%) followed by wheezing (69.2%) and shortness of breath (61.4%). Half of the respondents perceived their NT symptoms as moderate to very severe. Moreover, respondents reported that these symptoms affected their NT sleep, with 25.3% reporting difficulty falling asleep, 77.7% reporting slight to extreme sleep disturbances, and 34.4% reporting they were awakened at least once per night. Consequently, 59.1% of patients reported feeling anxious (slightly to extremely) due to their NT symptoms, and 25.3% used rescue medications on an average of 4.0 (standard deviation 2.3) nights over the past week.

Pattern and impact of EM symptoms

Similarly, respondents with EM symptoms (n=506) during the week prior to the survey also indicated that they had, on average, experienced EM symptoms for the previous 5 years, and 83% experienced at least three symptoms over the past week (Table 3). While cough (74.5%) was also the most frequently reported symptom in the morning, shortness of breath (73.9%) and bringing up phlegm or mucus (69.6%) were the next most common. More than half of respondents considered their EM symptoms to be moderate to very severe, which is slightly more than the reported severity of NT symptoms. Like NT symptoms, the impact of EM symptoms was observed, with 60.4% of respondents reporting limiting their morning activity due to EM symptoms and 27.8% having trouble concentrating in the morning. Also, 54.3% of respondents reported feeling anxious (slightly to extremely) due to their EM symptoms. Rescue medication use was also higher among respondents in the morning, with 43.4% of those with EM symptoms having used rescue medications on an average of 5.1 (standard deviation 2.4) mornings during the prior week.

Factors associated with symptoms

Multivariate analyses showed that, compared to patients without symptoms, those with both NT and EM symptoms were more likely to be current smokers (odds ratio [OR] =2.61; 95% confidence interval [CI], 1.18–5.78), have used oxygen in the past week (OR=2.2; 95% CI, 1.02–4.71), experienced dyspnea as measured by mMRC dyspnea scale (OR=2.73; 95% CI, 1.56–4.76), have poorer health status as measured by the COPD Assessment Test (OR=8.03; 95% CI, 4.33–14.89), demonstrate low (OR=2.58; 95% CI, 1.35–4.93) or moderate (OR=2.04; 95% CI, 1.13–3.76) adherence to COPD medications in the past year, and have experienced an exacerbation in the past year (OR=2.06; 95% CI, 1.08–3.9). In contrast, only worse health status (OR=2.78; 95% CI, 1.70–4.54) was a significant factor when comparing patients with either NT or EM symptoms versus those without any symptoms (Figure 2).

Discussion

Previous studies have shown that many patients with COPD experience symptoms in the morning and/or during the night,[9–11] which has highlighted the importance of investigating the occurrence of these symptoms and their association with measures of COPD burden for effective COPD management. Findings from this study indicate that symptoms during the NT and in the morning are common among COPD patients in the US. In addition, the presence of these symptoms has a substantial impact on patients' health-related quality of life and interferes with patients' lives through many factors, including worse sleep quality, limited morning activities, and anxiety.

Consistent with previous studies,[19–22] the majority of the respondents included in this study were current or former smokers. Being a current smoker, a well-known risk factor for COPD, was found to be independently associated with both NT and EM symptoms, suggesting that COPD patients who

Table 1 Demographic and clinical characteristics of survey respondents

	Total respondents N=752	Both NT and EM symptoms n=318	Either NT or EM symptoms n=246	Neither NT nor EM symptoms n=188	*P*-value[a]
Age (years), mean (SD)	60.2 (8.0)	58.6 (7.8)	61.0 (8.1)	62.0 (7.8)	<0.01
Female, %	60.5	57.6	63.8	61.2	0.31
White/Caucasian, %	91.6	92.7	91.0	90.4	0.61
Education status, %					0.05
High school or less	41.9	46.8	37.1	39.9	
Some college and above	58.1	53.2	62.9	60.1	
Household income, % (US$)					0.01
Less than $25,000	13.3	17.3	8.8	12.1	
$25,000 to $74,999	60.1	61.0	61.0	57.2	
$75,000 and over	26.7	21.7	30.3	30.6	
Employment status, %					0.12
Full-time	47.5	46.5	48.0	48.7	
Part-time	10.7	7.9	11.4	14.4	
Not working	41.8	45.6	40.7	36.9	
Age at COPD diagnosis (years), mean ± SD	53.5±9.2	51.5±9.1	54.7±8.7	55.5±9.4	<0.01
COPD duration (years),[b] mean ± SD	6.5±6.3	7.1±6.9	6.0±5.5	6.2±6.0	0.11
Smoking status, %					<0.01
Current smoker	28.9	38.1	24.0	19.9	
Former smoker	58.1	49.1	64.2	65.6	
Never smoked	12.9	12.9	11.8	14.5	
Overweight/obese,[c] %	69.7	72.4	66.7	69.2	0.33
Oxygen use in the past week, %	15.8	20.4	16.3	7.5	<0.01
Sleep medication use in the past week, %	33.4	39.0	32.9	24.5	<0.01
Oral steroid use in the past week, %	29.9	32.1	25.6	31.9	0.20
COPD exacerbation in the past year, %	21.5	29.3	18.7	12.2	<0.01
CAT score categories, %					<0.01
Low (<10)	26.4	6.6	27.9	57.8	
Medium (10–20)	43.1	39.2	54.1	35.3	
High (21–30)	24.5	39.9	18.0	7.0	
Very high (31–40)	6.0	14.2	0.0	0.0	
mMRC dyspnea score categories,[d] %					<0.01
0	28.3	13.9	32.4	48.1	
1–4	71.7	86.1	67.6	51.9	
MMAS-8 adherence level,[e] %					<0.01
Medication nonusers	14.5	10.1	12.6	24.5	
Low adherence (0–5)	23.3	30.9	19.9	14.9	
Moderate adherence (6–7)	31.2	35.3	31.3	23.9	
High adherence (8)	31.0	23.7	36.2	36.7	

Notes: [a]Analysis of variance was used for continuous variables whereas chi-square/Fisher's exact test was used for categorical variables. [b]Duration of COPD was calculated using age at the survey minus age at COPD diagnosis. [c]Overweight/obese was defined as body mass index ≥25 kg/m^2, which was calculated as weight in pounds divided by square of height in inches multiplied by 703. [d]Patients were considered as having dyspnea symptoms if mMRC dyspnea scale responses =1–4 and were considered as being without dyspnea symptoms if mMRC scale response =0. [e]Patients were categorized into four levels: 1) patients who did not take any COPD-related medications; 2) patients who took COPD-related medications and had a MMAS-8 score =0–5 (low adherence); 3) patients who took COPD-related medications and had a MMAS score =6–7 (moderate adherence); and 4) patients who took COPD-related medications and had a MMAS score =8 (high adherence).

Abbreviations: CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; EM, early morning; MMAS-8, Morisky Medication Adherence Scale; mMRC, modified Medical Research Council; NT, nighttime; SD, standard deviation.

continue to smoke may experience worse symptoms at night and in the morning. This study further showed that, compared with respondents without NT/EM symptoms, patients with both symptoms were more likely to report home oxygen use during the day or at night. Evidence has shown that oxygen therapy can alleviate hypoxemia and reduce dyspnea symptoms for patients with COPD;[23] however, clinical trials and studies on the efficacy or effectiveness of long-term oxygen therapy are needed, especially for severe COPD patients.[24] A greater proportion of respondents with symptoms reported

Table 2 Type, severity, and impact of NT symptoms

	Respondents with NT symptoms N=376	
Types of NT symptoms over past week		
Short of breath or breathless, n, %	231	61.4%
Nights with shortness of breath or breathlessness, mean ± SD	4.5	±2.0
Coughing, n, %	274	72.9%
Nights with coughing, mean ± SD	4.9	±2.1
Bringing up phlegm or mucus, n, %	229	60.9%
Nights with bringing up phlegm or mucus, mean ± SD	4.8	±2.1
Tightness in chest, n, %	164	43.6%
Nights with tightness in chest, mean ± SD	4.2	±2.2
Chest congestion, n, %	183	48.7%
Nights with chest congestion, mean ± SD	4.9	±2.0
Wheezing, n, %	260	69.2%
Nights with wheezing, mean ± SD	5.0	±2.1
Severity of NT symptoms over past week, n, %		
Did not experience any symptoms	9	2.4%
Mild	179	47.6%
Moderate	160	42.6%
Severe	23	6.1%
Very severe	5	1.3%
Impact of NT symptoms over past week		
Difficult to fall asleep, n, %	190	25.3%
Nights on which it felt difficult to fall asleep, mean ± SD	3.8	±2.1
Sleep disturbed, n, %		
Not at all	81	22.1%
Slightly	122	33.2%
Moderately	130	35.4%
Severely	21	5.7%
Extremely	12	3.3%
Refused to answer	1	0.3%
Woke up at least once, n, %	259	34.4%
Nights woke up, mean ± SD	3.8	±2.1
Felt rested in morning, n, %	230	30.6%
Mornings felt rested, mean ± SD	4.0	±2.0
Anxious, n, %		
Not at all anxious	150	40.9%
Slightly anxious	105	28.6%
Moderately anxious	67	18.3%
Considerably anxious	29	7.9%
Extremely anxious	16	4.4%
Used rescue medications, n, %	190	25.3%

Abbreviations: NT, nighttime; SD, standard deviation.

using sleep medications (including prescriptions, over-the-counter medications, and herbal remedies) during the week before the survey, although it was not shown to be a significant factor associated with NT/EM symptoms after adjusting for other covariates.

Existing literature has shown that sleep disturbance among patients with COPD can have a number of negative impacts. One study conducted in Europe found that 26.5% of patients reported their sleep quality was affected by frequent waking during the night and difficulty falling asleep,[10] which is similar to the 25.3% of respondents in this study who reported having difficulty falling asleep due to symptoms at NT. Our results are also consistent with the qualitative study conducted by Shackell et al[25] showing that patients with COPD experience nocturnal fear and anxiety; in addition, one-fourth of respondents reported the use of rescue medications (eg, albuterol) between their bedtime and the time when they woke up to start a day.

While sleep disturbance is worse with increased symptoms at night, sleep disturbance itself is multifaceted and can be caused by a number of factors, including suboptimal evening routines, which may disrupt normal sleeping patterns.[25]

Table 3 Type, severity, and impact of EM symptoms

	Respondents with EM symptoms N=506	
Types of EM symptoms over past week		
Short of breath or breathless, n, %	374	73.4%
Nights with shortness of breath or breathlessness, mean ± SD	5.0	±2.1
Coughing, n, %	377	74.5%
Nights with coughing, mean ± SD	5.6	±1.9
Bringing up phlegm or mucus, n, %	352	69.6%
Nights with bringing up phlegm or mucus, mean ± SD	5.4	±2.0
Tightness in chest, n, %	207	40.9%
Nights with tightness in chest, mean ± SD	4.3	±2.2
Chest congestion, n, %	233	46.1%
Nights with chest congestion, mean ± SD	4.9	±2.1
Wheezing, n, %	300	59.3%
Nights with wheezing, mean ± SD	5.0	±2.2
Severity of EM symptoms over past week, n, %		
Mild	222	43.9%
Moderate	234	46.3%
Severe	45	8.9%
Very severe	4	0.8%
Impact of EM symptoms over past week		
Activity limited, n, %		
Not at all	200	39.6%
Slightly	113	22.4%
Moderately	96	19.0%
Severely	62	12.3%
Extremely	34	6.7%
Trouble concentrating, n, %	209	27.8%
Mornings trouble concentrating, mean ± SD	4.3	±2.0
Anxious, n, %		
Not at all	229	45.4%
Slightly	145	28.7%
Moderately	74	14.7%
Considerably	41	8.1%
Extremely	14	2.8%
Refused to answer	2	0.4%
Used rescue medications, n, %	326	43.4%

Abbreviations: EM, early morning; SD, standard deviation.

This is important because while it may be difficult to treat all facets of sleep disruption, the reduction of COPD symptoms during the evening hours may be amenable to treatment with maintenance medications. In fact, evidence exists that some medications already available to patients with COPD may help reduce NT symptoms of COPD.[12,26]

The study results are also consistent with the small body of literature around EM symptoms of COPD. In an international study conducted within five European countries, morning was reported to be the worst time of day among COPD patients; 9.5% of patients required assistance with their morning activity routines, and of these patients, 67.5% felt worried that they were a burden to others.[10] Similarly, an internet survey study found that 74% of patients with COPD reported that their morning activities took longer to complete than usual, with 21% of patients requiring help to perform their morning routine.[11] Our results confirm those findings, with more than half of respondents reporting morning activity limitation and anxiety, and nearly half of respondents having used rescue medications on more than 5 days in the week prior to the survey. Most recently, a multinational study of patients with EM symptoms reported that those with symptoms had worse quality of life, more exacerbations, and more work days off per year.[27] The results support previous findings that breathlessness is highly prevalent at night and in the EM;[10,11,28] however, cough was the most frequently reported EM symptom (74.5%) and NT symptom (72.9%). Partridge et al[11] found that COPD symptoms significantly impact sleep quality and morning routine, which can, in turn, negatively affect patients' health status.[11,29] Our findings showed that experiencing either NT

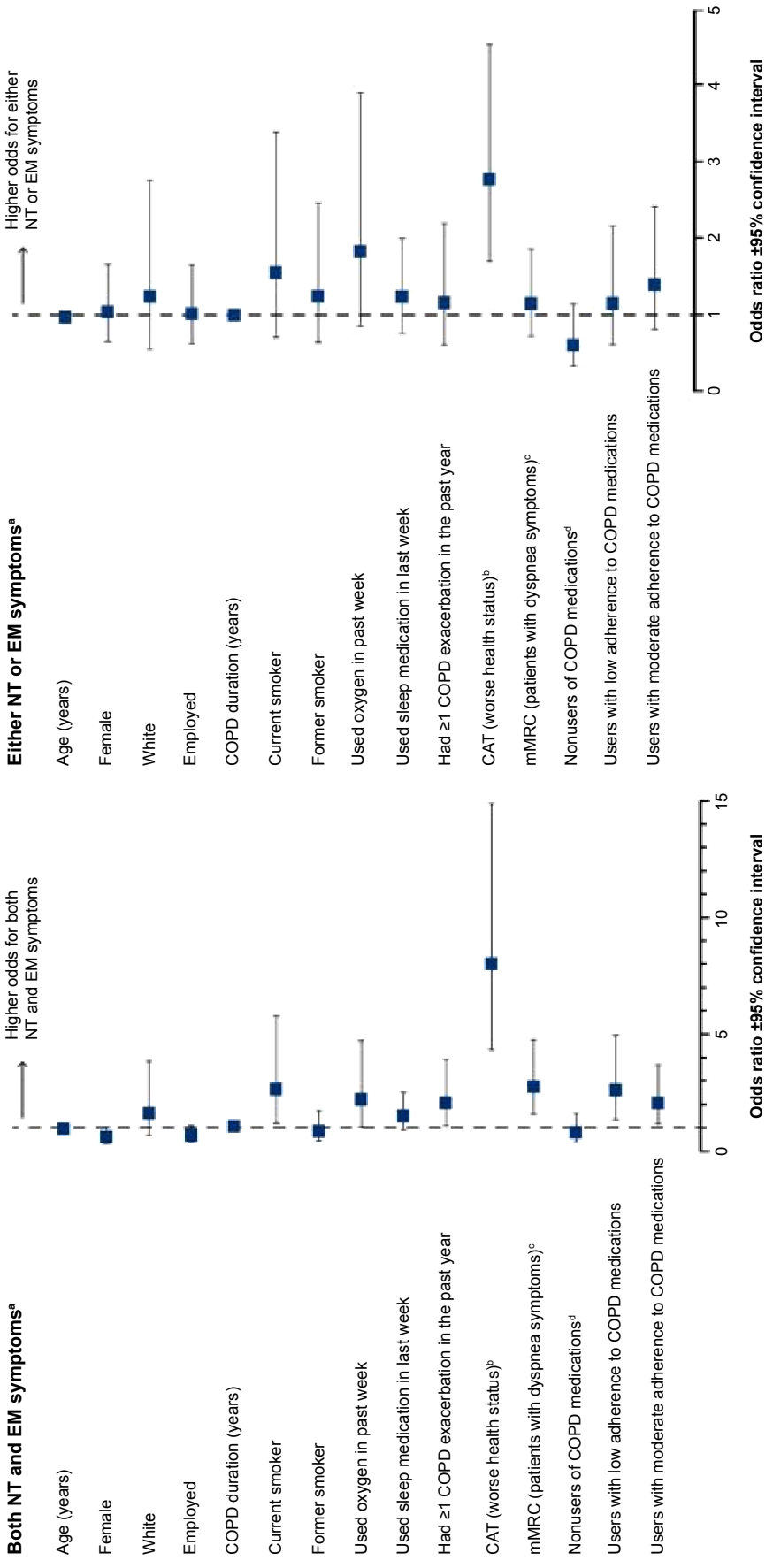

Figure 2 Factors associated with NT and/or EM symptoms in patients with COPD.

Notes: [a]Results were from a single multinomial model with neither NT nor EM symptoms as the reference group. [b]Represented by medium or high CAT scores. Patients were categorized into two levels: medium/high level if CAT score ≥10, and low level if CAT score <10 (reference group). [c]Patients were considered as having dyspnea symptoms if mMRC scale was within 1–4, and without dyspnea symptoms if mMRC =0 (reference group). [d]Patients were categorized into four levels: 1) patients who did not take any COPD-related medications; 2) patients who took COPD-related medications and had a MMAS score of 0–5 (low adherence); 3) patients who took COPD-related medications and had a MMAS score within 6–8 (moderate adherence); and 4) patients who took COPD-related medications and had a MMAS score >8 (high adherence as reference group).

Abbreviations: CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; EM, early morning; MMAS, Morisky Medication Adherence Scale; mMRC, modified Medical Research Council; NT, nighttime.

or EM symptoms was significantly associated with poorer health status, even after controlling for sociodemographic and clinical characteristics. Furthermore, experiencing both NT and EM symptoms had a greater overall impact than having only one of the two types of symptoms. That is, the presence of both NT and EM symptoms was not only significantly associated with poorer health status but also with the occurrence of previous exacerbations, dyspnea, and poor medication adherence.

The findings from this study should be interpreted in light of certain limitations. Patients were identified from medical and pharmacy claims in a large US administrative claims database, which may contain diagnostic or treatment coding errors. Although patients in this study confirmed their COPD diagnosis by answering self-reported screening questions, they were not asked whether or not they had asthma. It is possible that patients with ICD-9-CM codes for both asthma and COPD were first evaluated and diagnosed with asthma, and later diagnosed with only COPD. As the study respondents were identified from a large US administrative claims database, only individuals and/or their dependents with employer-provided health insurance were included. It is possible that the results from this study may not generalize to other populations consisting of uninsured individuals, Medicaid or Medicare recipients, or patients in countries other than the US with different health care systems. Additionally, the results were based on respondents' self-report and could not be independently verified through clinical documentation; thus, their accuracy may be subject to self-report and recall biases. Furthermore, some differences in terms of age, sex, and health plan region were observed between respondents and nonrespondents, but the differences were relatively minimal, with more respondents being female (6%), older (1.5 years), and having health plans in the Midwest region (9%). Lastly, this study did not collect objective ventilatory function data. Future studies should endeavor to correlate this data with NT and EM symptoms to further elucidate the impact of these symptoms.

Conclusion

In summary, most COPD patients with self-reported NT and EM symptoms consider their symptoms to be moderate to severe and perceive that symptoms affect their sleep, morning activities, and anxiety levels. Improvements in disease management approaches may decrease the burden associated with these symptoms, which could have significant humanistic impacts on patients, employers, and the health care system. Further study is needed to better understand the relationship of NT and EM symptoms with health-related quality of life, risk for exacerbations, as well as the effect of interventions on relieving these symptoms.

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Author contributions

All authors contributed to the study concept and design. QC performed data analysis, with assistance from JJS. All authors participated in interpretation of the data, development of the manuscript, and approved this manuscript for submission.

Disclosure

JJS, QC, and HT are employees of HealthCore Inc, a subsidiary of Anthem Inc., whose activities in the study were funded by Forest Research Institute, Inc., an affiliate of Actavis plc. MM was an employee of Forest Research Institute, Inc. at the time of the study and had stock/stock options. MM is currently employed by Novo Nordisk. JAD has received consulting fees from Forest Research Institute, Inc., Merck, and Boehringer Ingelheim and research grants from Pfizer and Amgen. SDS reports no conflicts of interest in this work.

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