Chronic Obstructive Pulmonary Diseases:
Journal of the COPD Foundation®

Original Research

Nighttime Symptom Burden in Chronic Obstructive Pulmonary Disease: A Qualitative Study

Sarah Miller, PhD, RN[1] Hayley D. Germack, PhD, RN[2] Meredith Bell, PharmD[3] Norbert Feigler, MD[3]
Randy Legg, PharmD, MBA[4] Kathleen Henderson[5] Chip Kreisman, BSB[5] Karen Winkler, MSc[6] Dorsa Khazaei, MSc[7]
Tommi Tervonen, PhD[8] Gerard J. Criner, MD[9]

Abstract

Rationale: Nighttime symptoms are clinically important but understudied in chronic obstructive pulmonary disease (COPD). This study explored patients' perceptions of nighttime symptoms, their effects on daily life, and symptom-management strategies.

Methods: Thirty U.S. adults with COPD and a moderate-to-high symptom burden (COPD Assessment Test score ≥10), without a hospitalization or emergency department visits for a severe exacerbation during the previous year, participated in semistructured interviews. All participants received single-inhaler dual or triple maintenance therapy and completed the 7-item COPD and Asthma Sleep Impact Scale (CASIS). Interviews were transcribed verbatim and thematically analyzed using the Symptom Management Theory framework.

Results: Participants (median age 63; 60% female; 90% White) reported a high burden of nighttime symptoms and sleep disruption (87% severely impacted based on CASIS). Participants described a pronounced nighttime symptom experience, most frequently shortness of breath, mucus/phlegm production, coughing, and difficulty staying asleep or frequent awakenings. A range of symptom management strategies was reported, including behavioral adaptations (routines, avoidance of technology, sleep hygiene), pharmacological management (antidepressants, sleep medications, rescue inhalers), and complementary and integrative approaches (meditation, acupuncture, relaxation techniques). Nighttime symptom outcomes extended beyond sleep disruption. Participants reported significant daytime consequences, including fatigue and impaired concentration. These effects contributed to activity avoidance and limitations in social participation.

Conclusions: Among symptomatic patients receiving single-inhaler dual or triple maintenance therapy, nighttime COPD symptoms were commonly reported and were associated with substantial physical, emotional, and functional impacts. The findings support further consideration of nighttime symptoms in clinical assessment and individualized COPD management.

1. College of Nursing, Medical University of South Carolina, Charleston, South Carolina, United States
2. U.S. Medical Evidence, BioPharmaceuticals Medical, AstraZeneca, Wilmington, Delaware, United States
3. U.S. Respiratory Medical, BioPharmaceuticals Medical, AstraZeneca, Wilmington, Delaware, United States
4. U.S. Clinical Value and Outcome, BioPharmaceuticals Medical, AstraZeneca, Wilmington, Delaware, United States
5. Patient Co-Investigator, United States
6. Kielo Research, Hamburg, Germany
7. Kielo Research, London, United Kingdom
8. Kielo Research, Zug, Switzerland
9. Department of Thoracic Medicine and Surgery, Lewis Katz School of Medicine, Temple University, Philadelphia, Pennsylvania, United States

Abbreviations:

ADLs=activities of daily living; **CASIS**=COPD and Asthma Sleep Impact Scale; **CAT**=COPD Assessment Test; **COD**=confirmation of diagnosis; **COPD**=chronic obstructive pulmonary disease; **CPAP**=continuous positive airway pressure; **FRAIL**=Fatigue-Resistance-Ambulation-Illnesses-Loss of weight; **GOLD**=Global initiative for chronic Obstructive Lung Disease; **GR**=group; **HCl**=hydrochloride; **ICS**=inhaled corticosteroid; **LABA**=long-acting beta2-agonist; **LAMA**=long-acting muscarinic antagonist; **Q1**=first quartile; **Q3**=third quartile; **SD**=standard deviation; **SMT**=Symptom Management Theory

Funding Support:

This study was funded by AstraZeneca

For personal use only. Permission required for all other uses.

Citation:

Miller S, Germack HD, Bell M, et al. Nighttime symptom burden in chronic obstructive pulmonary disease: a qualitative study. ***Chronic Obstr Pulm Dis***. 2026;13(6):500-512. doi: https://doi.org/10.15326/jcopdf.2026.0780

Publication Dates:

Date of Acceptance: October 16, 2026
Published Online Date: October 20, 2026

Address correspondence to:

Hayley D. Germack, PhD, RN
AstraZeneca
Email: hayley.germack@astrazeneca.com
Phone: (727) 678-8651

Keywords:

chronic airways obstruction; COPD Assessment Test; sleep medicine

This article has an online supplement.

Introduction

Chronic obstructive pulmonary disease (COPD), the fifth leading cause of death in 2023, imposes a substantial population burden in the United States, with an estimated 11 million individuals affected.[1,2] COPD is often associated with significant symptom burden, including ongoing dyspnea, chronic cough, mucus production, dry mouth, fatigue, pain, depression, and anxiety.[3,4] Symptoms have been reported as most problematic in the morning and have an impact on daily activities.[5]

Nighttime symptoms (including early morning symptoms) are a clinically significant yet understudied aspect of COPD.[6-8] COPD nighttime symptoms involve a complex interaction of perception, management behaviors, and consequent outcomes. Nighttime symptoms contribute to poor sleep quality, which can include difficulty falling asleep, frequent awakenings, and insomnia. One study estimated the prevalence of poor subjective sleep quality to be 55% in patients with moderate to severe COPD.[9] Poor sleep quality in turn worsens COPD burden, including daytime fatigue, reduced physical/mental functioning, and diminished quality of life.[9-16] As such, the Global initiative for chronic Obstructive Lung Disease (GOLD) report recommends assessing symptoms, including sleep disturbance and insomnia, at each routine COPD visit.[17]

To inform clinical practice and improve patient outcomes, it is essential to understand nighttime symptom experience, the burden of nighttime symptoms in patients with COPD, and strategies for managing nighttime symptoms. Inhaled triple therapy (inhaled corticosteroid [ICS]/long-acting beta2-agonist [LABA]/long-acting muscarinic antagonist [LAMA]) is a recommended maintenance treatment for patients with a history of COPD exacerbations. In clinical trials, triple therapy has been shown to improve lung function, reduce exacerbations, and enhance quality of life compared with LAMA alone, LABA/LAMA, or ICS/LABA.[17-21] With COPD symptoms often persisting despite medical management,[3] the extended therapeutic coverage of twice-daily therapies including the second peak in lung function with the evening dose may offer improved control of nighttime symptoms. The purpose of this study was to investigate how patients on single-inhaler dual or triple therapy and once-daily or twice-daily dosing perceive and manage nighttime symptoms associated with COPD.

Materials and Methods

Ethics Approval and Informed Consent

The study protocol was reviewed and approved as exempt by the Pearl Institutional Review Board before study procedures commenced. The study adhered to all applicable local regulations and good research practices. Each participant was provided with an informed consent form prior to their interview.

Methodology

The University of California-San Francisco's Symptom Management Theory (SMT)[22] served as the theoretical framework for this study. The SMT is essential for understanding individuals' symptom experiences, which comprise 3 components that interact simultaneously: symptom experience, management strategies, and outcomes. Symptom experience includes the individual perception and evaluation of the symptoms. Symptom management strategies are techniques aimed at preventing or mitigating the symptom experience, and symptom outcomes are the result of these strategies and experiences. While symptom experience was the primary focus of our study, we also examined the relational factors associated with symptom management strategies and outcomes.

Semistructured interviews (see the online supplement for the interview guide) used open-ended questions to explore several key topics, including the following: the frequency and severity of nighttime symptoms (including early morning symptoms), the impact of symptoms on daily life and sleep, coping techniques and strategies used for symptoms, potential perceived burden or benefit associated with taking a second daily dose of medication (if applicable), perception and efficacy of evening dosing in nighttime symptom alleviation, and the use of rescue medication before going to bed at night.

Sociodemographic and clinical data, including current medication use, the COPD Assessment Test (CAT),[23] the COPD and Asthma Sleep Impact Scale (CASIS),[12] and

For personal use only. Permission required for all other uses.

questions to assess frailty status (using the Fatigue-Resistance-Ambulation-Illnesses-Loss of weight [FRAIL] questionnaire[24]) were collected. Four investigators experienced in qualitative research conducted the interviews, with only the participant and the interviewer present. Interviews were conducted between March 11 and May 7, 2025. The interviews lasted approximately 60 minutes. Participants were compensated with $125 U.S. dollars for their time. All interviews were audio recorded through Zoom, transcribed verbatim, and de-identified to remove personally identifiable information.

Study Population

Thirty U.S. adults with a physician-confirmed diagnosis of COPD participated in this study. All participants reported moderate or high symptom burden (CAT score ≥10),[23] with no severe exacerbations resulting in hospitalizations or emergency department visits in the past year. A CAT score of ≥10 was required to ensure that participants had a clinically meaningful COPD symptom burden and were able to provide relevant experiential insight into the effects and management of nighttime symptoms. There were 10 patients in each of the following groups: single-inhaler once-daily triple therapy ("group[GR]1"), single-inhaler twice-daily triple therapy ("GR2"), and single-inhaler dual maintenance therapy ("GR3").

To qualify, patients needed to reside in the United States, have a confirmed diagnosis of COPD, be on single-inhaler triple therapy or on single-inhaler dual therapy as their maintenance treatment, and have at least 2 fills of their COPD maintenance therapy (or evidence of use for 60 days). Exclusion criteria included multi-inhaler ("open") maintenance therapy, taking ensifentrine nebulizer as maintenance therapy for COPD, taking a biologic treatment for COPD, having a diagnosis of lung cancer, asthma, or interstitial lung disease, or having a history of a lung transplant. The study was designed to examine experiences among patients receiving single-inhaler maintenance therapy, including experiences associated with once- versus twice-daily dosing. Patients receiving open triple therapy were, therefore, excluded to avoid conflating dosing experiences with the burden of managing multiple inhalers. Patients receiving single bronchodilator therapy were excluded because the study focused on patients with persistent symptom burden despite dual or triple maintenance therapy. Patients receiving ensifentrine were excluded to maintain a sample receiving established inhaled dual or triple maintenance regimens.

Patients unable to complete the interview due to language difficulties or cognitive impairment, as well as those with a lack of reliable internet access, were also excluded from the study. Participants were recruited primarily through a recruiter panel of nurse navigators and other nurses working in pulmonary and primary care settings. Recruitment also took place through a patient advocacy group (Pillar Patient Advocates).

Analysis

Interviews were analyzed by 3 researchers using a hybrid coding approach that began with deductive codes informed by the interview guide while remaining open to inductive codes that emerged during analysis. When new codes emerged from the interviews, they were added to the coding framework as part of the inductive process. Following the development of the preliminary coding dictionary, the research team prepared the first 2 transcripts for coding. An agreement of 84% was established, after which an intercoder agreement assessment was conducted using dual coding and reconciliation; minor coding discrepancies were discussed and resolved through consensus. The coders subsequently proceeded independently using the finalized coding dictionary. The analysis software used was Atlas.ti version 25 (ATLAS.ti GmbH; Berlin, Germany), with code frequency tabulated in R version 4.3 (The R Foundation; Vienna, Austria).

Results

A total of 2126 patients were invited to participate in the qualitative interviews. Of these, 406 patients completed the screening process, with 349 excluded. Fifty-seven patients met eligibility criteria and consented to participate. Thirty-five patients were scheduled for interviews, of whom 30 participated and completed the interview (Figure 1).

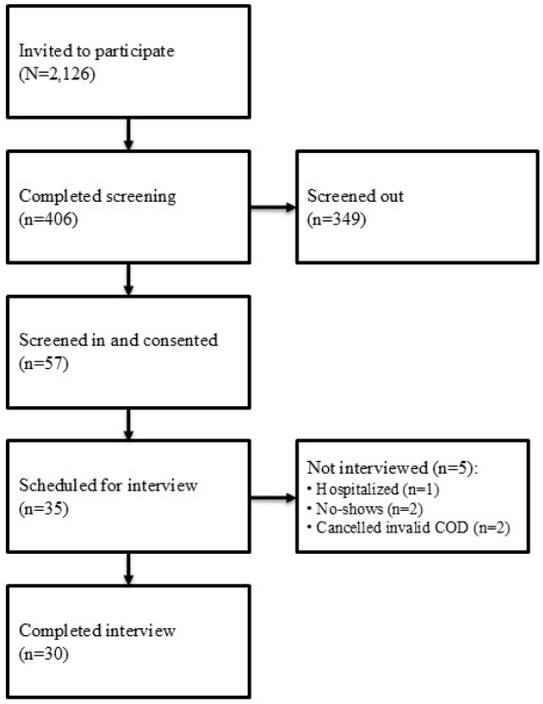
Patient Characteristics

Participants had a median age of 63 years; 60% were female, and 90% were White. Education varied, with nearly half having some college or university experience (47%). Insurance coverage varied, with the majority insured by Medicare (60%). Two-thirds of participants were receiving single-inhaler triple therapy, split evenly between fluticasone furoate/umeclidinium/vilanterol and budesonide/glycopyrrolate/formoterol fumarate (33% each). The remaining participants were receiving single-inhaler dual maintenance therapy, most commonly fluticasone propionate/salmeterol (13%), followed by tiotropium bromide and olodaterol (10%), budesonide/formoterol (6.7%), and fluticasone furoate/vilanterol (3.3%).

Detailed sociodemographic and clinical characteristics are presented in Table 1. The majority (87%) were severely impacted by nighttime symptoms and sleep disruption, as measured with CASIS. Based on established thresholds, severe sleep impairment was defined as a total CASIS score of ≥30. Participants differed in COPD severity, with most

For personal use only. Permission required for all other uses.

Figure 1. Participant Dispositions



COD=confirmation of diagnosis

reporting high (21–30) or very high (31–40) impact on the CAT patient-reported outcome (73%).

Qualitative Findings

Thematic analysis of the 30 interviews revealed 3 key themes aligned with the 3 components of the SMT: a high nighttime symptom burden, wide-ranging outcomes from nighttime symptoms, and various symptom management strategies.

Table 2 presents a structured summary of participant quotes organized according to the 3 primary components of the SMT, highlighting the movement from perception and evaluation of symptoms to concrete management behaviors, and finally, to the physical, emotional, and functional consequences reported by participants. The following sections describe the main findings, organized by key dimensions of the SMT.

Main Findings - Nighttime Symptom Experience

The most frequently reported nighttime symptoms, as shown in Figure 2, were shortness of breath (80%), mucus/phlegm production (80%), coughing (77%), and difficulty staying asleep or experiencing frequent awakenings (77%). Wheezing, sweating or night sweats, and snoring were each reported by 60% of participants.

- **Patient 15, GR2:** *"I'm up and I'm just coughing, but I'm not really producing anything to spit out, and it just makes sleeping very difficult because it's like I'm struggling with my breathing."*
- **Patient 12, GR3:** *"Yeah, hard for me to get a lot of sleep because I, you know, whenever I'm wheezing and I keep coughing and not getting any sleep."*

When asked about the top 3 most bothersome symptoms, participants most often identified difficulty staying asleep or frequent awakenings (40%), followed by shortness of breath (33%), mucus/phlegm production (33%), and coughing (33%). Wheezing and sweating or night sweats were less frequently ranked among the top 3 most bothersome, and snoring was not identified as a top concern by any participant.

- **Patient 26, GR2:** *"Well, I would say the wakefulness is more bothersome because it makes my day... I mean, I don't want to have no energy to do nothing through the day."*
- **Patient 19, GR1:** *"I think it's staying asleep. Falling asleep is not always an issue because I'm so exhausted from getting up from the night before that I can't really. You know, I'm kind of tired, so I will fall asleep."*

Main Findings - Nighttime Symptoms Outcomes

Nighttime symptoms were reported to have wide-ranging impacts (see Figure 3). Physical impacts were the most frequently

For personal use only. Permission required for all other uses.

Table 1. Sociodemographic Characteristics, COPD Assessment Test, and COPD and Asthma Sleep Impact Scale

Characteristic	Total Sample (N=30)
Age, median (Q1, Q3)	63 (57, 66)
Gender[a]	
Female	18 (60)
Male	12 (40)
Education[a]	
Elementary/Primary School	1 (3.3)
Middle School/Junior High School	3 (10)
High School	4 (13)
Some College/University	14 (47)
College/University (BA, BSc)	5 (17)
Postgraduate Degree (Masters, MD, PhD)	3 (10)
Ethnicity[a]	
White	27 (90)
Black or African American	3 (10)
Insurance[a]	
Medicare	18 (60)
Medicaid	7 (23)
Employer-provided Insurance	7 (23)
Self-provided Insurance	2 (6.7)
Veteran Affairs/Military Health Care	1 (3.3)
Current Maintenance Treatment[a]	
Fluticasone Propionate/Salmeterol	4 (13)
Tiotropium Bromide & Olodaterol	3 (10)
Budesonide/Formoterol	2 (6.7)
Fluticasone Furoate/Vilanterol	1 (3.3)
Fluticasone Furoate/Umeclidinium/Vilanterol	10 (33)
Budesonide/Glycopyrrolate/Formoterol Fumarate	10 (33)
CAT Category[a]	
Medium Impact (10-20)	8 (27)
High Impact (21-30)	18 (60)
Very High Impact (31-40)	4 (13)
CASIS Category[a]	
Less Severe Sleep Impairment (<30)	4 (13)
Severe Sleep Impairment (≥30)	26 (87)

[a] n (%)

Q=quartile; CAT=COPD Assessment Test; CASIS= COPD and Asthma Sleep Impact Scale

reported consequence of nighttime symptoms. Nearly all participants (93%) reported experiencing physical effects, and these were most often mentioned spontaneously (80%) without probing.

- **Patient 06, GR2:** *"It affects me because if I'm doing housework, running the vacuum cleaner, I've got to take a break. I'll do one room and I'm like, I've got to sit down for a minute. It slows me down. Just like to make a bed, it takes my breath. It's just I get really winded."*
- **Patient 23, GR3:** *"When I'm up in the night and I have broken sleep, I have a terrible breathing day. Because I think my body's tired and it takes more of an impact on me. So, if I sleep well, I feel better during the day. If I don't, then a lot of times I have to take a nap during the day because I'm so tired."*
- **Patient 59, GR1:** *"The fatigue. And it kind of all runs together because I don't think if I wasn't so fatigued, I wouldn't be so snappy."*

Emotional (77%), reduced sleep quality (77%), cognitive (63%), and social impacts (60%) were also frequently reported. Emotional impacts were evenly split between spontaneous and probed reporting, while cognitive and social impacts were more commonly identified following probing. Anxiety was the most frequently reported emotional impact, affecting 78% of participants who described emotional consequences.

For personal use only. Permission required for all other uses.

Table 2. Participant Quotes Framed Within the Symptom Management Theory

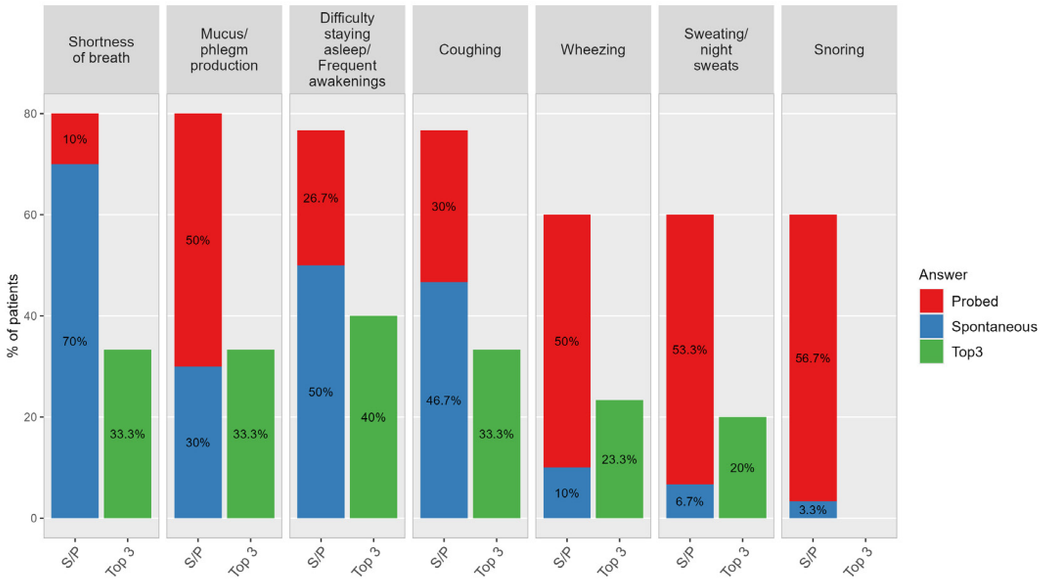
Dimension	Sub-Domain	Participant Quotes
Symptom Experience	Perception	**Patient 15, GR2:** *"Basically, I go to bed and I wake up a lot in the middle of the night and I just feel, I guess maybe it's the dripping of whatever into my lung and I feel like a lump and I just cough a lot. I'm up and I'm just coughing, but I'm not really producing anything to spit out and it just makes sleeping very difficult because it's like I'm struggling with my breathing."*
	Evaluation	**Patient 20, GR3:** *"And just generally at night, my symptoms do seem to be worse. I've got this my lungs hurt a little bit, not extremely bad, but they do hurt. And I've got this, I don't know, shortness of breath feeling in them."* **Patient 12, GR3:** *"…whenever I'm having a hard time breathing or whatever, you know, it kind of gets you get a lot of anxiety because you know you're just, you know, hoping you can keep on you know, to the night…"*
	Response	**Patient 22, GR3:** *"…the feeling of restlessness, so an inability to relax. Do you have those at all? Yeah, no, that's a 10 right there."* **Patient 12, GR3:** *"Yeah, hard for me to get a lot of sleep because I, you know, whenever I'm wheezing and I keep coughing and not getting any sleep. So, it's like sometimes I sleep 2 or 3 hours. Then I get up and then come back and sleep another hour or 2 and get up like stuff like that. Sometimes it's just off and on. Sleep like 3 or 4 segments. Instead of sleeping all the way through the night."*
Symptom Management Strategies	Behavioral Adaptations *(Routines, Sleep Hygiene)*	**Patient 09, GR1:** *"I'm very regimented to manage this disease.* **Patient 14, GR2:** *"I just stick to a routine. I go to bed at a certain time."* **Patient 15, GR2:** *"I don't use my phone at night, I use during the day..."* **Patient 15, GR2:** *"I do external things like I don't use my phone, and I'll turn off the TV, because so these distractions interrupt with sleep. So, I, you know, keep a dark room and, you know, I keep the, you know, a little cooler. And, so, in addition to my sleeping medicines, you know, I've adopted other practices, like, you know, no technology and stuff to help."*
	Pharmacological Management	**Patient 10, GR3:** *"With the sleeping, the amitriptyline. That is what I totally give all credit to that. Because I guarantee if I didn't pay, if I wouldn't take it, it would be bad. It would be like 18 hours up, and the other hours very, very, very restless."* **Patient 16, GR3:** *"I just got a dosage of hydroxyzine, increased to 50 milligrams because the 25 milligrams wasn't working."* **Patient 09, GR1:** *"I start out with the rescue inhaler and then I have a long acting Breztri after that and I have my medicine that I take for my anxiety and depression…I take, some anxiety meds because sometimes they don't work. Especially if I start coughing and it won't go away, that's like. It's very, you know, scary."*
	Complementary and Integrative Approaches	**Patient 26, GR2:** *"It is very difficult to fall asleep…like depending with the pillows and trying to get comfortable. And then I have coughing and it's like, "Oh my God, I'm not going to fall asleep." I use sleep meditation, sleep hypnosis to help me fall asleep, so it does help..."* **Patient 09, GR1:** *"I have 10 supplements you know, to try to maintain my energy. I drink electrolytes all day long because I've noticed how much the energy had, my energy has been affected, so I have an electrolyte drink that I drink that I'm hoping helps me with my energy."* **Patient 19, GR1:** *"I take supplements to help me fall back asleep. I don't like to take a sleeping pill. So, I take a, you know, like stuff with melatonin in it. And sometimes it works, sometimes, sometimes it doesn't."* **Patient 03, GR2:** *"I do acupuncture every single Monday, and that gives me one hour a week to relax and reset and just get grounded. And during that hour of acupuncture, I listen to this meditation, a Deepak Chopra, something the acupuncturist puts on me…So on those nights when I have difficulty falling back to sleep, when I wake up in the middle of the night, what I do in my head is I start listening to the chakras."*
Symptom Outcomes	Activity Avoidance	**Patient 09, GR1:** *"I can't get up in the morning and go somewhere. I have to plan my day around my symptoms. There's no getting up in the morning and going and of course then if I'm having a flare up then I don't get to do things maybe I planned it's very disruptive to life."* **Patient 62, GR1:** *"Sometimes, depending on the day, I might not take a trip because of that. I'm like, "Oh, y'all going to be walking all fast, I'm not going to go." So sometimes it does hold you back."* **Patient 03, GR2:** *"If I wanted to go to the movies, I couldn't do it. I'd be coughing. So, I feel like I'm interrupting everybody. So, the coughing is my biggest one that bothers me."*
	Daytime Effects	**Patient 22, GR3:** *I can't sleep and it affects my whole during the daytime and I'm not focused."* **Patient 23, GR3:** *"When I'm up in the night and I have broken sleep, I have a terrible breathing day. Because I think my body's tired and it takes more of an impact on me. So, if I sleep well, I feel better during the day. If I don't, then a lot of times I have to take a nap during the day because I'm so tired."*
	Life/ADLs	**Patient 19, GR1:** *"I have a lot of clients that I help and there are times where I just can't concentrate or think good. It's not as good as it used to be."* **Patient 06, GR2:** *"If I'm doing housework, running the vacuum cleaner, I've got to take a break. I'll do one room and I'm like, I've got to sit down for a minute. It slows me down. Just like to make a bed, it takes my breath. It's just I get really winded."*

GR=group; ADLs=activities of daily living

- **Patient 03, GR2:** *"…when I get the anxiety or anxious feeling, that's bothersome, because I feel like I'm lost. Okay. And anxiety, is it at nighttime as well? Well, it starts in the afternoon."*
- **Patient 12, GR3:** *"When I'm having a hard time breathing or whatever, you know, it kind of gets you get a lot of anxiety, hoping you can keep on you know, to the night and get by through everything and stuff and everything."*

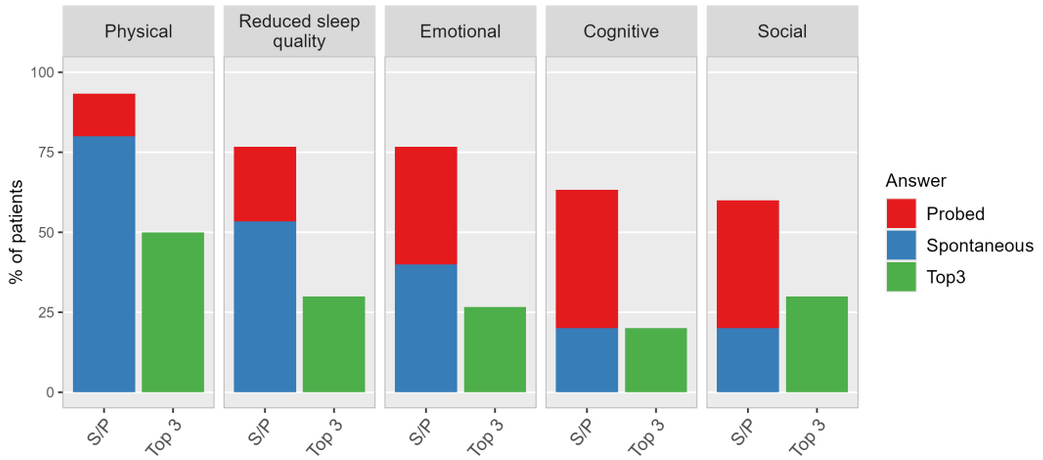
For personal use only. Permission required for all other uses.

Figure 2. Frequently Reported Nighttime Symptoms



S/P=spontaneous/probed

Figure 3. Frequently Reported Impacts of Nighttime Symptoms



S/P=spontaneous/probed

- **Patient 12; GR3:** *I was struggling to breathe. I was having to write things on paper for my wife, because I couldn't even talk."*

When participants ranked the most bothersome impacts, physical impacts were selected most often, identified by 50% of participants. Reduced sleep quality and social impacts were both ranked among the top 3 most bothersome (30% each), and emotional impacts were reported as the most bothersome by 27% of the participants.

Main Findings – Nighttime Symptom Management Strategies

Participants reported a combination of behavioral adaptations, complementary and integrative approaches, and pharmacological symptom management strategies (Table 3).

To manage sleep disruptions, participants most commonly relied on consistent sleep routines (33%), sleep hygiene, and relaxation techniques such as meditation or breathing exercises (33%).

- **Patient 14, GR2:** *"I just stick to a routine. I go to bed at a certain time."*
- **Patient 15, GR2:** *"I do acupuncture every single Monday, and that gives me one hour a week to relax and reset and just get grounded. And during that hour of acupuncture, I listen to this meditation, a Deepak Chopra, something the acupuncturist puts on me…So on those nights when I have difficulty falling back to sleep, when I wake up in the middle of the*

For personal use only. Permission required for all other uses.

Table 3. Strategies for Dealing With Sleep Disruption

Strategy, n (%)	Total Sample (N=30)
Coping Mechanisms	
Sticking to a Sleeping Routine	10 (33)
Stress-Management/Relaxations Techniques	10 (33)
Taking Antidepressant Medications	9 (30)
Drinking Liquid Before Bed	3 (10)
Having A Distraction, Such as TV or Reading, Before Bed	4 (13)
Medications Such as Painkillers or Muscle Relaxants	3 (10)
Pre-Emptying Cough Technique Before Going to Bed	2 (7)
Reducing Media or TV Consumption Before Bed	2 (7)
Avoid Caffeine	1 (3)
Sleep Environment	
Change pillow/bed/body position (e.g., head elevated)	9 (30)
Light	7 (23)
Temperature	6 (20)
Humidity	5 (17)
Reduce noise	1 (3)
Sleep Supplements	
Magnesium	4 (13)
Tylenol PM[a]	4 (13)
Melatonin	2 (7)
Electrolyte Drink	1 (3)
Valerian	1 (3)
Other Medical Management Methods for Nighttime Symptoms	
COPD Medication or Nebulizer	14 (47)
Oxygen Therapy	6 (20)
CPAP Machine	3 (10)
Preventive Rescue Inhaler Use to Help With Aleep	11 (37)

[a] Nighttime pain reliever and sleep aid (acetaminophen and diphenhydramine hydrocloride)

COPD=chronic obstructive pulmonary disease; CPAP=continuous positive airway pressure

night, what I do in my head is I start listening to the chakras."

- **Patient 35, GR3:** *"For the sleep, and then, I'll listen to YouTube. I listen to frequencies, like the 528, 423 frequency, the theta waves, binaural beats delta waves. Anything that'll make me sleep."*
- **Patient 03, GR2:** *"Most of the time, I can talk myself out of it. I don't know if that makes sense, but I'm like, relax, relax, relax, relax. And I, like, meditate myself out of it."*

Around one-third (30%) used non-COPD medications, mainly antidepressants, to support sleep.

- **Patient 10, GR3:** *"With the sleeping, the amitriptyline. That is what I totally give all credit to that. Because I guarantee if I didn't pay, if I wouldn't take it, it would be bad. It would be like 18 hours up, and the other hours very, very, very restless."*
- **Patient 16, GR3:** *"I just got a dosage of hydroxyzine, increased to 50 milligrams because the 25 milligrams wasn't working. They also got me on melatonin as well."*
- **Patient 40, GR1:** *"I'm on medication for my mental health and he's trying to help my sleeping."*

Inhaler device use was common: 83% reported using a rescue inhaler at night, with more than half describing them as very effective, and some (37%) used them preventatively before bedtime.

- **Patient 23, GR3:** *"Sometimes I use it before I go to bed. I'm not very good at keeping track of when the last time it is, I used it. ...I'll do it, so that I don't wake up in the night all winded. Because if I don't use it, I definitely have exacerbations."*
- **Patient 15, GR2:** *"I find I need it more at night, for example, when I had to walk up the sixth flight of stairs, ... Like, I feel like I need it, but I don't want to get up...at night, when I'm laying there, and then I, I guess I said earlier, I think everything just kind of settles, and then it comes up at night."*

For personal use only. Permission required for all other uses.

- **Patient 31, GR3:** *"I think I notice symptoms more at night, and also just because I know it'll probably help me sleep a little better."*

Additional management strategies included nebulizer use (47%), oxygen therapy (20%), and CPAP machines (10%).

Table 4 summarizes participant experiences with twice-daily maintenance therapy among those with existing and/or prior exposure to a second daily dose (80%). Participants described a number of perceived benefits from the second daily dose, including improved symptom control (25%), better sleep (21%), and prolonged effectiveness (21%). Smaller proportions (13%) reported feeling no noticeable changes, and some participants described challenges, such as difficulty remembering the second dose or disruptions to daily routines (38%).

- **Patient 09, GR1:** *"Yes [the second dose provides additional relief] because I'll cough more without it. [The twice-daily] totally helped with my coughing that is what made my coughing manageable. So, if I don't do that nighttime dose, I wake up crappy in the morning, and I'm sluggish, and I don't know. It does something. I'm better if I do 2 doses."*
- **Patient 57, GR1:** *"I don't get exacerbations. And to me that's very important because I don't want to go back to the hospital. I don't like being in the hospital, so controlling exasperations is very important to me."*
- **Patient 35, GR3:** *"[The twice-daily] gets you through the day and night."*

Discussion

This study provides in-depth insight into the nighttime symptom experiences of symptomatic patients with COPD receiving single-inhaler dual or triple maintenance therapy. The findings suggest that nighttime symptoms represent a considerable burden to these patients and may impact daily functioning and quality of life. The SMT[22] provided the guiding conceptual framework for interpreting these findings, situating nighttime symptoms within the dynamic relationship between symptom experience, management strategies, and outcomes.

Nighttime symptoms in this study encompassed evening, night, and early morning manifestations, most participants reporting CASIS scores indicative of considerable nighttime symptom burden and sleep disruption. These findings align with prior studies, including the ASSESS study, which similarly demonstrated high nighttime symptom burden among patients with COPD.[16] Participant narratives emphasized that symptoms were often perceived as more severe at night, using descriptions such as distressing, persistent, and difficult to control. Dyspnea, cough and mucus production disrupted sleep and were physically and emotionally taxing.

Consistent with prior evidence, nocturnal symptoms were perceived to contribute to frequent awakenings, difficulty initiating and maintaining sleep, and reliance on rescue or nebulized medications during the night.[9-15] Within the SMT framework, findings reflect a heightened symptom experience beyond physical symptoms, including emotional responses such as anxiety or fear related to breathlessness. Nearly all participants reported physical consequences of nighttime symptoms, and 4 out of 5 reported reduced sleep quality, consistent with prior literature showing pervasive daytime fatigue and impaired functioning.[9,11,12,15,25]

Emotional and psychological consequences were commonly reported and appeared clinically meaningful, with patients describing nocturnal anxiety, panic related to breathlessness, and anxiety attacks, further diminishing quality of life across physical, social, and emotional domains.[9,15,26] Difficulty staying asleep or frequent awakenings emerged as the most bothersome nighttime symptom, while physical impacts were most often identified as the most burdensome consequence, suggesting that disrupted sleep may be one pathway through which nighttime symptoms affect daytime functioning.

Within the SMT framework, the findings suggest that nighttime symptom burden and inadequate symptom control extend beyond nocturnal discomfort to influence functional outcomes and daily behaviors. Activity avoidance emerged as a salient symptom outcome, with participants describing reduced participation in social activities, household tasks, and physical exertion. Such avoidance may contribute to progressive physical deconditioning and reduced independence, reinforcing a cyclical relationship between symptom burden and functional limitation in COPD.

Participants described a wide range of symptom management and coping strategies aimed at mitigating symptoms and improving sleep. Behavioral adaptations, such as structured sleep routines and a controlled sleep environment (e.g., adjusting sleep positioning, lighting, and temperature), were commonly reported and have been described in prior research as beneficial for improving sleep quality and symptom relief.[27-29] These strategies reflect the adaptive efforts and active patient engagement in symptom self-management.

Pharmacological management was also frequently employed. Approximately one-third of participants reported using antidepressant medications to aid sleep, with some also using supplements like melatonin, both of which have been shown to have potential effects on sleep latency or sleep quality.[30] Notably, limited prior research has examined real-world sleep management strategies among individuals

For personal use only. Permission required for all other uses.

Table 4. Experience With Twice-Daily Therapy

Aspects of the Second Dose, n (%)	Patients With Twice-Daily Therapy Experience (N=24)
Positive	
Better COPD Symptom Control	6 (25)
Works Well With Patients' Schedules	6 (25)
Better Nighttime Symptom/Sleep Management	5 (21)
Prolonged Effectiveness	5 (21)
Easy to Remember	4 (17)
Neutral	
No Difference Was Noticed With the Second Dose	3 (13)
Negative	
Difficulties With Remembering/Disruption to Daily Activities	9 (38)

COPD=chronic obstructive pulmonary disease

with COPD, particularly from the patient perspective. The present findings, therefore, add insights into how patients combine prescribed treatments with self-initiated strategies to manage nighttime symptoms in COPD.

The findings of the current study suggest that participants used a comprehensive and individualized approach to sleep management, which integrates behavioral, complementary and integrative approaches, and pharmacological strategies. Participants described actively balancing clinician-directed treatment plans with self-management behaviors and taking an active role in their sleep management. Clinicians may wish to consider that patients often engage in substantial self-management efforts alongside prescribed therapies to address nighttime symptoms.

Inhaler use was commonly mentioned as a symptom management strategy; one-third of individuals used rescue inhalers preventively at night, while others relied on maintenance therapy, particularly twice-daily regimens, which some participants perceived to be beneficial for nighttime symptom control and sleep outcomes. These observations are consistent with prior studies suggesting that extended-dosing regimens may contribute to nighttime symptom control.[31,32]

Despite longstanding recognition of nighttime symptom burden, the GOLD report,[17] as of the 2025 edition, still lacks explicit recommendations for managing sleep disturbance or nighttime COPD symptoms. Findings from this study support further consideration of nighttime symptoms in clinical care and may help inform future guideline development and recommendations to address the full 24-hour symptom experience in COPD.

Limitations

The sample size and homogeneous composition of the sample impose constraints on the generalizability and transferability of findings. Although efforts were made to ensure an equal number of participants within the 3 groups, the limited number of participants per group does not allow for group-specific conclusions. Another limitation is that it was not always possible to distinguish whether impacts, such as reduced sleep quality or emotional effects, were primarily driven by nighttime symptoms or the overall burden of disease and treatment. This may have influenced the accuracy of data on nighttime-specific experiences. The eligibility criteria may also limit the transferability of the findings. Requiring a CAT score of ≥10 and current single-inhaler dual or triple maintenance therapy selected a symptomatic population with persistent burden despite maintenance treatment. Consequently, the nighttime symptoms and associated impacts reported may be more pronounced than those experienced by people with lower CAT scores, milder COPD, or different treatment profiles. The findings are most applicable to symptomatic patients receiving single-inhaler dual or triple therapy. The exclusion of open triple therapy means that the findings may not reflect the treatment burden associated with managing multiple inhalers. The findings may also have limited applicability to patients receiving single-bronchodilator regimens or newer maintenance options such as ensifentrine. A detailed exacerbation history was not collected beyond confirming the absence of a severe exacerbation resulting in hospitalization or an emergency department visit during the previous 12 months. The relationship between prior exacerbation burden and the reported nighttime experiences, therefore, could not be assessed.

Conclusions

This study suggests that nighttime symptoms represent a substantial burden in COPD among symptomatic patients receiving single-inhaler dual or triple maintenance therapy. Patients described persistent nighttime symptom distress and relied on a combination of pharmacological, complementary, and integrative approaches to manage nighttime symptoms, indicating both adaptive self-management and areas where additional support may be needed. These findings highlight the potential value of a more systematic assessment of nighttime symptoms, comprehensive and early patient

For personal use only. Permission required for all other uses.

education, and integration of multidisciplinary care to support COPD management across the full 24-hour cycle. Clinicians may wish to consider nighttime symptoms as part of COPD care and tailor management discussions to individual symptom patterns, treatment needs, and dosing schedules where clinically appropriate.

Acknowledgements

Author contributions: All authors—SM, HDG, MB, NF, RL, KH, CK, KW, DK, TT, and GJC—were involved in the conception and/or design of the study, reviewing the article and approval of the final manuscript. TT, DK, and KW were involved in data acquisition, data analysis, and interpretation. SM and HDG were involved in data interpretation and writing of the article. Medical writing assistance, under the guidance of the authors, was provided by Colin Lightfoot for this manuscript, in accordance with Good Publication Practice 2022 guidelines.

Data Sharing Statement: No data are available. Data are not available as no consent was sought from patients to allow sharing of data with third parties.

Declaration of Interest

HDG, MB, NF, and RL are employees of AstraZeneca Pharmaceuticals LP and hold AstraZeneca stock. GJC has received grants/contracts and consulting fees from AstraZeneca, GSK, Chiesi, Boehringer Ingelheim, Pulmonx, and Apreo. He has also received consulting fees from Intuitive and Uniquity. He is part of an advisory board for Chiesi and Sanofi Regeneron. SM has received funding and consulting fees from AstraZeneca as well as grants from the National Institutes of Health and the National Institute for Nursing Research. She is also the current South Carolina State Captain for the COPD Foundation. KH and CK are patient participants and receive consulting fees and financial assistance for meetings/travel from the COPD Foundation. DK, KW, and TT are employees of Kielo Research, which received fees from AstraZeneca related to this work. TT holds stock in Kielo Research.

For personal use only. Permission required for all other uses.

References

1. American Lung Association (ALA). COPD in your state. ALA website. Updated September 2025. Accessed December 2025. https://www.lung.org/lung-health-diseases/lung-disease-lookup/copd/for-health-professionals/copd-in-your-state

2. Weeks JD, Elgaddal N. National Center for Health Statistics, Centers for Disease Control and Prevention (CDC). Chronic obstructive pulmonary disease in adults age 18 and older: United States, 2023. CDC website. Published May 2025. Accessed December 2025. https://www.cdc.gov/nchs/products/databriefs/db529.htm .

3. Roberts M, Smith T, Wheatley J, Cho JG. Symptom burden of patients with chronic obstructive pulmonary disease attending the Westmead Breathlessness Service: prevalence, associations, and sex-related differences. *Int J Chron Obstruct Pulmon Dis.* 2023;18:2825-2837. https://doi.org/10.2147/COPD.S433541

4. Duffy PS, Criner JG. Chronic obstructive pulmonary disease. *Med Clin North Am.* 2019;103(3):453-461. https://doi.org/10.1016/j.mcna.2018.12.005

5. Kessler R, Partridge MR, Miravitlles M, et al. Symptom variability in patients with severe COPD: a pan-European cross-sectional study. *Eur Respir J.* 2011;37(2):264-272. https://doi.org/10.1183/09031936.00051110

6. Price D, Small M, Milligan G, Higgins V, Gil EG, Estruch J. Impact of night-time symptoms in COPD: a real-world study in five European countries. *Int J Chron Obstruct Pulmon Dis.* 2013;8:595-603. https://doi.org/10.2147/COPD.S48570

7. Sampol J, Miravitlles M, Saez M, Pallero M, Sampol G, Ferrer J. Poor sleep quality, COPD severity and survival according to CASIS and Pittsburgh questionnaires. *Sci Rep.* 2023;13:18656. https://doi.org/10.1038/s41598-023-45717-9

8. Stephenson JJ, Cai Q, Mocarski M, Tan H, Doshi JA, Sullivan SD. Impact and factors associated with nighttime and early morning symptoms among patients with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis.* 2015;10:577-586. https://doi.org/10.2147/COPD.S76157

9. Kauffman KS, Doede M, Diaz-Abad M, et al. Experience of insomnia, symptom attribution and treatment preferences in individuals with moderate to severe COPD: a qualitative study. *Patient Prefer Adherence.* 2014;8:1699-1704. https://doi.org/10.2147/PPA.S71666

10. Agusti A, Hedner J, Marin JM, Barbé F, Cazzola M, Rennard S. Night-time symptoms: a forgotten dimension of COPD. *Eur Respir Rev.* 2011;20(121):183-194. https://doi.org/10.1183/09059180.00004311

11. Budhiraja R, Parthasarathy S, Budhiraja P, Habib MP, Wendel C, Quan SF. Insomnia in patients with COPD. *Sleep.* 2012;35(3):369-375. https://doi.org/10.5665/sleep.1698

12. Glasser I, Wang F, Reardon J, et al. Improving COPD care in a medically underserved primary care clinic: a qualitative study of patient perspectives. *COPD.* 2016;13(5):616-621. https://doi.org/10.3109/15412555.2015.1126570

13. Hareendran A, Palsgrove AC, Mocarski M, et al. The development of a patient-reported outcome measure for assessing nighttime symptoms of chronic obstructive pulmonary disease. *Health Qual Life Outcomes.* 2013;11:104. https://doi.org/10.1186/1477-7525-11-104

14. Khan N, Vestbo J, Garrow A, et al. The Manchester Respiratory-related Sleep Symptoms scale for patients with COPD: development and validation. *Int J Chron Obstruct Pulmon Dis.* 2018;13:3885-3894. https://doi.org/10.2147/COPD.S171140

15. Shackell BS, Jones RC, Harding G, Pearse S, Campbell J. 'Am I going to see the next morning?' A qualitative study of patients' perspectives of sleep in COPD. *Prim Care Respir J.* 2007;16(6):378-383. https://doi.org/10.3132/pcrj.2007.00078

16. Miravitlles M, Worth H, Soler Cataluna JJ, et al. Observational study to characterise 24-hour COPD symptoms and their relationship with patient-reported outcomes: results from the ASSESS study. *Respir Res.* 2014;15:122. https://doi.org/10.1186/s12931-014-0122-1

17. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2025 report. GOLD website. Published December 2025. Accessed December 19, 2025. https://goldcopd.org/2025-gold-report/

18. Lipson DA, Barnacle H, Birk R, et al. FULFIL trial: once-daily triple therapy for patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2017;196(4):438-446. https://doi.org/10.1164/rccm.201703-0449OC

19. Martinez FJ, Rabe KF, Calverley PMA, et al. Determinants of response to roflumilast in severe chronic obstructive pulmonary disease: pooled analysis of two randomized trials. *Am J Respir Crit Care Med.* 2018;198(10):1268-1278. https://doi.org/10.1164/rccm.201712-2493OC

20. Pollack M, Rapsomaniki E, Anzueto A, et al. Effectiveness of single versus multiple inhaler triple therapy on mortality and cardiopulmonary risk reduction in COPD: the SKOPOS-MAZI study. *Am J Med.* 2024;138(4):650-659. https://doi.org/10.1016/j.amjmed.2024.11.007

21. Singh D, Papi A, Corradi M, et al. Single inhaler triple therapy versus inhaled corticosteroid plus long-acting beta2-agonist therapy for chronic obstructive pulmonary disease (TRILOGY): a double-blind, parallel group, randomised controlled trial. *Lancet.* 2016;388(10048):963-973. https://doi.org/10.1016/S0140-6736(16)31354-X

22. Dodd M, Janson S, Facione N, et al. Advancing the science of symptom management. *J Adv Nurs.* 2001;33(5):668-676. https://doi.org/10.1046/j.1365-2648.2001.01697.x

23. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD Assessment Test. *Eur Respir J.* 2009;34(3):648-654. https://doi.org/10.1183/09031936.00102509

For personal use only. Permission required for all other uses.

24. van Kan GA, Rolland YM, Morley JE, Vellas B. Frailty: toward a clinical definition. *J Am Med Dir Assoc*. 2008;9(2):71-72. https://doi.org/10.1016/j.jamda.2007.11.005

25. Partridge MR, Karlsson N, Small IR. Patient insight into the impact of chronic obstructive pulmonary disease in the morning: an internet survey. *Curr Med Res Opin*. 2009;25(8):2043-2048. https://doi.org/10.1185/03007990903103006

26. Collacott H, Zhang D, Heidenreich S, Tervonen T. A systematic and critical review of discrete choice experiments in asthma and chronic obstructive pulmonary disease. *Patient*. 2022;15:55-68. https://doi.org/10.1007/s40271-021-00536-w

27. Chan RR, Giardino N, Larson JL. A pilot study: mindfulness meditation intervention in COPD. *Int J Chron Obstruct Pulmon Dis*. 2015;10(1):445-454. https://doi.org/10.2147/COPD.S73864

28. Lin T, SS. Effects of breathing-based meditation on dyspnea in COPD, a single-case study. *Eur Respir J*. 2022;60(Suppl 66):37. https://doi.org/10.1183/13993003.congress-2022.37

29. Nolan CM, Brighton LJ, Mo Y, et al. Meditative movement for breathlessness in advanced COPD or cancer: a systematic review and meta-analysis. *Eur Respir Rev*. 2023;32(168):220243. https://doi.org/10.1183/16000617.0243-2022

30. Halvani A, Mohsenpour F, Firouz Abadi EE. Effect of melatonin on sleep quality of COPD patients. *Eur Respir J*. 2012;40(Suppl 56):3477. https://publications.ersnet.org/content/erj/40/suppl56/p3477?utm_source=chatgpt.com

31. D'Urzo A, Kerwin E, Rennard S, He T, Gil EG, Caracta C. One-year extension study of ACCORD COPD I: safety and efficacy of two doses of twice-daily aclidinium bromide in patients with COPD. *COPD*. 2013;10(4):500-510. https://doi.org/10.3109/15412555.2013.791809

32. Kerwin E, Rennard S, Gelb A, Rekeda L, Gil EG, Caracta C. ACCORD COPD I: improvements in nighttime symptoms and rescue medication use in COPD with twice-daily aclidinium bromide. *Eur Respir J*. 2014;38(55):873. https://doi.org/10.1183/13993003/erj.38.Suppl_55.p873

For personal use only. Permission required for all other uses.