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Original Research

Ambient Air Pollution Exposure and Sleep Quality in COPD

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Abstract

Rationale: Ambient air pollution exposure is associated with respiratory morbidity among individuals with chronic obstructive pulmonary disease (COPD), particularly among those with concomitant obesity. Although people with COPD report high incidence of poor sleep quality, no studies have evaluated the association between air pollution exposure, obesity, and sleep disturbances in COPD.

Methods: We analyzed data collected from current and former smokers with COPD enrolled in the Subpopulations and Intermediate Outcome Measures in COPD -Air Pollution ancillary study (SPIROMICS AIR). Socio-demographics and anthropometric measurements were collected, and 1-year mean historical ambient particulate matter ($PM_{2.5}$) and ozone concentrations at participants' residences were estimated by cohort-specific spatiotemporal modeling. Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI), and regression models were constructed to determine the association of 1-year $PM_{2.5}$ (1Yr-$PM_{2.5}$) and 1-year ozone (1Yr-ozone) with the PSQI score, and whether obesity modified the association.

Results: In 1308 participants (age: 65.8 ± 7.8 years, 42% women), results of regression analyses suggest that each $10\mu g/m^3$ increase in 1Yr-$PM_{2.5}$ was associated with a 2.1-point increase in PSQI (P=0.03). Obesity modified the association between 1Yr-$PM_{2.5}$ and PSQI (P=0.03). In obese and overweight participants, a $10\mu g/m^3$ increase in 1Yr-PM2.5 was associated with a higher PSQI (4.0 points, P<0.01, and 3.4 points, P<0.01, respectively); but no association in lean-normal weight participants (P=0.51). There was no association between 1 Yr-ozone and PSQI.

Conclusion: Overweight and obese individuals with COPD appear to be susceptible to the effects of ambient $PM_{2.5}$ on sleep quality. In COPD, weight and ambient $PM_{2.5}$ may be modifiable risk factors to improve sleep quality.

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air pollution; sleep quality; COPD; obesity

Introduction

Air pollution exposure is a major public health concern thought to be an important determinant of lung and sleep health.[1-3] More than 4 in 10 Americans live in counties across the nation with unhealthy levels of ozone or particulate matter pollution.[4] Air pollution exposure may have implications for sleep quality and health outcomes, especially in patients with respiratory disorders.

Chronic obstructive pulmonary disease (COPD) is a highly prevalent respiratory disorder characterized by poor sleep quality.[5-7] Sleep disturbance in COPD patients is largely attributed to nocturnal breathing difficulties, hypoxemia, and medications.[6-8] It is unclear, however, if ambient air pollution exposure is also a risk factor for poor sleep quality among COPD patients. Several studies conducted in the general population have revealed that those who live in areas with greater ambient air pollution have poorer sleep quality, particularly those with concomitant sleep apnea.[9,10] Given the compromise in lung function, COPD patients may be uniquely vulnerable to the effect of air pollution exposure on sleep quality. In addition, factors such as obesity and smoking may modulate the relationship between air pollution exposure and sleep quality in COPD, since they predispose to sleep apnea,[11-13] and are known to be associated with inflammation.[14-17]

Our goal was to examine the association between ambient air pollution exposure and sleep quality in COPD patients. We analyzed ambient air and sleep quality data collected from the Subpopulations and InteRmediate Outcome Measures In COPD Study (SPIROMICS)[18] and SPIROMICS Air Pollution (SPIROMICS AIR) ancillary study. We hypothesized that: (1) ambient air pollution exposure would be associated with worse sleep quality in patients with COPD, and that (2) the association of ambient air pollution exposure and sleep quality would be modified by obesity, such that obese patients are more susceptible to the adverse effects of ambient pollution exposure. We also hypothesized that (3) the association of ambient air pollution exposure and sleep quality would be modified by smoking status, such that current smokers are more susceptible to the adverse effects of ambient pollution exposure.

Methods

Study Population

The current cross-sectional analysis was conducted on data collected from current and former smokers (≥20 pack years) with COPD enrolled in the SPIROMICS AIR study.[18] Participants were enrolled at 7 (New York City, New York; Baltimore, Maryland; Los Angeles, California; Ann Arbor, Michigan; San Francisco, California; Salt Lake City, Utah; and Winston-Salem, North Carolina) of the 12 SPIROMICS clinical sites.[18]

SPIROMICS participants who were current or former smokers with COPD (postbronchodilator forced expiratory volume in 1 second [FEV$_1$] to forced vital capacity [FVC] ratio <70%) and who had available air pollution exposure and sleep quality data were included in our analyses (Figure 1). SPIROMICS was approved by the institutional review board at each of the clinical centers. All study participants provided written informed consent.

Assessment of Ambient Particulate Matter and Ozone

Participant addresses were obtained and geocoded with a geographic information system (ArcGIS 10.3; ESRI). Two-

Figure 1. Consort Diagram of Study Participants
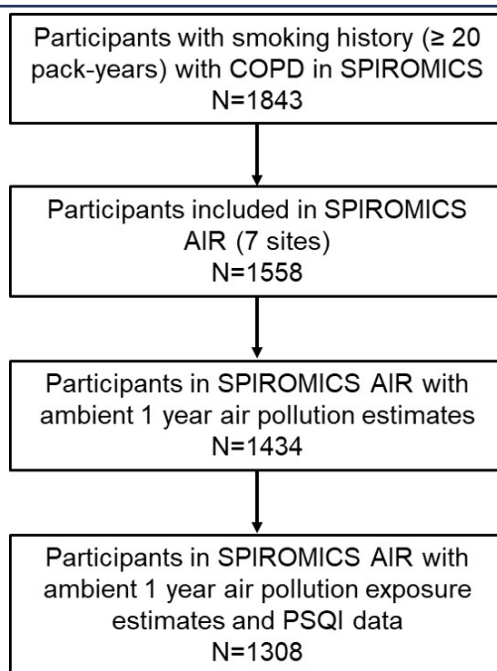
SPIROMICS=SubPopulations and InteRmediate Outcome Measures in COPD Study; PSQI=Pittsburgh Sleep Quality Index

week mean outdoor concentrations of fine particulate matter (PM$_{2.5}$) and ozone outside each participant's home were predicted using spatiotemporal modeling methods.[19,20] The 2-week air pollution exposures were used to calculate the mean 1-year PM$_{2.5}$ (1 Yr-PM$_{2.5}$) and 1-year ozone (1 Yr-ozone) levels,[19,20] which we used for our analyses.

Assessment of Sleep Quality

We assessed sleep quality with the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a validated self-rated survey that evaluates sleep quality and disturbances over a 4-week period. It is an 18-item questionnaire comprising 7 sub-sections, each scored 0–3, allowing for total scores ranging from 0–21, with higher scores representing poorer sleep quality.[21]

Statistical Analyses

Participant characteristics were described using the median with interquartile range (IQR) for continuous variables and n (%) for the categorical variables. We modeled 1 Yr-PM$_{2.5}$ and 1 Yr-ozone as continuous variables by increments of 10μg/m^3 and 5 parts per billion (ppb) respectively. PSQI was examined as a continuous composite score and also as a dichotomous outcome based on PSQI total scores above and below the threshold for poor sleep quality (>5 and ≤5).[21] To address our hypotheses, we examined the association of 1 Yr-PM$_{2.5}$ and 1 Yr-ozone as the independent variables and PSQI as the dependent variable using linear and logistic regression in unadjusted and adjusted models. In adjusted models, we adjusted for age, sex, race, education,

income, current smoking status, smoking pack years, FEV$_1$% predicted, body mass index (BMI) (continuous), and occupational exposure, which refers to self-reported exposure to vapor, gases, dust, and fumes in the longest held job. The adjusted model also included study site and neighborhood poverty rate, which represents the percentage of families below the poverty level in a census tract based on 2010 American Community Survey 5-year estimates.[22] We performed sequential covariate adjustments to check against potential over-adjustment and checked for multicollinearity in the fully adjusted model using the variance inflation factor (VIF).[23,24] We examined whether BMI category (lean/normal weight, <25kg/m^2; overweight, ≥25kg/m^2 and <30kg/m^2; and obese, ≥30kg/m^2) and smoking status modified the association of ambient air pollution exposure and PSQI. Effect modification was tested by introducing an interaction term of categorical BMI and smoking status in the adjusted models.

Since sex-related differences in fat distribution can impact tidal volumes[25-27] and potential air pollutant deposition in the lungs, in post-hoc analyses we examined whether sex modified the association of ambient air pollution exposure and PSQI in the 3 BMI categories (lean/normal weight, overweight, and obese).

All analyses were performed using STATA (version 15.1).

Results

Participant Characteristics

A total of 1308 SPIROMICS AIR participants with COPD

had available PSQI scores as well as 1-Yr historical $PM_{2.5}$ and ozone exposure data. As shown in Table 1, the median age was 67 years and the median BMI was $26.9 kg/m^2$, with women comprising 42% of the participants. The group had a median 1-Yr $PM_{2.5}$ exposure of $8.8 \mu g/m^3$ and a median 1-Yr ozone exposure of 10.5 ppb. The median PSQI score was 6.0 and approximately half (51.3%) of the participants had PSQI scores greater than 5, which is the validated threshold for poor sleep.[21]

Association of Ambient Air Pollution Exposure and Pittsburgh Sleep Quality Index

Linear regression analyses revealed a positive association between 1 Yr-$PM_{2.5}$ and PSQI, such that a $10 \mu g/m^3$ increase in 1 Yr-$PM_{2.5}$ was associated with a 2.1 point (95% confidence interval [CI]: 0.8–3.3, $P<0.01$) increase in PSQI in the unadjusted model, and a 2.1-point increase (95% CI: 0.2–4.0, $P=0.03$) in the adjusted models. Logistic regression also revealed a positive association between 1 Yr-$PM_{2.5}$ and the odds of poor sleep quality (PSQI>5) in the unadjusted

(OR=2.6, 95% CI: 1.3–5.0, $P=0.01$), and adjusted (OR=2.7, 95% CI: 0.9–7.9, $p=0.07$) models. 1 Yr-Ozone was not associated with PSQI either as continuous or categorical (Table 2 and Table 3).

Additionally, in comparison to lean-normal weight, the linear association between 1-Yr $PM_{2.5}$ and PSQI was amplified among overweight ($\beta_{interaction}=4.2$, 95% CI: 1.5–7.0, $P<0.01$) and obese participants ($\beta_{interaction}=4.8$, 95% CI: 1.9–7.7, $P<0.01$). For example, a $10 \mu g/m^3$ increase in 1 Yr-$PM_{2.5}$ was associated with a 3.4 point (95% CI: 1.0–5.8, $P=0.01$) increase among the overweight, a 4.0 point (95% CI: 1.5–6.5, $P<0.01$) increase in PSQI among the obese but was not associated with PSQI among the lean-normal weight ($\beta=-0.8$, 95% CI: -3.4–1.7, $P=0.52$). Similarly, the relationship between 1-Yr $PM_{2.5}$ and the odds of poor sleep quality was amplified among current smokers compared to former smokers (OR interaction=3.6, 95% CI: 0.8–15.4, $P=0.09$), as a $10 \mu g/m^3$ increase in 1-Yr $PM_{2.5}$ was associated with a 6 times higher odds of poor sleep quality among current smokers (OR=6.7, 95% CI: 1.5–30.0, $P=0.01$) but not associated with the odds of poor sleep quality among former smokers (OR=1.9, 95%

Table 1. Participant Characteristics[a]

	Median (IQR) or n (%)
Demographics	
Age, years.	67.0 (60.0, 72.0)
Sex, n (% female)	549 (42.0%)
Race, n (% white)	1101 (84.2%)
Education, n (% above HS degree)	840 (64.2%)
Income	
Under $35,000	442 (33.8%)
$35,000-$74,999	383 (29.3%)
$75,000 or Above	237 (18.1%)
Declined to Answer	246 (18.8%)
Smoking Status	429 (32.8%)
Pack Years	46.0 (35.0, 60.9)
FEV_1 % Predicted	63.6 (45.8, 79.8)
BMI, kg/m^2, continuous	26.9 (23.7, 31.1)
BMI, categorical	
Lean/Normal Weight (BMI<25)	451 (34.4%)
Overweight (BMI≥25 &<30)	448 (34.3%)
Obese (BMI≥30)	409 (31.3%)
Occupational Exposure, n (% yes)	629 (48.1%)
% Poverty Rate	6.1 (2.7,12.9)
Ambient Pollution Exposure	
1 Yr-$PM_{2.5}$, $\mu g/m^3$	8.8 (7.8, 10.2)
1 Yr-Ozone, ppb	10.5 (6.5,15.7)
PSQI Score	
Continuous	6.0 (3.0, 9.0)
Dichotomous, n (%>5)	671 (51.3%)

[a]N=1308

Data are presented as median with IQR (25%tile, 75%tile) for continuous variables, and n (%) for categorical variables.

Occupational exposure refers to self-reported exposure to vapor, gas, dust, and fumes at the longest job.

IQR=interquartile range; HS=high school; FEV_1=forced expiratory volume in 1 second; BMI=body mass index; PM=particulate matter; Yr=year; ppb=parts per billion; PSQI=Pittsburgh Sleep Quality Index

Table 2. Association of Ambient Air Pollution Exposure and the Pittsburgh Sleep Quality Index

	PSQI Total Score Continuous			PSQI Total Score (>5 vs ≤5)		
	β	95% CI	P	OR	95% CI	P
1 Yr-PM$_{2.5}$ (per 10μg/m^3)						
Unadjusted	2.1	0.8 - 3.3	<0.01	2.6	1.3 - 5.0	0.01
Adjusted	2.1	0.2 - 4.0	0.03	2.7	0.9 - 7.9	0.07
1 Yr-ozone (per 5 ppb)						
Unadjusted	-0.0	-0.2 - 0.2	0.75	1.0	0.9 - 1.1	0.37
	0.1	-0.3 - 0.5	0.59	1.1	0.9 - 1.3	0.66

Adjusted model includes age, gender, race, education, income, smoking status, pack years, FEV$_1$ % predicted, BMI, occupational exposure, neighborhood poverty rate, study sites, and the other ambient pollutant (PM$_{2.5}$ or ozone).

PSQI=Pittsburgh Sleep Quality Index; CI=confidence interval; OR=odds ratio; YR=year; PM=particulate matter; ppb= parts per billion; FEV$_1$=forced expiratory volume in 1 second; BMI=body mass index

Table 3. Association of Ambient Air Pollution Exposure and Pittsburgh Sleep Quality Index in Multivariable Model

	PSQI Total Score Continuous			PSQI Total Score (>5 vs ≤5)		
	β	95% CI	P	OR	95% CI	P
Variables in the Multivariable Model						
1 Yr-PM2.5 (per10 μg/m^3)	2.1	0.2 - 4.0	0.03	2.7	0.9 - 7.9	0.07
Age, years	-0.1	-0.0 - -0.5	<0.01	0.9	0.9 - 1.0	<0.01
Sex, female	0.9	0.5 - 1.3	<0.01	1.5	1.2 - 1.9	<0.01
Race, White	0.2	-0.4 - 0.9	0.53	1.1	0.8 - 1.5	0.75
Education > High School	-0.2	-0.7 - 0.3	0.43	1.0	0.8 - 1.3	0.84
Income (< $35,000)						
$35,000 - $74,999	-0.9	-1.4 - -0.4	<0.01	0.7	0.5 - 0.9	0.02
≥ $75,000	-1.2	-1.8 - -0.5	<0.01	0.5	0.4 - 0.8	<0.01
Declined to answer	-0.1	-0.8 - 0.6	0.08	1.0	0.7 - 1.4	0.87
FEV$_1$, % Predicted	0.0	0.0 - 0.0	0.33	1.0	1.0 - 1.0	0.54
Smoking Status, yes	0.6	0.1 - 1.1	0.02	1.3	1.0 - 1.7	0.07
Pack Years	0.0	0.0 - 0.0	0.46	1.0	1.0 - 1.0	0.27
BMI, kg/m^2	0.0	0.0 - 0.1	0.55	1.0	1.0 - 1.0	0.11
Occupational Exposure, yes	0.5	0.0 - 0.9	0.04	1.4	1.1 - 1.8	0.01
% Poverty Rate	0.0	0.0 - 0.0	0.80	1.0	1.0 - 1.0	0.99
Site (CU-New York)						
JH-Baltimore	0.3	0.7 - 1.3	0.51	1.0	0.5 - 1.6	0.84
UCLA-Los Angeles	-0.7	-1.6 - 0.3	0.15	0.6	0.3 - 1.0	0.03
MI-Ann Arbor	-0.2	-1.1 - 0.7	0.68	0.7	0.4 - 1.2	0.24
UCSF-San Francisco	0.5	-0.5 - 1.4	0.33	1.0	0.6 - 1.7	0.90
UT-Salt Lake City	0.9	-0.3 - 2.0	0.14	1.2	0.7 - 2.3	0.49
WF-Winston Salem	0.2	-0.7 - 1.2	0.63	0.8	0.5 - 1.4	0.50
1 Yr-Ozone (per 5 ppb)	0.1	-0.3 - 0.5	0.59	1.1	0.9 - 1.3	0.66

Occupational exposure refers to self-reported exposure to vapor, gas, dust, and fumes at the longest job.

PSQI=Pittsburgh Sleep Quality Index; CI=confidence interval; OR=odds ratio; PM=particulate matter; YR=year; FEV$_1$=forced expiratory volume in 1 second; BMI=body mass index; CU=Columbia University; JH=Johns Hopkins; UCLA=University of California-Los Angeles; MI=Michigan; UCSF=University of California-San Francisco; UT=Utah; ppb=parts per billion

CI: 0.6–5.9, P=0.27) (Table 4). Within obese participants (n=409), the adverse linear association of 1 Yr-PM$_{2.5}$ with PSQI tended to be greater among women than among men (β$_{interaction}$=3.9, 95% CI: -0.4–8.2, P=0.07), with a 10μg/m^3 increase in 1 Yr-PM$_{2.5}$ associated with a 7.3 point (95% CI: 3.1–11.5, P<0.01) increase in PSQI among women and a 3.4 point (95% CI: -0.1–6.9, P=0.06) increase in PSQI in men.

There was no sex difference in the relationship between 1 Yr-PM$_{2.5}$ and PSQI among overweight (β$_{interaction}$=-1.1, 95% CI: -5.1–2.8, P=0.57) or lean-normal participants (β$_{interaction}$=1.3, 95% CI: -3.2–5.7, P=0.57). The modifying effect of weight and sex on the relationship between 1 Yr-PM$_{2.5}$ and PSQI is shown in Figure 2.

The sequential covariate adjustment for checking

Table 4. Association of Ambient Air Pollution Exposure and Pittsburgh Sleep Quality Index by Smoking Status

	PSQI Total Score Continuous			PSQI Total Score (>5 vs ≤5)		
	β	95% CI	*P*	OR	95% CI	*P*
Former Smokers						
1 Yr-PM$_{2.5}$ (per 10µg/m^3)	1.8	-0.2 - 3.8	0.08	1.9	0.6 - 5.9	0.27
1 Yr-Ozone (per 5 ppb)	0.1	-0.3 - 0.5	0.79	1.1	0.9 - 1.4	0.50
Current Smokers						
1 Yr-PM$_{2.5}$ (per 10µg/m^3)	2.7	0.0 - 5.4	0.05	6.7	1.5 - 30.0	0.03
1 Yr-Ozone (per 5 ppb)	0.2	-0.3 - 0.7	0.42	1.0	0.8 - 1.3	0.90
All Participants						
1 Yr-PM$_{2.5}$ (per 10µg/m^3)	2.1	0.2 - 4.0	0.03	2.7	0.9 - 7.9	0.07
Smoking Status, yes	0.6	0.1 - 1.1	0.02	1.3	1.0 - 1.7	0.07
1 Yr-PM$_{2.5}$[a] Smoking Status	0.9	-1.7 - 3.5	0.48	3.5	0.8 - 15.4	0.09

[a]Interaction term testing effect modification by smoking status.

All models were adjusted for age, sex, race, education, income, pack years, FEV$_1$ % predicted, BMI, occupational exposure, neighborhood poverty rate, and study sites.

PSQI=Pittsburgh Sleep Quality Index; CI=confidence Interval; OR=odds ratio; Yr=Year; PM=particulate matter; ppb=parts per billion; BMI=body mass index

Figure 2. Predicted Changes in the Total Pittsburgh Sleep Quality Index Score Per 10µg/m^3 Increase in Mean Yearly Ambient Fine Particulate Matter
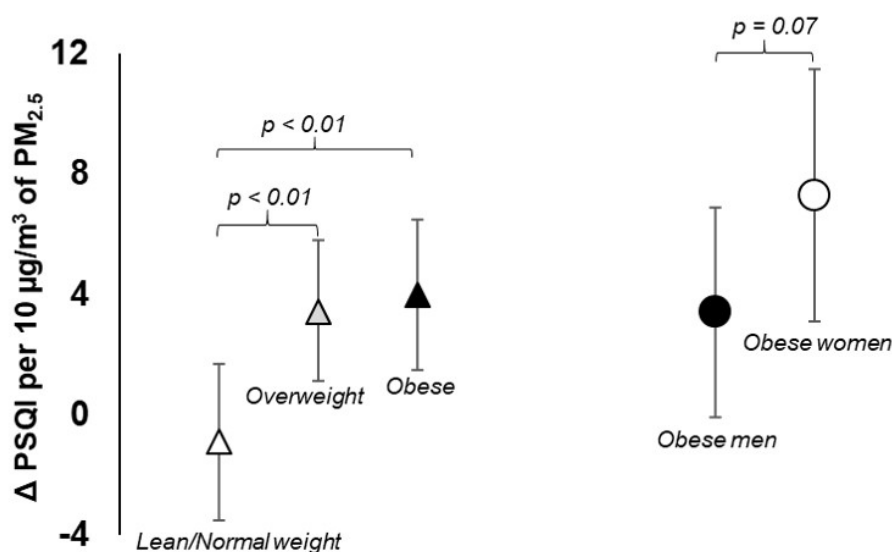
PSQI=Pittsburgh Sleep Quality Index; PM=particulate matter

against potential over-adjustment showed that our results were robust across inclusion of different covariates and, in our final fully adjusted model, none of our predictors' VIF exceeded the conventional benchmark[23,24] of 4, suggesting no serious multicollinearity issue.

Discussion

In this cross-sectional analysis of ambient air pollution exposure and subjective sleep quality in the SPIROMICS cohort, we found that an increased ambient 1 Yr-PM$_{2.5}$ but not 1 Yr-ozone was associated with a higher PSQI, indicating worse sleep quality. We also found that the association of 1 Yr-PM$_{2.5}$ and PSQI was modified by obesity and smoking status, such that overweight-obese participants were more susceptible to the adverse effects of air pollution exposure compared to normal weight adults and current smokers more susceptible compared to former smokers. Furthermore, female obese participants seemed to be more susceptible than male obese participants.

A recent systematic review by Liu et al showed that in a general population cohort, ambient pollution exposure was associated with poor sleep quality.[2] Our study confirms this finding in the SPIROMICS cohort, a nationally diverse group of COPD patients. Our results indicate that a 10µg/m^3 increase in 1 Yr-PM$_{2.5}$ is associated with a 2.1 unit increase in PSQI, a self-reported measure of poor sleep quality, and a 3 times higher odds of having poor sleep quality defined[21] by a PSQI score greater than 5. Previous studies have reported a minimum clinically important difference of 3 units for

PSQI,[28,29] suggesting that an increase of $15\mu g/m^3$ in $PM_{2.5}$ exposure can result in clinically significant worsening in sleep quality. Although poor sleep quality is prevalent in COPD, our results imply that ambient $PM_{2.5}$ is a potential contributor.

Associations between ambient $PM_{2.5}$ and sleep quality in COPD may be driven by several mechanisms. The deposition of particulate matter in the lungs could lead to alveolar inflammation and a worsening of the inefficient gas exchange[3] already present in COPD. Inefficient gas exchange will promote hypercapnia and hypoxia increasing respiratory drive and sympathetic activation, which would culminate in micro-arousals and sleep disruption. Air pollutants may also irritate the nasal and pharyngeal mucosa leading to upper airway inflammation, exacerbating sleep apnea, and yielding more breathing difficulties that can disrupt sleep. Alteration of CNS control of sleep, increased depression, and anxiety are other mechanisms by which air pollution exposure may contribute to poor sleep.[30,31]

Our findings further suggested interactions between weight and ambient $PM_{2.5}$, sex and ambient $PM_{2.5}$, and between smoking status and ambient $PM_{2.5}$. For example, ambient $PM_{2.5}$ was associated with sleep quality only in overweight-obese participants, suggesting that this COPD subgroup is more vulnerable to the effect of air pollution exposure on sleep. In the overweight-obese patients who may have COPD-obstructive sleep apnea overlap, increased risk for sleep-disordered breathing due to air pollution exposure[32] may explain poorer sleep quality. It is also possible that the inflammation provoked by air pollution exposure is synergistic with the chronic inflammatory state of obesity,[14-16] thereby promoting sleep-disordered breathing. Overweight-obese persons also have greater minute ventilation given the greater metabolic demand,[33,34] possibly increasing the dose of inhaled air pollutants over time.[27] Increased minute ventilation may also explain why there was a stronger association of ambient $PM_{2.5}$ and sleep quality in obese women compared to obese men, since obesity in men is associated with visceral fat deposition unlike subcutaneous adiposity in women,[25,26] which is more likely to allow for lung expansion and air pollutant deposition in the lungs.[35,36] The lack of an interaction between sex and ambient $PM_{2.5}$ in the lean/normal weight and overweight BMI categories suggests that differential fat distribution is most likely to impact the relationship of air pollution exposure and sleep quality at BMI levels above $30kg/m^2$. On the other hand, increased upper airway inflammation and susceptibility to sleep apnea might explain the stronger association of ambient $PM_{2.5}$ and sleep quality observed in the current smokers compared to former smokers. Our results also show that current smokers have worse sleep quality compared to former smokers (Table 3 and Table 4), which implies that smoking cessation might improve sleep quality.

Of note, there was no association between ambient ozone and sleep quality, suggesting that the effect of air pollution exposure on sleep may be dependent on the type of air pollutant. The lack of an association could mean that ozone does not irritate the upper airway mucosa, nor does it persist in the alveoli long enough to significantly alter gas exchange nocturnally. It also suggests that ozone does not provoke inflammation as much as $PM_{2.5}$. In addition, it is possible that ambient ozone levels were not substantial enough to disrupt sleep.

We acknowledge, however, several limitations in interpreting our findings. First, our study lacked objective assessment of sleep and diagnostic validation of sleep-disordered breathing. Recognizing this limitation, it is pertinent that future projects investigating the effect of air pollution on sleep quality, characterize sleep and breathing with gold standard polysomnography. It will also be useful to employ rigorously tested patient-reported sleep assessment tools such as the PROMIS Sleep-Related Impairment and Sleep Disturbance questionnaires that capture unique psychometric domains of sleep quality.[37,38] Furthermore, focused assessments like home-based actigraphy may reveal movement disorders and changes in circadian rhythm as potential links between air pollution exposure and sleep health disruption. Second, we did not account for the level of indoor air pollution exposure, which could have been different between participants and, therefore, confounded our results. Finally, we realize that even though environmental air pollution measurement provides an index of patient exposure, it does not represent the dose or volume of air pollutants inhaled. Future studies should, therefore, include methods to estimate the amount of air pollutants deposited in the airways and alveoli, and also quantify tidal volume and minute ventilation. Nevertheless, there are several strengths of this study. Our analysis is based on a large, well-defined, nationally diverse cohort with fine spatiotemporal modeling of ambient air pollution exposure. In addition, this is the first study, to our knowledge, which has evaluated the association between air pollution exposure, obesity, and sleep disturbances in COPD.

Implication

Air pollution exposure may be an important predisposing factor for poor sleep in COPD, with smokers, overweight-obese, and in particular, obese female subgroups, being the most vulnerable. Hence, adopting strategies to mitigate air pollution exposure may improve sleep quality in these vulnerable patient groups. Identification of vulnerable groups in our study also highlights potential mechanisms by which air pollution exposure might affect sleep quality. Future work should, therefore, adopt a multi-dimensional approach to sleep health assessment[39,40] to improve the characterization of sleep quality, while investigating the

possible role of inflammation, sleep-disordered breathing, and lung mechanics on the effect of air pollution exposure on sleep quality.

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