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Associations of fine particulate matter exposure with sleep disorder indices in adults and mediating effect of body fat

Cheng-Yu Tsai [a,b], Huei-Tyng Huang [c,1], Ming Liu [d,1], Wun-Hao Cheng [e,f], Wen-Hua Hsu [e], Arnab Majumdar [a], Kang-Yun Lee [b], Po-Hao Feng [b], Chien-Hua Tseng [b], Kuan-Yuan Chen [b], Yi-Chun Kuan [g,h,i,j], Jiunn-Horng Kang [k,l], Hsin-Chien Lee [m], Cheng-Jung Wu [n], Wen-Te Liu [b,e,g,k,*]

[a] Department of Civil and Environmental Engineering, Imperial College London, South Kensington Campus, London, SW7 2AZ, United Kingdom
[b] Division of Pulmonary Medicine, Department of Internal Medicine, Taipei Medical University-Shuang Ho Hospital, No. 291, Zhongzheng Rd., Zhonghe District, New Taipei City, 235041, Taiwan
[c] Department of Medical Physics and Biomedical Engineering, University College London, Gower Street, London, WC1E 6BT, United Kingdom
[d] Department of Biology, University of Oxford, 11a Mansfield Road, Oxford, Oxfordshire, OX1 3SZ, United Kingdom
[e] School of Respiratory Therapy, College of Medicine, Taipei Medical University, No. 250, Wuxing Street, Taipei, 110301, Taiwan
[f] Respiratory Therapy, Division of Pulmonary Medicine, Department of Internal Medicine, Taipei Medical University-Wan Fang Hospital, No.111, Sec. 3, Xinglong Rd., Taipei, 116079, Taiwan
[g] Sleep Center, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan
[h] Department of Neurology, Taipei Medical University-Shuang Ho Hospital, No.291, Zhongzheng Rd., Zhonghe District, New Taipei City, 235041, Taiwan
[i] Department of Neurology, School of Medicine, College of Medicine, Taipei Medical University, No. 250, Wuxing Street, Taipei, 110301, Taiwan
[j] Taipei Neuroscience Institute, Taipei Medical University, No. 250, Wuxing Street, Taipei, 110301, Taiwan
[k] Research Center of Artificial Intelligence in Medicine, Taipei Medical University, No. 250, Wuxing Street, Taipei, 110301, Taiwan
[l] Graduate Institute of Nanomedicine and Medical Engineering, College of Biomedical Engineering, Taipei Medical University, No. 250, Wuxing Street, Taipei, 110301, Taiwan
[m] Department of Psychiatry, Taipei Medical University Hospital, No. 252, Wuxing Street, Taipei, 110301, Taiwan
[n] Department of Otolaryngology, Taipei Medical University-Shuang Ho Hospital, No. 291, Zhongzheng Rd., Zhonghe District, New Taipei City, 235041, Taiwan

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ABSTRACT

Exposure to particulate matter (PM) may be a risk factor for obstructive sleep apnea (OSA) and obesity. However, whether body fat accumulation exerts mediating effects on the association between air pollutant exposure and OSA aggravation remains unclear.

This study retroactively acquired the polysomnographic data (sleep variables) and body composition information from 2893 patients in a northern Taiwan sleep center. The levels of exposure to various air pollutants were estimated using an adjusted method based on data from governmental air quality monitoring stations near registered residential addresses instead of only referencing the nearest station. The sleep disorder indices and body fat metrics, which served as the outcomes of interest, were transformed using the Box-Cox transformation. Multiple linear regression models and causal mediation analysis were employed to investigate the associations between the analyzed parameters and the estimated air pollutant exposure at various time scales (1-, 6-, and 12-month).

Significant associations were observed between the increased interquartile range (IQR) of short-term (1-month) exposure to $PM \leq 10 \ \mu m$ (PM_{10}), $PM \leq 2.5 \ \mu m$ ($PM_{2.5}$), and the apnea–hypopnea index (AHI), oxygen desaturation index (ODI), and arousal index (ArI). Short-term (1-month) exposure to PM_{10} and $PM_{2.5}$ was significantly associated with increased trunk fat percentage. Causal mediation analysis revealed that short-term (1-month) exposure to PM_{10} and $PM_{2.5}$ affected trunk fat percentage, thereby partially meditating the elevations in AHI, ODI, and ArI.

PM exposure may directly increase sleep disorder indices and alter body fat, thereby mediating the worsening of OSA manifestations (i.e., increased AHI, ODI, and ArI).

1. Introduction

Obstructive sleep apnea (OSA) is a sleep disorder characterized by the repetitive blocking of the upper respiratory tract partially (hypopnea) or completely (apnea) during sleep, which results in restricted air flow and reduced oxygen delivery (Stansbury and Strollo, 2015). OSA globally affects an estimated 1 billion people between the ages of 30 and 65 years, making it a major health concern worldwide (Benjafield et al., 2019). The prevalence of OSA was reported to be 26% from 1990 to 2012 in the United States (Peppard et al., 2013). A systemic review reported an average prevalence of 7% in Asia, with a wide range of prevalence rates between 3.7% and 97.3%, which were obtained using different data sets (Mirrakhimov et al., 2013). Regarding gender differences, a study conducted in Switzerland reported a prevalence of moderate-to-severe OSA of 23.4% in women and 49.7% in men between 2009 and 2013 (Heinzer et al., 2015). OSA may be related to anatomical structural abnormalities (Lee et al., 2012), and body fat accumulation may further aggravate its prevalence (Gottlieb and Punjabi, 2020). The association between air pollution and OSA has been studied, but the results vary across different countries, seasons, and temperatures (Clark et al., 2020). Therefore, robust and consistent evidence of the association between OSA and particulate pollution is lacking, and it is unclear on whether exposure to such pollutants has synergistic effects that lead to increased sleep disorder indices, which in turn aggravate OSA manifestations. Further research is therefore required to investigate this association and to reduce the increasing prevalence.

OSA severity is evaluated through polysomnography (PSG), which is the gold standard for measuring various physiological signals to quantify sleep disorder indices, such as the apnea–hypopnea index (AHI), oxygen desaturation index (ODI), and arousal index (ArI) (Rundo and Downey, 2019). Studies have investigated the associations between sleep disorder indices measured through PSG, anthropometric data, and air pollution data. For instance, obese patients, whose body mass index (BMI) ranged between 30 and 39.9 kg/m^2, had higher mean values of AHI and ODI (AHI: 28.5 ± 1.22 events/h; ODI: 32.1 ± 1.20 events/h) than did normal weight patients (BMI: <25 kg/m^2; AHI: 14.3 ± 1.40 events/h; ODI: 15.8 ± 1.40 events/h) (Ernst et al., 2016). Specifically, a significant correlation was found between body fat level and AHI (r = 0.65), and abdominal fat level was reported to be a selection marker for differentiating OSA patients from healthy individuals (p < 0.001) (Pinto et al., 2011). A study reported that annual exposure to particulate matter (PM) affected sleep apnea; that is, a 5-μg/m^3 increase in exposure to PM with a diameter of ≤ 2.5 μm ($PM_{2.5}$) was associated with a 60% higher odds ratio (OR) of moderate-to-severe OSA, which is defined as an AHI score of ≥ 15 events/h (95% confidence interval [CI]: 0.98, 2.62) (Billings et al., 2019). Another study analyzed the impact of air pollutant exposure in bedroom environments and demonstrated that 1-year mean exposure to PM with a diameter of ≤ 10 μm (PM_{10}, 16.86 μg/m^3) was significantly associated with increased AHI (p = 0.021) (Lappharat et al., 2018). Thus, both obesity and PM exposure may independently exacerbate OSA manifestations in terms of increased AHI and ODI.

PM exposure may be associated with body fat formation or accumulation and, therefore, with further increases in sleep disorder indices. Analyses of fixed exposure increments indicated that a 10-μg/m^3 increase in exposure to both $PM_{2.5}$ and PM_{10} (OR: 1.04, 95% CI: 1.01, 1.06) was associated with an increased risk of being overweight for people who had been living in the study areas for more than 5 years (Yang et al., 2019). A UK Biobank–based study analyzed the data of approximately 500,000 participants aged 40–69 years to investigate the relationship between the annual averaged PM exposure and various

body fat measures. The results of that study revealed that exposure to $PM_{2.5}$ and PM_{10} was associated with increased BMI, waist-to-hip ratio, and body fat percentage, either at enrollment or during long-term follow-up (median follow-up time: 4.4 years) (Furlong and Klimentidis, 2020). An animal study discovered that exposure to fine PM may induce adipose tissue inflammation and the redistribution of visceral adiposity (Marchini et al., 2020). Another study suggested that PM upregulates the expression of genes involved in lipid-droplet formation, lipogenesis, and adipocyte differentiation (Mendez et al., 2013). Consequently, interactions between PM and body fat percentage may occur. However, the underlying mechanisms or mediating effects between OSA, body fat distribution, and particulate pollutant exposure require further clarification.

The present retrospective study explored the associations between particulate pollutant exposure, body fat percentage, and sleep disorder indices. Moreover, the present study examined the mediating effects of body fat percentage on the association between PM exposure and OSA severity.

2. Materials and methods

2.1. Ethics approval

The Taipei Medical University–Joint Institutional Review Board reviewed and approved the protocol of the current study (TMU–JIRB: N202212067). All the procedures concerning data retrospection and determination, individual detail deidentification, statistical analysis, and subsequent data storage or maintenance were conducted per the approved protocol.

2.2. Retrospective collection of data and patient enrollment

The current study retrospectively collected data from an established sleep database in northern Taiwan (Taipei Medical University-Shuang Ho Hospital, New Taipei City, Taiwan). This sleep database contains sleep parameters measured using PSG for participants who underwent a PSG examination between July 2019 and February 2022. Data of participants who met the following criteria were included in further statistical examinations: (1) had an age between 18 and 80 years, (2) completed a full PSG examination (total recording time lasting more than 6 h), (3) had not received prior medical treatment for OSA (i.e., upper airway surgery or use of noninvasive devices), as determined at the time of performing the PSG, (4) did not regularly use hypnotics or psychotropics, and (5) did not have a diagnosis of central nervous system (e.g., stroke, epilepsy, or brain tumor) or lung (e.g., chronic obstructive pulmonary disease or lung cancer) disease. The baseline demographic characteristics of the eligible individuals were then extracted (i.e., age, sex, surgery history, and medication use) from clinical records, and their residential address and anthropometric data (i.e., BMI, neck and waist size, and body composition variables) were acquired. All the retrieved data were employed for subsequent statistical examinations.

2.3. Anthropometric data measurement

Because anthropometric data were routinely determined before PSG, the current study accessed anthropometric data from the abovementioned sleep database. Specifically, we acquired data on waist and neck size quantified using a tape measure and data on body composition quantified using the Tanita MC-780 system (Tanita, Tokyo, Japan). All

individuals were required to fast for at least 3 h and urinate to evacuate the bladder before undergoing anthropometric measurements. Thereafter, certified PSG technologists directed the participants to stand still and measured the size of their neck and waist. Subsequently, they were instructed to stand straight shoulder width apart on the platform of the bioelectrical impedance measurement machine and grip the metal induction handles with both arms placed down on the sides of the thighs. After approximately 15 s of measurement, the body weight and information regarding body composition (i.e., fat, muscle, and bone mass and water content in total body and in local areas such as trunk and arms) were automatically obtained. To obtain more detailed data on body fat, we determined the total body fat percentage and the body fat distribution in areas including the trunk (trunk fat percentage, which was estimated as the fat mass in trunk divided by the limb weight) and limbs (limb fat percentage, which was estimated as the fat mass in limbs divided by the limb weight); these parameters represented the overall percentage of body fat accumulation or the body fat accumulation in specific areas.

2.4. Sleep variables in polysomnography

The retrospective study was conducted using the data obtained from a sleep center. The sleep center used three types of laboratory-based PSG equipment for data collection, namely Embla N7000 (ResMed, San Diego, CA, USA), Embletta MPR (Natus Medical, Pleasanton, CA, USA), and Nox-A1 (Nox Medical, Alpharetta, GA, USA). Regarding the PSG scoring software, two types of scoring interfaces were employed according to the type of hardware device, namely RemLogic software (version 3.41; Embla Systems, Thornton, CO, USA) and the Noxturnal system (version 6.2.2; Nox Medical). Regarding their routine scoring procedures, licensed PSG technologists first scored the data (to determine sleep stage and sleep event) according to the manual published by the American Academy of Sleep Medicine in 2017 (Berry et al., 2017). Subsequently, to prevent bias or scoring unreliability caused by different scorers, an independent technologist reviewed the scoring outcomes separately, and the inconsistencies were extracted for further discussion to reach an agreement. Several sleep variables from the database were analyzed; two types of respiratory events were primarily examined: apnea (scored based on a ≥90% oronasal signal decline measured using a thermistor) and hypopnea (scored based on a ≥30% nasal signal decline measured using a nasal cannula and combined with at least a 3% reduction in oxygen desaturation or arousal occurrence). Arousal, another sleep variable included in the database, was also incorporated into this study, which was scored based on changes in the electroencephalography signal preceded by at least 10 s of stable sleep. The duration of arousal events was at least 3 s, and these events exhibited high-frequency patterns, including alpha waves (8–12 Hz), theta waves (4–8 Hz), and other high-frequency wave patterns, but not sleep spindles (>16 Hz). Notably, the sleep disorder indices included in the analysis, namely AHI, ODI, and ArI, were automatically computed by the software program by dividing the number of events by the corresponding total sleep time. Based on the AHI values, OSA severity was classified into four levels, namely normal (AHI <5 events/h), mild (AHI between 5 and 15 events/h), moderate (AHI between 15 and 30 events/h), and severe (AHI ≥30 events/h) (Quan et al., 1999).

2.5. Estimation of air pollutant exposure levels

According to the air quality data monitored by the Taiwan Environmental Protection Administration, this study estimated the air pollutant exposure levels based on the participants' residential address. Specifically, this study determined hourly data on background atmospheric information (temperature and humidity) and the level of various air pollutants from the monitoring stations in northern Taiwan, subsidized and organized by the governmental agency. To estimate the exposure levels, this study referenced a previously proposed approach,

whereby exposure estimates are only based on the data of the nearest station, and proposed an adjusted approach (He et al., 2022). Fig. S1 presents the principle of the adjusted approach used in this study, which involves weighted estimation using data obtained from nearby air pollution monitoring stations. In brief, stations located within a maximum distance of 3 km from the residential address of the participants were selected as nearby stations. Next, weights were assigned to the selected stations according to the distances between the stations and the participants' residences, and the weighted average of daily exposure levels was subsequently computed. Fig. S2 illustrates a comparison of outcomes of both PM_{10} and $PM_{2.5}$ obtained using these two estimation methods, namely the nearest station estimation method and the method in which data from nearby stations were referenced. Regarding air pollutant categories, the data on PM_{10}, $PM_{2.5}$, carbon oxide (CO), neutral oxide (NO), NO_2, sulfur dioxide (SO_2), and O_3 were acquired, and all data are presented as the medians with the IQRs. All the estimated data on an individual's exposure to air pollutants were determined from the date of PSG examination, and the exposure data were retrospectively enrolled in various time scales, namely short-term (1-month), medium-term (6-month), and long-term (12-month).

2.6. Statistical analysis

All statistical analyses, including regression and causal mediation analyses, were conducted using SPSS (version 20.0; IBM, Armonk, NY, USA), and the level of significance was set as $p < 0.05$. First, multiple linear regression models were employed to examine the associations between exposure to fine particles, sleep disorder indices, and body fat metrics, including total body fat, trunk fat percentage, and limb fat percentage (which are indicative of the overall degree of obesity and the spatial distribution of fat within the body). Various covariates including age, sex, BMI, and other gaseous pollutants were adjusted for in the models. Additional linear regression analyses were conducted to explore the associations between fine particle exposure and sleep disorder indices while considering the effects of body fat metrics. These analyses were adjusted for covariates including age, sex, BMI, other gaseous pollutants, and body fat metrics. Box–Cox transformation was applied to analyze the results for sleep disorder indices and body fat metrics from the regression models (Gurka et al., 2005). This transformation was implemented to meet the distribution requirements and satisfy the assumptions of the linear regression models. Next, a mediation analysis was performed to investigate the mediating effects of body fat percentage on the association between PM exposure and sleep disorder indices. More precisely, the indices for body fat distribution at specific sites (i.e., trunk fat percentage) were used as intermediary variables, and multiple linear regression was conducted to investigate the association between PM exposure and sleep disorder indices. In other words, four associations between independent variables (i.e., fine particles), intervening variables (i.e., body fat accumulation), and dependent variables (i.e., AHI, ODI, and ArI) were determined separately (Paths A, B, C, and C*). Specifically, Path A focused on the relationship between fine particle exposure and trunk fat percentage, with adjustments for age, sex, BMI, temperature, relative humidity, and gaseous pollutants; Path B focused on the relationships between trunk fat percentage and sleep disorder indices, with adjustments for age, sex, and BMI; and Path C focused on the relationships between fine particle exposure and sleep disorder indices (total effect), with adjustments for age, sex, BMI, temperature, relative humidity, and gaseous pollutant exposure. Path C* focused on the relationships between fine particle exposure and sleep disorder indices (including mediating effects), with adjustments for age, sex, BMI, temperature, relative humidity, and gaseous pollutant exposure. Next, the mediation proportions were determined (Nevo et al., 2017). In supplementary analyses, the participants were classified into two groups: those without and with OSA. Next, multivariable logistic regression models were used to examine the ORs between fine particle exposure and the risk of having OSA (AHI ≥5 events/h) between these

Table 1
Demographics, body profiles, and sleep parameters from the polysomnography data of the study population ($N = 2873$).

Categorical variable	N/Mean	%/SD
Age (years)	47.61	13.23
Sex (n, %)		
Male/female	1896/977	65.99/34.01
Body profile		
BMI (kg/m^2)	26.76	4.84
Body fat percentage (%)	28.62	8.78
Muscle percentage (%)	17.8	4.57
Body water percentage (%)	49.74	5.58
Bone mass percentage (%)	3.84	0.38
Visceral fat level (score)	11.68	4.86
Body fat distribution (%)		
Trunk fat percentage	30.26	9.54
Limb fat percentage	26.75	8.33
Sleep disorder index (events/h)		
ODI	24.48	24.22
AHI	30.15	24.18
ArI	21.38	14.55
OSA severity (n, %)		
Normal	292	10.17
Mild	656	22.83
Moderate	774	26.94
Severe	1151	40.06

Abbreviations: *SD*, standard deviation; BMI, body mass index; ODI, oxygen desaturation index; AHI, apnea–hypopnea index; ArI, arousal index; OSA, obstructive sleep apnea.
Note: Trunk fat percentage = trunk fat mass (kg)/trunk weight (kg); limb fat percentage = limb fat mass (kg)/limb weight (kg).
Note: ODI: Cumulative frequency of desaturation episodes ($\geq$3%) occurring per hour.

two groups. The present study employed IQR alteration as an indicator of individual pollutant exposure to investigate the effects of PM exposure on sleep parameters. In this model, the non-normality of PM data was considered to avoid the interference of extreme values (Bose et al., 2019).

3. Results

3.1. Basic characteristics and sleep parameters of the study population

Table 1 provides a summary of the demographics and sleep parameters of the recruited participants. The total sample size was 2873. Additionally, Table S1 presents the parameters categorized for

Table 2
Participants' exposure levels to air pollutants and background atmospheric information.

Categorical variable	Median (IQR)		
	Short term (1 month)	Medium term (6 months)	Long term (12 months)
Air pollutant			
PM$_{10}$ (μg/m^3)	23.41 (3.45)	23.85 (2.31)	24.77 (1.7)
PM$_{2.5}$ (μg/m^3)	12.36 (2.45)	12.41 (1.49)	12.92 (0.63)
NO$_2$ (ppb)	14.47 (2.21)	14.41 (1.6)	15.06 (1.11)
SO$_2$ (ppb)	1.84 (0.27)	1.86 (0.22)	1.92 (0.21)
O$_3$ (ppb)	28.57 (4.06)	28.5 (1.31)	28.9 (0.6)
Background			
Ambient temperature (°C)	23.61 (4.65)	24.25 (3.03)	24.08 (0.32)
Relative humidity (%)	73.49 (4.72)	73.05 (2.59)	72.92 (1.52)

Abbreviations: IQR, interquartile range; PM$_{10}$, particulate matter with an aerodynamic diameter of $\leq$10 μm; PM$_{2.5}$, particulate matter with an aerodynamic diameter of $\leq$2.5 μm; NO$_2$, nitrogen dioxide; SO$_2$, sulfur dioxide; O$_3$, ozone.
Date are expressed as median (interquartile range).

Table 3
Associations between sleep disorder indices and interquartile range (IQR) alterations for short-, medium-, and long-term exposure to fine particles.

Variable	Beta coefficient (95% confidence interval)		
	Short term (1 month)	Medium term (6 months)	Long term (12 months)
AHI (X$^{events/h}$)			
PM$_{10}$ (μg/m^3)	0.33 (0.23–0.44) **	−0.04 (−0.14 to 0.05)	−0.08 (−0.3 to 0.13)
PM$_{2.5}$ (μg/m^3)	0.54 (0.41–0.67) **	−0.06 (−0.17 to 0.05)	−0.07 (−0.27 to 0.13)
ODI (X$^{events/h}$)			
PM$_{10}$ (μg/m^3)	0.34 (0.23–0.45) **	−0.05 (−0.15 to 0.05)	−0.11 (−0.34 to 0.11)
PM$_{2.5}$ (μg/m^3)	0.58 (0.44–0.71) **	−0.08 (−0.2 to 0.03)	−0.15 (−0.36 to 0.07)
ArI (X$^{events/h}$)			
PM$_{10}$ (μg/m^3)	0.12 (0.06–0.17) **	−0.01 (−0.06 to 0.04)	0.01 (−0.1 to 0.12)
PM$_{2.5}$ (μg/m^3)	0.15 (0.07–0.21) **	−0.01 (−0.06 to 0.05)	−0.02 (−0.13 to 0.09)

Abbreviations: AHI, apnea–hypopnea index; ODI, oxygen desaturation index; ArI, arousal index; PM$_{10}$, particulate matter with an aerodynamic diameter of $\leq$10 μm; PM$_{2.5}$, particulate matter with an aerodynamic diameter of $\leq$2.5 μm.
Note: Multivariable linear regression models were adjusted for age, sex, body mass index, temperature, relative humidity, and exposure to gaseous pollutants, including nitrogen dioxide, sulfur dioxide, and ozone.
Note: The unit of outcome (i.e., sleep disorder indices) was subjected to Box-Cox transformation.
Note: The IQRs were 3.45 μg/m^3 for PM$_{10}$ and 2.45 μg/m^3 for PM$_{2.5}$.
**p < 0.01.

Table 4
Associations between body fat and interquartile range (IQR) alterations for short-, medium-, and long-term exposure to fine particles.

Variable	Beta coefficient (95% confidence interval)		
	Short term (1 month)	Medium term (6 months)	Long term (12 months)
Body fat percent ($X^{[\%]}$)			
PM$_{10}$ (µg/m^3)	0.02 (−0.01 to 0.05)	−0.02 (−0.04 to 0.01)	0.01 (−0.04 to 0.07)
PM$_{2.5}$ (µg/m^3)	0.02 (−0.01 to 0.06)	−0.01 (−0.04 to 0.03)	0.01 (−0.04 to 0.07)
Trunk fat percent ($X^{[\%]}$)			
PM$_{10}$ (µg/m^3)	0.06 (0.01–0.11) *	−0.03 (−0.08 to 0.02)	0.02 (−0.09 to 0.13)
PM$_{2.5}$ (µg/m^3)	0.07 (0.01–0.13) *	−0.01 (−0.07 to 0.05)	0.03 (−0.08 to 0.14)
Limb fat percent ($X^{[\%]}$)			
PM$_{10}$ (µg/m^3)	0.01 (−0.01 to 0.03)	−0.01 (−0.02 to 0.0)	0.01 (−0.02 to 0.04)
PM$_{2.5}$ (µg/m^3)	0.01 (−0.02 to 0.01)	−0.0 (−0.02 to 0.01)	0.0 (−0.02 to 0.03)

Abbreviations: PM$_{10}$, particulate matter with an aerodynamic diameter of ≤10 µm; PM$_{2.5}$, particulate matter with an aerodynamic diameter of ≤2.5 µm.
Note: Multivariable linear regression models were adjusted for age, sex, body mass index, temperature, relative humidity, and exposure to gaseous pollutants, including nitrogen dioxide, sulfur dioxide, and ozone.
Note: The unit of outcome (i.e., body fat details) was subjected to Box–Cox transformation.
Note: The IQRs were 3.45 µg/m^3 for PM$_{10}$ and 2.45 µg/m^3 for PM$_{2.5}$.
*p < 0.05.

Table 5
Associations between sleep disorder indices and interquartile range (IQR) alterations for short-term exposure to fine particles while considering effects of trunk fat.

Variable	Beta coefficient (95% confidence interval)
AHI ($X^{[events/h]}$)	
PM$_{10}$ (µg/m^3)	0.32 (0.23–0.43) **
PM$_{2.5}$ (µg/m^3)	0.53 (0.41–0.67) **
ODI ($X^{[events/h]}$)	
PM$_{10}$ (µg/m^3)	0.33 (0.23–0.45) **
PM$_{2.5}$ (µg/m^3)	0.57 (0.44–0.71) **
ArI ($X^{[events/h]}$)	
PM$_{10}$ (µg/m^3)	0.11 (0.06–0.17) **
PM$_{2.5}$ (µg/m^3)	0.14 (0.07–0.21) **

Abbreviations: AHI, apnea–hypopnea index; ODI, oxygen desaturation index; ArI, arousal index; PM$_{10}$, particulate matter with an aerodynamic diameter of ≤10 µm; PM$_{2.5}$, particulate matter with an aerodynamic diameter of ≤2.5 µm.
Note: Multivariable linear regression models were adjusted for age, sex, body mass index, trunk fat percentage, temperature, relative humidity, and exposure to gaseous pollutants, including nitrogen dioxide, sulfur dioxide, and ozone.
Note: The unit of outcome (i.e., sleep disorder indices) was subjected to Box–Cox transformation.
Note: The IQRs were 3.45 µg/m^3 for PM$_{10}$ and 2.45 µg/m^3 for PM$_{2.5}$.
**p < 0.01.

participants without OSA (N = 285) and those with OSA (N = 2588). The mean age of the participants was 47.61 years, and 65.99% of them were male. In terms of body composition measures, their mean BMI value was 26.76 kg/m^2, and their percentages of body fat, muscle, water, and bone mass were 28.62%, 17.8%, 49.47%, and 3.84%, respectively. In terms of body fat distribution, the mean trunk fat percentage of the participants was 30.26%, and the limb fat percentage was 26.75%. Regarding the distribution of OSA severity, 292 (10.17%) participants had normal breathing, 656 (22.83%) had mild OSA, 774 (26.94%) had moderate OSA, and 1151 (40.06%) had severe OSA. In terms of PSG variables, among participants, the mean ODI was 24.48 ± 24.22 events/h, mean AHI was 30.15 ± 24.18 events/h, and mean ArI was 21.38 ± 14.55 events/h.

3.2. Levels of exposure to air pollutants among recruited participants

Table 2 provides a summary of the levels of exposure to various air pollutants among the enrolled participants and the relevant background atmospheric information. The pollutant exposure data were estimated through back-extrapolation from the time of participant enrollment into this study. The short-term IQRs for PM$_{10}$ and PM$_{2.5}$ were 3.45 and 2.45 µg/m^3, respectively. The medium-term IQRs for PM$_{10}$ and PM$_{2.5}$ were 2.31 µg/m^3 and 1.49 µg/m^3, respectively. Lastly, the long-term IQRs for PM$_{10}$ and PM$_{2.5}$ were 1.7 µg/m^3 and 0.63 µg/m^3, respectively.

3.3. Associations between fine particle exposure, sleep disorder indices, and body fat profiles

Table 3 presents the associations between sleep disorder indices (after Box–Cox transformation) and fine particle exposure across multiple time scales, with adjustment for age, sex, BMI, and exposure to various gaseous pollutants. A 1-unit increase in the short-term IQRs of PM$_{10}$ exposure was positively associated with a 0.33-unit increase in AHI (95% CI: 0.23, 0.44 units, p < 0.01), a 0.34-unit increase in ODI (95% CI: 0.23, 0.45 units, p < 0.01), and a 0.12-unit increase in ArI (95% CI: 0.06, 0.17 units, p < 0.01). Similarly, a 1-unit increase in the short-term IQRs of PM$_{2.5}$ exposure was associated with a 0.54-unit increase in AHI (95% CI: 0.41, 0.67 units, p < 0.01), a 0.58-unit increase in ODI (95% CI: 0.44, 0.71 units, p < 0.01), and a 0.15-unit increase in ArI (95% CI: 0.07, 0.21 units, p < 0.01). The associations between exposure to particulate pollutants and body fat profiles (after Box–Cox transformation) are presented in Table 4. A 1-unit increase in the IQR of
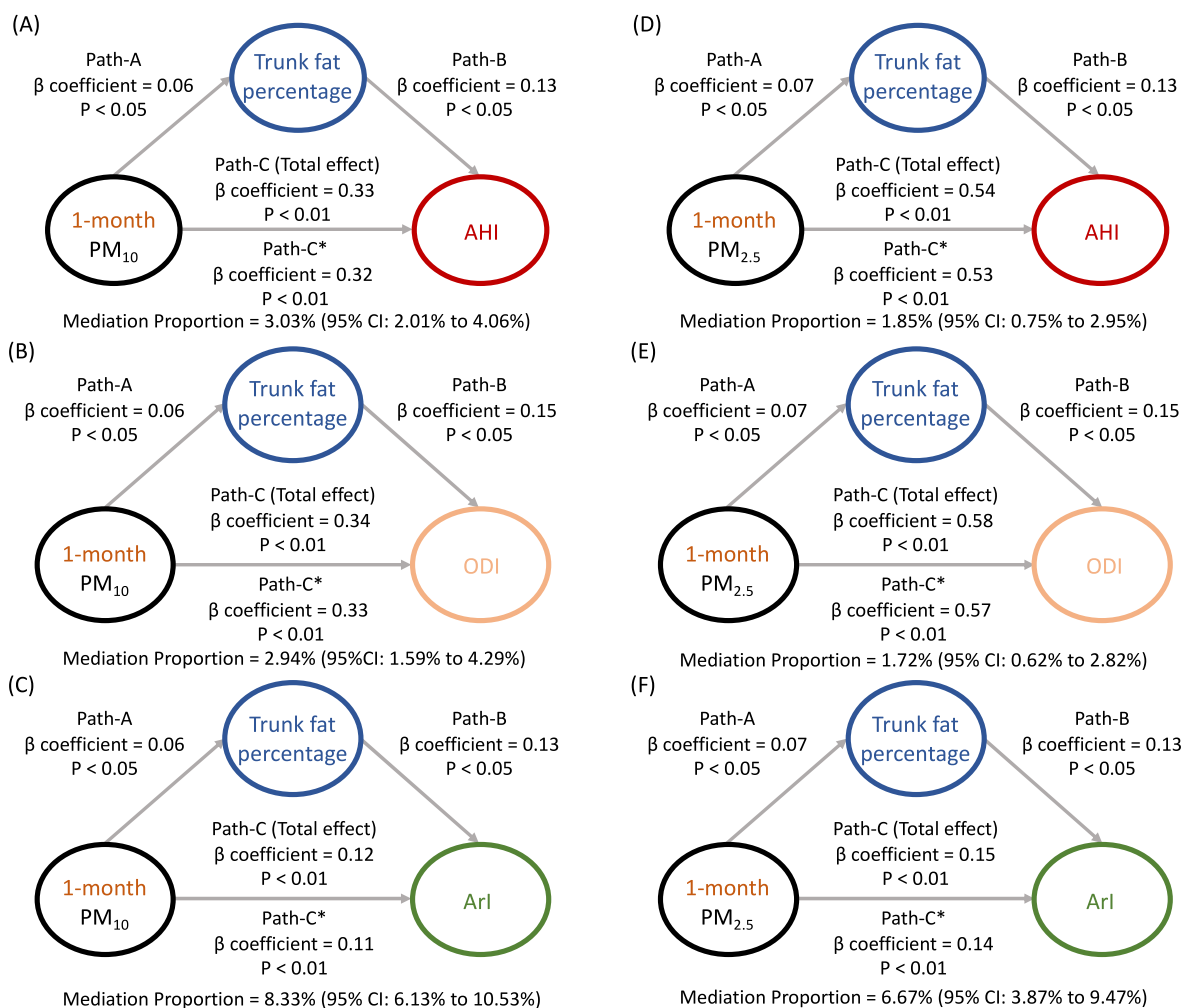
Fig. 1. Causal mediation analysis revealing association between short-term exposure to fine particles and sleep disorder indices, with trunk fat percentage being a partial mediator

Abbreviations: AHI, apnea–hypopnea index; ODI, oxygen desaturation index; ArI, arousal index; PM_{10}, particulate matter with an aerodynamic diameter of ≤ 10 µm; $PM_{2.5}$, particulate matter with an aerodynamic diameter of ≤ 2.5 µm; CI, confidence interval.

Note: Path-A, effect of exposure on mediator with adjustments for age, sex, body mass index, temperature, relative humidity, and exposure to gaseous pollutants, including nitrogen dioxide, sulfur dioxide, and ozone; Path-B, effect of mediator on outcome with adjustments for age, sex, and body mass index; Path-C, effect of exposure on outcome (total effect) without accounting for mediation and after adjusting for age, sex, body mass index, temperature, relative humidity, and exposure to gaseous pollutants, including nitrogen dioxide, sulfur dioxide, and ozone; and Path-C*, effect of exposure on outcome after considering mediating effects and adjusting for factors such as age, sex, body mass index, temperature, relative humidity, and exposure to gaseous pollutants, including nitrogen dioxide, sulfur dioxide, and ozone.

short-term exposure to PM_{10} was significantly associated with a 0.06-unit increase in trunk fat percentage (95% CI: 0.01, 0.11 units, $p < 0.05$) after adjustment for age, sex, BMI, and gaseous pollutants. Additionally, significant associations were observed between the IQR of short-term exposure to $PM_{2.5}$ and trunk fat percentage (0.07 units, 95% CI: 0.01, 0.13 units, $p < 0.05$).

3.4. Associations between fine particle exposure and sleep disorder indices stratified by body fat profile (effects of body fat metrics)

Because significant associations were observed between short-term PM exposure, sleep disorder indices, and trunk fat percentage, the associations between PM exposure and sleep disorder indices (after Box–Cox transformation) were investigated while considering the effect of trunk fat percentage; the results are summarized in Table 5. A 1-unit increase in the IQRs of PM_{10} exposure was positively associated with a 0.32-unit increase in AHI (95% CI: 0.23, 0.43 units, $p < 0.01$), a 0.33-unit increase in ODI (95% CI: 0.23, 0.45 units, $p < 0.01$), and a 0.11-unit increase in ArI (95% CI: 0.06, 0.17 units, $p < 0.01$). Similarly, a

1-unit increase in the short-term IQRs of $PM_{2.5}$ was associated with a 0.53-unit increase in AHI (95% CI: 0.41, 0.67 units, $p < 0.01$), a 0.57-unit increase in ODI (95% CI: 0.44, 0.71 units, $p < 0.01$), and a 0.14-unit increase in ArI (95% CI: 0.07, 0.21 units, $p < 0.01$).

3.5. Causal relationships between short-term fine particle exposure, trunk fat percentage, and sleep disorder indices

In the present study, a mediation analysis of the causal relationships between sleep disorder indices, trunk fat percentage, and fine particle exposure (i.e., short-term exposure to PM_{10} and $PM_{2.5}$) was conducted. The analysis included exposure to PM_{10} and $PM_{2.5}$ because exposure to these pollutants was significantly and separately associated with sleep disorder indices and trunk fat percentage. Fig. 1 reveals that, after adjustments for age, sex, BMI, temperature, relative humidity, and gaseous pollutants (e.g., nitrogen dioxide, sulfur dioxide, and ozone), 1-month exposure to PM_{10} was significantly associated with elevated trunk fat percentage, which partially mediated increases in AHI (Fig. 1A, total effect: 0.33 units; effect after considering the mediating effect: 0.32

units; mediation proportion: 3.03%; 95% CI: 2.01%, 4.06%), ODI (Fig. 1B, total effect: 0.34 units; effect after considering the mediating effect: 0.33 units; mediation proportion: 2.94%; 95% CI: 1.59%, 4.29%), and ArI (Fig. 1C, total effect: 0.12 units; effect after considering the mediating effect: 0.11 units; mediation proportion: 8.33%; 95% CI: 6.13%, 10.53%). Similarly, 1-month exposure to $PM_{2.5}$ was significantly associated with elevated trunk fat percentage, which partially meditated increases in AHI (Fig. 1D, total effect: 0.54 units; effect after considering the mediating effect: 0.53 units; mediation proportion: 1.85%; 95% CI: 0.75%, 2.95%), ODI (Fig. 1E, total effect: 0.58 units; effect after considering the mediating effect: 0.57 units; mediation proportion: 1.72% 95% CI: 0.62%, 2.82%), and ArI (Fig. 1F, total effect: 0.15 units; effect after considering the mediating effect: 0.14 units; mediation proportion: 6.67%; 95% CI: 3.87%, 9.47%).

3.6. Associations between fine particle exposure and OSA

This study further investigated the ORs for the association between the risk of OSA (AHI ≥5 events/h) and exposure to particulate pollutants; the results are presented in Table S2. An increased IQR of short-term exposure to PM_{10} and $PM_{2.5}$ was associated with an elevated risk of OSA (PM_{10}: OR: 1.61, 95% CI: 1.17, 2.22, $p < 0.01$; $PM_{2.5}$: OR: 1.62, 95% CI: 1.16, 2.23, $p < 0.01$). The results obtained from logistic regression indicate that increased short-term exposure to fine particles increases the risk of OSA.

4. Discussion

Robust evidence on the association between particulate pollutant exposure and increased sleep disorder indices is lacking. Therefore, whether PM exposure mediates the association between body fat formation and OSA severity must be investigated. Thus, the present retrospective study retrieved the PSG data and anthropometric data of participants, and their levels of exposure to particulate pollutants was estimated; the associations and mediating effects between body fat formation and OSA severity were analyzed. Short-term (1-month) exposure to PM_{10} and $PM_{2.5}$ was significantly associated with OSA severity aggravation (increased AHI, ODI, and ArI) and positively associated with trunk fat accumulation. In addition, short-term exposure to PM_{10} and $PM_{2.5}$ may be associated with an elevated risk of OSA. Regarding the presence of a mediating effect, the results suggest that short-term exposure to PM had a mediating effect on trunk fat accumulation, which in turn partially aggravated OSA manifestations by increasing AHI, ODI, and ArI scores.

This study estimated the median annual exposure to $PM_{2.5}$ as 12.92 µg/m^3 (IQR: 0.63 µg/m^3) and that to PM_{10} as 24.77 µg/m^3 (IQR: 1.7 µg/m^3). Compared with the suggested mean annual exposure to $PM_{2.5}$ (5 µg/m^3) and PM_{10} (15 µg/m^3) in the 2021 air quality guidelines proposed by the World Health Organization (Salud, 2021), the levels of exposure to these two types of fine PM in the current study were higher. Thus, the current estimations of levels of exposure to PMs in northern Taiwan were higher than the value recommended by the air quality guidelines, which suggests that air pollution levels in Taipei metropolitan area may be detrimental to individuals' health. Next, the current study used an adjusted approach in which the data from nearby stations, while setting a maximum distance of the stations from the participants' residence, were referenced rather than only considering measurements from the nearest station as a unitary data source. The supplementary material indicates that the approach of considering data from multiple stations provides a more accurate approximation of the actual data compared with the method that solely relies on measurements from the nearest station as a single data source. Moreover, this approach improves the reliability of the data by mitigating potential inaccuracies in estimation that may arise from relying solely on a single data source (e.g., the nearest station may still be considerably far and may lead to unreliable assessments).

The present study discovered that short-term exposure to both PM_{10} and $PM_{2.5}$ was significantly associated with increases in AHI and ODI, which aligns with the findings of other studies. For example, a study analyzed the data collected from approximately 25,000 participants and examined the relationships between particulate pollution and the score on a subjective sleep quality index that is a valid screening instrument for OSA (Wang et al., 2022). Their results indicated that individuals with higher scores had higher monthly exposure levels to both PM_{10} and $PM_{2.5}$ compared with those with lower scores. Another study explored the relationships between PSG parameters and average PM_{10} exposure levels during winter (December and January) and summer (June and July) periods (Yıldız Gülhan et al., 2020). Those findings indicated higher AHI values during winter months, which corresponded to higher levels of PM10, compared to the summer months. Several plausible underlying mechanisms may explain these relationships. First, short-term exposure to PM can trigger inflammatory responses in the airway, which may cause airway constriction (Ghorani-Azam et al., 2016; Schaumann et al., 2004). Short-term PM exposure can also activate signaling pathways that result in the hypersecretion of mucus in the airway, and this reaction may be associated with increased airway resistance (Liu et al., 2020). Additionally, short-term PM exposure may be associated with lower respiratory infections and may directly contribute to unstable bronchial physiology (Zhuang et al., 2021). These reactions may partially contribute to the increased risk of worsening OSA. PM accumulation in the respiratory tract is also associated with oxidative stress and active oxidative responses, which may partially increase the risk of nocturnal hypoxia (Ren et al., 2020; Zhao et al., 2016). The aforementioned physiological responses in the respiratory system may lead to respiratory tract instability, which can exacerbate OSA manifestations (e.g., elevated AHI, ODI, and ArI) and further impair sleep quality. However, because these studies did not directly examine PM exposure, more comprehensive studies are required to validate the causal relationship between short-term exposure to fine particles and its adverse effects on the respiratory system and, consequently, sleep quality. Thus, further investigation is warranted to clarify the relationships between PM exposure, increases in sleep disorder indices, and the pathobiological mechanisms or reactions resulting from the exposure of the respiratory system to PM.

The findings of the present study indicated that short-term exposure to both PM_{10} and $PM_{2.5}$ was significantly associated with an increased ArI, suggesting that PM stimulates the sleep arousal response by influencing the central nervous system. More precisely, short-term exposure to PM may cause damage to neurons, thereby affecting the central nervous system (Song et al., 2022). A systematic review indicated that elevations in short-term (hours to days) exposure to PM may induce unstable hemodynamics in the brain (Wang et al., 2014). An animal study revealed that short-term exposure (1–3 months) to PM may lead to the accumulation of metal and inflammatory biomarkers in the rat brain (Ljubimova et al., 2018). Another animal study suggested that after short-term exposure to PM (4–24 h), PM can indirectly reach the central nervous system through the peripheral system, ultimately crossing the blood–brain barrier and affecting its permeability (Sharma et al., 2009). The disruptions in the physiology of the central nervous system may contribute to increased sleep arousal or interrupted sleep cycles. Similarly, another relevant study reported positive associations between short-term exposure (monthly) to fine PM and ArI (Lo et al., 2021), which is consistent with the current findings. Taken together, these results indicate that PM exposure affects the physiology of the central nervous system, thereby increasing the frequency of sleep arousal. However, additional studies must be conducted to confirm the causal relationship between short-term exposure to fine particles and its detrimental impact on the central nervous system, potentially leading to sleep disturbances.

The study findings indicated that short-term exposure to PM was associated with trunk fat accumulation in analyses adjusted for age, sex, BMI, and other gaseous pollutants. A previous study reported that short-

term (monthly) exposure to particulate pollutants can disrupt body fat metabolism by reducing the uptake of free fatty acids (Yang et al., 2021). Another study suggested that short-term exposure to $PM_{2.5}$ (i.e., 30 days) leads to vascular insulin resistance and adipose tissue inflammation, which is triggered by pulmonary oxidative stress (Haberzettl et al., 2016). Another relevant study demonstrated that short-term exposure to ambient $PM_{2.5}$ (a week to month) can affect fasting blood glucose levels and metabolism (Zhan et al., 2021). Furthermore, short-term exposure to particulate pollutants may serve as toxicity stimuli, leading to increased oxidative stress and systemic inflammatory responses in adipose tissue (Xu et al., 2012). The organic components and heavy metals present in PM are additional risk factors that may promote oxidative stress and dysregulate the cell metabolism pathway (Nassan et al., 2021). Taken together, these mechanisms indicate that short-term exposure to fine PM may activate inflammatory responses or induce metabolism dysfunction, ultimately altering body fat accumulation. Nevertheless, the causal effect of short-term exposure to PM on body fat accumulation requires further research.

Regarding the mediating effect, the study findings suggest that short-term exposure to PM exerted mediating effects on trunk fat accumulation, which in turn partially aggravated OSA manifestations, as indicated by the increases in AHI, ODI, and ArI (1.72%–8.33%). To the best of our knowledge, this is the first study to indicate that body fat in the abdominal area can serve as an intermediary variable for assessing the causal relationship between fine particle exposure and sleep disorder indices. Studies have revealed that short-term exposure to PM (2 weeks) can affect glucose metabolism (Chen et al., 2020). Another relevant study found that exposure to high concentrations of $PM_{2.5}$ for approximately 1 week (5 days) was associated with hypothalamic inflammation, increased fat mass accumulation, and elevated food intake, whereas 3-month exposure impaired hypothalamus function by interfering with leptin signaling, resulting in hyperphagia (increased appetite) and decreased energy expenditure (Campolim et al., 2020). These mechanisms may contribute to elevated body fat percentage. Furthermore, trunk fat may directly serve as an indicator for predicting OSA severity (Tsai et al., 2022). Specifically, abdominal fat may aggravate OSA manifestations, such as detrimental intermittent hypoxia, because the presence of excessive adipose tissue in the trunk area may restrict lung volume, place additional strain on ventilatory muscles, and lead to narrowing of the space in the respiratory tract (Ryan et al., 2019). Intermittent hypoxia during sleep may cause dyslipidemia because oxygen desaturation can bidirectionally inhibit lipoprotein clearance (Drager et al., 2010). This may jointly result in trunk fat accumulation, which may partially increase sleep disorder indices. Overall, the current findings indicate that exposure to fine PM may affect trunk fat accumulation, which may increase sleep disorder indices and thereby worsen OSA manifestations.

Across various time scales, the present study identified significant associations between sleep disorder indices (i.e., AHI, ODI, and ArI), trunk fat percentage, and short-term exposure to fine particles; however, these associations were not observed in the medium or long term. This discrepancy in findings across different time scales may be attributed to variations in data distribution. Specifically, the IQRs for PM exposure exhibited a decreasing trend with the increasing time scale, whereas the medians exhibited similar ranges at all examined time scales. Thus, the data on short-term PM exposure exhibited a dispersed distribution, resulting in a higher IQR, whereas the data on long-term PM exposure were concentrated, leading to a lower IQR. Consequently, a significant association between sleep and body fat was observed for short-term exposure, which was characterized by a high IQR, but not for long-term exposure, which was characterized by low IQR values. Other studies have also presented diverse outcomes, emphasizing the need for further research in this area. For example, a study reported that a 1-unit IQR increment in the annual exposure to $PM_{2.5}$ (3.4 μg/m^3) was associated with increased AHI and ODI (Shen et al., 2018). Another recent study reported that an increase in the IQR for annual $PM_{2.5}$ exposure

(3.38 μg/m^3) was associated with a 6.8% increase in ODI in patients with mild OSA (He et al., 2022). By contrast, another study investigated the effects of $PM_{2.5}$ exposure and humidity on the AHI and severity of OSA. Its results indicated that an increased mean exposure to $PM_{2.5}$ (per 1 μg/m^3) was significantly associated with an increased AHI in patients with mild-to-moderate OSA (0.04–0.08 events/h) and in those with severe OSA (0.05–0.08 events/h); these results were observed at various time scales, including 1-day, 1-week, and 1-month mean exposure (Bai et al., 2023). Hence, further studies are required to determine the differences in the effects of short-term and long-term exposure on sleep quality and body fat.

Some limitations of this study should be considered or addressed in future. First, the exposure levels of air pollutants were estimated according to the data from government-subsidized air quality monitoring stations. The estimated levels of air pollutants can only represent the ambient air quality, and indoor exposure can also disturb sleep health and alter body composition, but the latter was not estimated or measured in the present study (Yang et al., 2020). Next, this study adopted the adjusted approach for estimating exposure levels, which aimed to overcome the limitation (i.e., misestimation of outliers if only a single data source is considered) of only using the air quality measurements based on the nearest monitoring station to participant residences. However, this approach does not consider land use information or traffic flow, which can contribute to the levels of particulate pollutant exposure. Other factors, such as socioeconomic status (e.g., occupation type) and other air pollution sources (e.g., secondhand smoke) in the residential environment of individuals, may also affect the levels of particulate pollution exposure (Hoebel et al., 2018). Estimations conducted without considering these factors may provide inaccurate results compared with actual exposure. Moreover, considering the non-normality of air pollution data, the present study employed IQR to investigate the associations of interest, which can mitigate the effects of extreme values in the analysis. With respect to the practical applications based on our current observations, a short-term (1-month) increase in IQR of PM_{10} (3.45 μg/m^3) and $PM_{2.5}$ (2.45 μg/m^3) exposure was significantly associated with increased sleep disorder indices after adjustment for confounding factors such as age, sex, BMI, trunk fat percentage, temperature, relative humidity, and gaseous pollutant exposure. These results suggest that increased PM exposure exacerbated OSA manifestations, as demonstrated by the increased AHI, ODI, and ArI; these findings may serve as evidence for reducing the exposure of the public to such pollutants. However, similar median values were observed across multiple timescales. Under specific conditions, low median values with scattered data points could result in a higher IQR relative to high median values with tightly clustered data points. This finding should be considered in future studies. Thus, additional transformations of data and the incorporation of IQR and derived coefficient values may be necessary to increase the precision of research results in the future. Failure to consider these aspects may limit the generalizability and accessibility of the results of the present study. Regarding the effect of comorbidities, this study did not extract data of those who regularly used hypnotic medications and with central nervous system disorders or pulmonary system illnesses. Cardiovascular or renal diseases may also affect the clinical manifestations (e.g., intermittent hypoxia and sleep fragmentation) or severity of OSA, but these diseases were not considered in the present study (Gildeh et al., 2016). Further, lifestyle habits, including cigarette smoking or alcohol consumption, which may serve as residual confounding factors in estimating air pollution levels and partially cause imprecise or bias in current exposure data, were not collected in this study (do Nascimento et al., 2022; Song et al., 2015). Thus, further studies with more comprehensive data dimensions are warranted to enhance the robustness of the current findings.

5. Conclusion

This study proposed an estimation method that utilized data from stations located near the residences of the study participants. This method yielded higher prediction accuracies (higher R-square values) than the traditional method that solely relies on data from the nearest single station. The estimation of air pollution levels in this study revealed that short-term (1-month) exposure to high concentrations of PM (both PM_{10} and $PM_{2.5}$) was significantly associated with an increased trunk fat percentage and aggravated OSA manifestations, as evidenced by increased AHI, ODI, and ArI. The results of causal mediation analysis suggest that short-term exposure to PM mediates the relationship between air pollution and trunk fat accumulation, thereby increasing AHI, ODI, and ArI scores. Additionally, short-term exposure to both PM_{10} and $PM_{2.5}$ was found to increase the risk of OSA. These findings indicate that reducing exposure to PM may prevent trunk fat accumulation; alleviate OSA manifestations by decreasing AHI, ODI, and ArI; and prevent OSA development.

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Authors' contributions

Cheng-Yu Tsai: Conceptualization, Methodology, Writing – original draft. Huei-Tyng Huang: Formal analysis, Methodology, Writing – original draft. Ming-Liu: Methodology, Writing – original draft. Wun-Hao Cheng: Data curation, Investigation, Validation. Wen-Hua Hsu: Data curation, Investigation, Visualization. Arnab Majumdar: Methodology, Writing – review & editing. Kang-Yun Lee: Funding acquisition, Supervision. Po-Hao Feng: Resources, Validation. Chien-Hua Tseng: Resources. Kuan-Yuan Chen: Resources. Yi-Chun Kuan: Data curation. Jiunn-Horng Kang: Project administration. Hsin-Chien Lee: Resources, Funding acquisition. Cheng-Jung Wu: Resources. Wen-Te Liu: Conceptualization, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.apr.2023.101886.

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