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Review

Association of air pollution with risk and severity of obstructive sleep apnea: A systematic review and meta-analysis

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ABSTRACT

Background: Obstructive Sleep Apnea (OSA) is a significant health concern characterized by recurrent upper airway blockages during sleep, causing various health issues. There's growing evidence of a link between air pollution and OSA, though research results have been inconsistent. This systematic review and meta-analysis aims to consolidate and examine data on the relationship between air pollution and OSA's risk and severity.

Methods: A literature search across PubMed, EMBASE, and Web of Science was conducted until January 10, 2024. The selection criteria targeted studies involving OSA participants or those at risk, with quantitative air pollution assessments. The Nested Knowledge software facilitated screening and data extraction, while the Newcastle-Ottawa Scale was used for quality assessment. Meta-analyses, utilizing random-effects models, computed pooled odds ratios (ORs) for the OSA risk associated with PM2.5 and NO2 exposure, analyzed using R software version 4.3.

Results: The systematic review included twelve studies, four of which were analyzed in the meta-analysis. The meta-analysis revealed diverse results on the association of PM2.5 and NO2 with OSA risk. PM2.5 exposure showed a pooled OR of 0.987 (95 % CI: 0.836–1.138), indicating no substantial overall impact on OSA risk. Conversely, NO2 exposure was linked to a pooled OR of 1.095 (95 % CI: 0.920–1.270), a non-significant increase in risk. Many studies found a relationship between air pollution exposure and elevated Apnea-Hypopnea Index (AHI) levels, indicating a relationship between air pollution and OSA severity.

Conclusion: The findings suggest air pollutants, especially NO2, might play a role in worsening OSA risk and severity, but the evidence isn't definitive. This highlights the variability of different pollutants' effects and the necessity for more research. Understanding these links is vital for shaping public health policies and clinical approaches to address OSA amidst high air pollution.

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1. Introduction

Obstructive Sleep Apnea (OSA) is a common and significant health issue, marked by repeated occurrences of total or partial blockage of the upper airway while sleeping (Qureshi et al., 2003; Bushi et al., 2023a). These obstructions lead to recurrent arousals and significant reductions in blood oxygen saturation. OSA affects a substantial proportion of the global population, contributing to a myriad of health complications, including cardiovascular disease, hypertension, metabolic syndrome, and impaired cognitive function. In recent years, there has been growing interest in the potential environmental determinants of OSA, with air pollution emerging as a significant area of concern (Urbanik et al., 2020).

Air pollution, a complex mixture of particulate matter, gases, and chemical substances is a recognized global health hazard (Mutlu and Peker, 2019). The World Health Organization (WHO) has classified outdoor air pollution as a leading environmental risk factor for mortality, primarily due to its association with cardiovascular and respiratory diseases (Hoek et al., 2013). Urbanization and industrialization have led to increasing levels of air pollution in many parts of the world, heightening the urgency to understand its broader health implications (Manisalidis et al., 2020). The relationship between air pollution and OSA is biologically plausible and supported by emerging evidence. Air pollutants, particularly particulate matter with a diameter of less than 2.5 micrometers (PM2.5), can induce systemic inflammation, oxidative stress, and autonomic imbalance. These pathophysiological changes are known to contribute to the development and exacerbation of respiratory disorders. In the context of OSA, air pollution may aggravate upper airway inflammation and dysfunction, thereby increasing the propensity for airway collapse during sleep (Wang et al., 2022).

Several epidemiological studies have investigated the relationship between air pollution and the risk of OSA (Wang et al., 2022; Billings et al., 2019; Laratta et al., 2017; Qiu et al., 2022). However, the results have been somewhat inconsistent, possibly due to differences in population characteristics, study design and methods of air pollution and OSA assessment. This variability calls for the need for a comprehensive synthesis of the available evidence to ascertain the strength and nature of this association (Tsai et al., 2023). The hypothesized pathways include enhanced upper airway inflammation and edema due to pollutant-induced oxidative stress, heightened neural reflexes leading to airway hyperresponsiveness, and systemic inflammatory responses that may affect central control of breathing (Cheng et al., 2019). Given the global burden of OSA and the ubiquity of air pollution, elucidating their relationship is of significant public health importance. Individuals with OSA are often unaware of their condition, and delayed diagnosis and treatment can lead to severe health consequences. If air pollution is established as a modifiable risk factor for OSA, it could have substantial implications for prevention and management strategies.

Recent studies have explored the relationship between air pollution and OSA (Tsai et al., 2023; Bai et al., 2023; He et al., 2023a, 2023b). This study is motivated by the necessity to integrate existing knowledge on this topic. By systematically collecting and analyzing data from a range of studies, this review aims to elucidate the extent to which air pollution contributes to the risk of OSA. The findings are expected to enhance clinical practice, guide future research, and potentially influence environmental and public health policies. The main objective of this study is to perform a thorough review and meta-analysis of observational studies that investigate the link between air pollution and the risk of obstructive sleep apnea.

2. Methods

This study adhered to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), as outlined in Table S1 (Page et al., 2021). We utilized Nested Knowledge® web software (Nested-Knowledge, MN, USA) for the screening and extraction process. Nested Knowledge® provides an all-encompassing software solution for conducting systematic literature reviews and meta-analyses. The AutoLit® function in the software facilitated the processes of screening, data extraction. We registered the study protocol in PROSPERO.

3. Selection criteria

Our inclusion criteria encompassed observational studies of any design (cohort, case-control, cross-sectional) involving participants diagnosed with or at risk of OSA, regardless of age, gender, or ethnicity. We focused on studies that quantitatively assessed air pollution, specifically measuring particulate matter (PM2.5 and PM10), nitrogen dioxide (NO2), ozone (O3), sulfur dioxide (SO2), carbon monoxide (CO), and other relevant pollutants. Outcomes of interest was risk of OSA as confirmed through established diagnostic methods. We considered peer-reviewed articles published in English without date restrictions. Our exclusion criteria ruled out non-observational studies such as reviews, editorials, and case reports, as well as studies with insufficient data on air pollution and OSA outcomes, non-English publications, reports with duplicated data from previously included studies, and studies focusing solely on indoor air pollution or unrelated environmental factors. The inclusion criteria is detailed in Table S2.

4. Literature search

We implemented a comprehensive literature search strategy to investigate the association between air pollution and OSA. Our search spanned multiple electronic databases, including PubMed, EMBASE, and Web of Science, selected for their extensive coverage of medical and environmental science literature. We used a combination of keywords and MeSH terms related to "air pollution" (such as "particulate matter," "airborne pollutants," "environmental pollution") and "obstructive sleep apnea" (including "OSA," "sleep apnea syndromes," "sleep-disordered breathing"), using Boolean operators for effective term combination. Our search, not restricted by publication date to ensure comprehensiveness, was initially conducted up until December 10, 2023, and then re-run on January 2, 2024. The search strategy is documented in Table S3. All records and data from the studies were organized and managed using Nested Knowledge web software, ensuring an efficient and systematic approach in handling the extensive data involved in this review.

5. Screening

Initially, following a comprehensive literature search, we compiled all identified records. We then removed duplicates using Nested Knowledge web software, complemented by manual checks, to ensure each study was uniquely represented. The titles and abstracts of these records were reviewed by two reviewers to exclude studies that did not meet the inclusion criteria or were irrelevant. For records that passed this initial screening, two independent reviewers conducted a detailed full-text review, assessing each study against our predefined criteria. Discrepancies between reviewers were resolved through discussing with a third reviewer when necessary.

6. Data extraction and quality assessment

In the data extraction process, two independent reviewers extracted relevant information from each included study, such as sample size, study design, participant demographics, details of air pollution exposure, and OSA-related outcomes. This was facilitated by a standardized data extraction form and managed through the tagging function using Nested Knowledge web software, ensuring consistency and organization. Discrepancies during this phase were resolved through discussion or consultation with a third reviewer. For the quality assessment, we

employed the Newcastle-Ottawa Scale for cohort and case-control studies, focusing on criteria such as selection and comparability of study groups, exposure and outcome ascertainment, and follow-up adequacy (Bushi et al., 2023b).

7. Statistical analysis

We conducted narrative summarization and statistical analysis to elucidate the association between air pollution and OSA. Studies reporting odds ratios (OR) and confidence intervals (CI) for the association between NO2 and PM2.5 with the risk of developing OSA were pooled through the meta-analysis. Meta-analysis refers to the statistical method that aggregates and analyzes the outcomes from several studies that are similar in nature. These studies may exhibit variations in their design and implementation, resulting in heterogeneity in their underlying effects. Our analysis primarily employed random-effects models to address potential heterogeneity among the studies. This model typically assumes a normal distribution of the underlying effects across studies. The Restricted Maximum Likelihood (REML) random effect model was employed. It is a statistical method used for estimating the variance components in models. The REML approach adjusts the likelihood calculations to account for the degrees of freedom used in estimating the parameters of random effects in a statistical model. This adjustment is crucial for providing unbiased estimates of variance components in models with random effects, such as those used in mixed-effects models or meta-analysis with random-effects models. By making this adjustment, REML helps to avoid the underestimation of these variance components, which can occur if simple maximum likelihood (ML) estimation is used. For pooling the ORs and CIs we used the 'metagen' function in the 'meta' package of R software. This function is specifically designed for the meta-analysis of studies that provide effect sizes and their corresponding standard errors (Schwarzer, 2007). The heterogeneity was assessed using the I^2 and Tau^2 statistics. The computation of Tau^2 was conducted using the maximum likelihood method (Langan et al., 2019; Gandhi et al., 2023a). Additionally, we included 95 % prediction intervals to understand the range of potential effects and the consistency of the results, with a threshold of $p<0.05$ set for statistical significance. A prediction interval is a statistical measure that estimates the range within which the values of future observations are expected to fall and for evaluating the heterogeneity across the studies included in the analysis (IntHout et al., 2016; Gandhi et al., 2023b). This interval reflects not only the uncertainty of the effect size estimate but also the additional uncertainty about where the effect size of a new study will fall, considering the observed between-study variability (Nagashima et al., 2019). All statistical analyses were conducted using 'Meta' package in the R statistical software (version 4.3) (Shamim et al., 2023). RStudio is favored for its capability to perform a wide array of statistical analyses and its ability to produce appealing graphical plots.

8. Results

8.1. Literature search

The PRISMA diagram illustrates the systematic review and meta-analysis study selection workflow (Fig. 1), starting with 6790 records identified from databases. After removing 2094 duplicates, the remaining 4696 records were screened, leading to 214 reports being retrieved and 241 full-text reports assessed for eligibility. Ultimately, only one study was included from this group. Concurrently, citation searching identified three additional records, all of which were retrieved and assessed, but only one met the eligibility criteria due to the others lacking outcomes of interest. In total, 4482 records were excluded after screening, with 203 full-text articles being excluded for various reasons, including being letters to the editor, reviews, case reports, or not including the outcomes of interest. The selection process culminated in 12 studies included in the qualitative synthesis and four in the quantitative synthesis.

8.2. Characteristics of included studies

The characteristics of included studies are summarized in Table 1. The studies included in the review spanned various countries and utilized different study designs to explore the impact of environmental factors on OSA. Seven studies were from Taiwan, Each from USA,

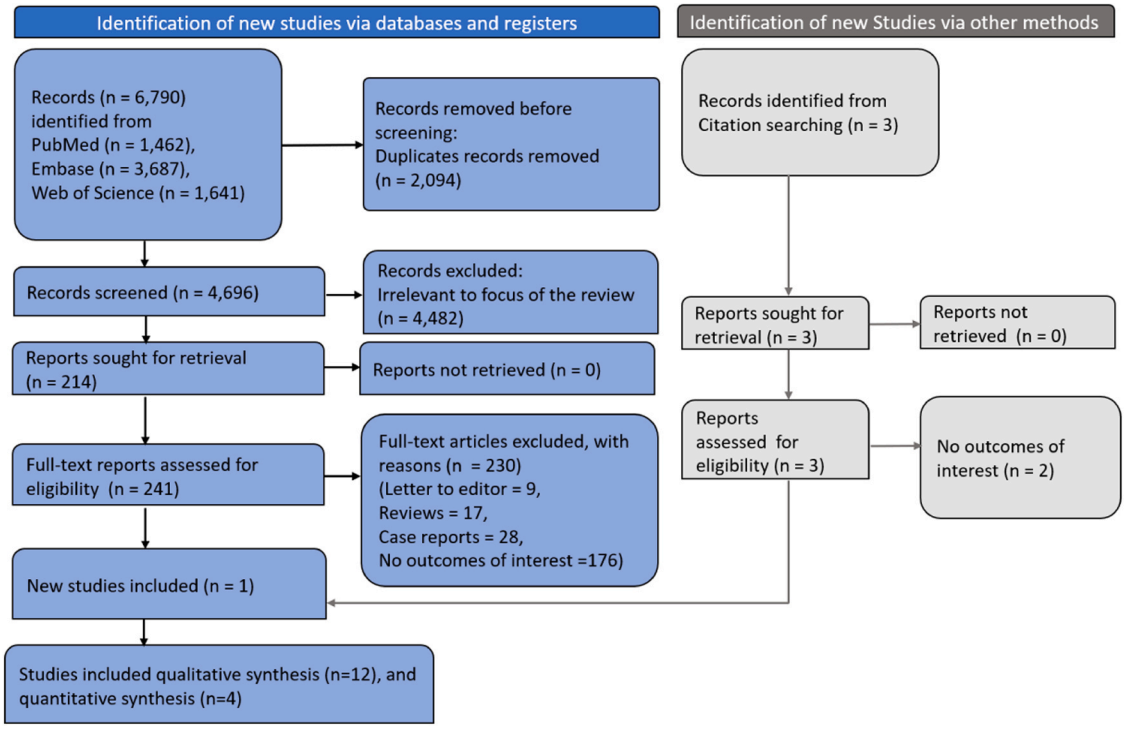

Fig. 1. PRISMA flow diagram depicting article screening and selection process.

Table 1
Characteristics of included studies.

Study	Country	Study design	Participants	Age (mean)	Male %	BMI (kg/m2)	OSA assessment	Total sample	Key findings
Bai et al. (2023)	Taiwan	Case-control study	Participants aged 20–80 who completed a one-night PSG test	48.9	68.4	27	Polysomnography	8628	Fluctuations in short-term RH and fine PM2.5 levels were linked to alterations in AHI among patients with OSA, notably with RH during colder months.
Billings et al. (2019)	USA	Retrospective study	Participants from the Multi-Ethnic Study of Atherosclerosis (MESA) involved in both the Sleep and Air studies.	68.4	45.9	28.7	Polysomnography	1974	People exposed to higher yearly levels of NO2 and PM2.5 had an increased likelihood of developing sleep apnea.
Cassol et al. (2012)	Brazil	Retrospective study	Patients aged 18 years and older who were referred to a university-affiliated sleep clinic for suspected sleep disorders during January 2000 to December 2009	46	66	28	Polysomnography	7523	Inverse correlation exists between the AHI and ambient temperature, and a positive correlation with atmospheric pressure, relative air humidity, and carbon monoxide concentrations. Notably, RH was identified as a significant influence on AHI.
Cheng et al. (2019)	Taiwan	Retrospective study	Patients referred by physicians for a PSG diagnostic study at the Sleep Center of the China Medical University Hospital, Taichung, Taiwan, between 2008 and 2015	46.54	76.78	27.18	Polysomnography and CPAP Titratio	5413	In patients with severe OSA, factors such as PM10 or smaller, ozone, sulfur dioxide, RH were linked to variations in the AHI
Yıldız Gülhan et al. (2020)	Turkey	Retrospective study	Patients admitted to the Chest Disease Polyclinic for Sleep Disorders at Duzce University, School of Medicine between January 2015 and December	47.3	63.2	33.4	PSG digital system was used (Alice 5 SleepSystem, Philips, Respironics, Murrysville, PA)	500	The study found a significant correlation between the AHI and PM10 levels during winter, indicating that PM10 greatly elevates the risk for OSA when air pollution is high.
He et al. (2023a)	Taiwan	Cross-sectional stud	Adults from urban areas in northern Taiwan, including Taipei and New Taipei City, who visited the Sleep Center of Taipei Medical University Hospital for polysomnography tests between January 2015 and September 2021, seeking treatment for sleep disorders.	46.43	51.65	24.27	Polysomnography	3330	Extended periods of sleeping on the back significantly raised the risk of mild OSA, especially in men and obese individuals.
He et al. (2022)	Taiwan	Cross-sectional stud	Adults who underwent polysomnography tests at Taipei Medical University Hospital's Sleep Center between January 2015 and April 2019, using data from the Taipei Sleep Center and Taiwan's Environmental Protection Administration	49.6	69.2	26.7	Polysomnography	4634	Exposure to traffic-related air pollution, both short-term and long-term, was linked to an increased risk of mild Obstructive Sleep Apnea, with this association being influenced by the REM sleep stage.
He et al. (2023b)	Taiwan	Cross-sectional study	Participants were urban residents of northern Taiwan referred to Taipei Medical University Hospital's Sleep Center for polysomnography tests between May 2019 and November 2021.	47.6	66.2	26.7	Polysomnography	3550	NO2 exposure is linked to mild OSA and affects night-time body composition changes, like fat accumulation and muscle depletion in lower limbs, in patients with mild OSA (AHI <15). PM2.5 is only associated with nocturnal lower-limb composition changes, not mild OSA.
Laratta et al. (2017)	Canada	Retrospective cohort study	Patients suspected of having OSA and undergoing PSG between 2007 and 2013	57.6	69.6	NA	Polysomnography	1339	No link was found between air pollution exposure and OSA severity or inflammatory biomarkers in the cohort.
Qiu et al. (2022)	Taiwan	Cross-sectional study	Individuals aged 20–85 years, without cardiopulmonary diseases or central sleep apnea, and exposed to air pollution in the Taipei metropolitan area from the sleep center at Taipei Medical University Hospital between January 2015 and April 2019.	49.6	66.4	26.7	Polysomnography	4634	The traffic-related air pollution correlates with sleep disorder symptoms, noting a reduction in sleep duration and efficiency, alongside increased sleep disruptions. It also observed a increasing risk of OSA linked with LAT.
Tsai et al. (2023)	Taiwan	Retrospective study	Patients aged 18–80 who completed a full PSG examination at Taipei Medical University-Shuang Ho Hospital's sleep center from July 2019 to February 2022, excluding those with certain medical treatments or diagnoses.	47.44	66.28	26.7	Polysomnography	2906	Exposure to PM2.5 and PM10 is a risk factor for OSA, potentially worsening its symptoms and affecting body fluid distribution. The study found that increased short-term exposure to PM10 and PM2.5 significantly raises the odds of OSA.
Wang et al. (2022)	China	Cross-sectional study	Patients aged 18 and older at Peking University Third Hospital's Department of Respiratory Medicine from April 2020 to May 2021.	49.4	68.6	26.2	ApneaLink® (ResMed, MAP Medicine Technology, Martinsried, Germany).	2524	Air pollutants, especially PM10 and O3, significantly affect sleep-disordered breathing in OSA patients, with more pronounced effects in females and during warm seasons. There are notable links between SO2, O3, CO, and the AHI in OSA patients.

Abbreviations: AHI: Apnea-Hypopnea Index, BMI: Body Mass Index, CO: Carbon Monoxide, CPAP: Continuous Positive Airway Pressure, LAT: Local Air Temperature, NA: Not Available, NO2: Nitrogen Dioxide, O3: Ozone, OSA: Obstructive Sleep Apnea, PSG: Polysomnography, REM: Rapid Eye Movement, RH: Relative Humidity, SO2: Sulfur Dioxide.

Canada, China, Turkey and Brazil. Participants' mean ages ranged from the mid-40 s to late 60 s, with a majority of studies reporting a predominance of male participants (Laratta et al., 2017; Cheng et al., 2019; Yıldız Gülhan et al., 2020). Body Mass Index (BMI) across studies was consistently in the overweight to obese range, reflecting a common risk factor for OSA (Wang et al., 2022; Qiu et al., 2022; Tsai et al., 2023). All studies employed polysomnography (PSG) as the primary method for OSA assessment, with one study augmenting this with CPAP titration and another utilizing a PSG digital system (Alice 5 SleepSystem) (Cheng et al., 2019; Yıldız Gülhan et al., 2020). Sample sizes varied widely, from a low of 500 to a high of 8628 participants, offering a broad perspective on the interaction between air pollution and sleep apnea severity (Bai et al., 2023; Yıldız Gülhan et al., 2020). Key findings from the studies highlighted the correlation between air quality parameters, such as relative humidity (RH), PM2.5, PM10, NO2, O3, SO2, CO, and the AHI (Wang et al., 2022; Cheng et al., 2019; Cassol et al., 2012). Several studies noted seasonal variations, with colder months and winter conditions exacerbating the effects of pollution on AHI (Tsai et al., 2023; Yıldız Gülhan et al., 2020). Others identified specific risks associated with traffic-related air pollution and the influence of sleeping positions on OSA severity (Qiu et al., 2022; He et al., 2023a, 2022). The quality of the studies were found to be moderate to high overall (Table S4).

8.3. Association of air pollution and OSA

Many studies reported assessment of air pollutants with risk of developing OSA (Table 2). He et al. (2023a) focused on the role of NO2 in OSA. Their study revealed that both short-term and long-term NO2 exposure significantly affects body composition and is linked with the occurrence of mild OSA, especially in individuals with an AHI under 15. Notably, they found no correlation between PM2.5 exposure and OSA. Qiu et al. (2022) delved into how air pollutants impact OSA risk, particularly focusing on NO2. Their findings showed that short- to medium-term exposure to NO2 increases the risk of latency-associated OSA (LAT OSA). They observed that an interquartile range (IQR) increase in NO2 (7.7 ppb) over 0–6 days led to a 15 % increased risk of LAT OSA, which further escalated to 21 % after adjusting for PM2.5 levels. However, their research did not establish a significant link between NO2 and non-LAT OSA, nor between PM2.5 exposure and OSA. Tsai et al. (2023) research explored the relationship between short-term exposure to PM10 and PM2.5 with OSA. Their results indicated a significant association, with higher short-term exposure to these particulates leading to an increased risk of developing OSA. Specifically, an IQR increase in PM10 and PM2.5 exposure corresponded to increased OR for OSA of 1.35 and 1.42, respectively. Yıldız Gülhan et al. (2020) highlighted the combined influence of PM10, air temperature, age, and Body Mass Index (BMI) on OSA risk. Their findings suggested that these factors collectively contribute to an increased OR for developing OSA. Billings et al. (2019) presented comprehensive research showing a strong association between NO2 and OSA. They found that a 10-ppb increase in NO2 over 1 or 5 years was linked to a nearly 40 % higher odds of OSA. For PM2.5, they observed an association with OSA with 1-year average exposure but not with 5-year averages. Each 5 μg/mˆ3 increase in annual mean PM2.5 exposure corresponded to 60 % higher odds of OSA, a connection that was particularly significant when excluding site factors. However, short-term PM2.5 levels were not significantly linked to OSA. The Los Angeles site in their study showed a distinct correlation between PM2.5 exposure and sleep apnea. He et al. (2023a) study, significant associations between both short- and long-term NO2 exposure and the increased risk of mild OSA were discovered. The research indicated that higher NO2 levels led to higher risks of mild OSA. Specifically, an IQR increase in NO2 exposure was linked to a 16.0 % increased risk for lag (0–7 days) exposure (7.7 ppb) and a 13.0 % increase for an average exposure over the previous two years (6.4 ppb). Notably, these associations were more pronounced in individuals with higher BMIs, although there was no significant interaction found between NO2 levels and mild OSA across different BMI values.

Table 2
Summary of studies reported risk of OSA with NO2 and PM.

Study	Exposure for OSA	Effect size (95% CI)
Qiu et al. (2022)	PM2.5 (0–2Y)	RRR=1.07 (0.91–1.26)
	PM2.5 (0–1Y)	RRR=1.06 (0.92–1.23)
	NO2 (0–2Y)	RRR=1.11 (0.99–1.24)
	NO2 (0–1Y)	RRR= 1.11 (0.99–1.24)
He et al. (2022)	PM2.5 (0–2Y)	OR=1.107 (0.90–1.35)
	NO2 (0–2Y)	OR=1.24 (1.085–1.435)
	PM2.5 (0–2Y)	OR=1.06 (0.89–1.26)
	NO2 (0–1 Y)	OR=1.18 (1.03–1.36)
Tsai et al. (2023)	PM2.5 (0–2Y)	OR=0.83 (0.7–1.0)
	PM10 (0–1 Y)	OR=1.04 (0.85–1.27)
	NO2 (0–1 Y)	OR=0.88 (0.74–1.03)
Billings et al. (2019)	NO2 (0–1 Y)	OR=1.39 (1.03–1.87)
	NO2 (0–5 Y)	OR=1.41 (1.04–1.92)
	PM2.5 (0–1 Y)	OR= 1.60 (0.98–2.62)
	PM2.5 (0–5 Y)	OR= 1.31 (0.78–2.20)
He et al. (2023a)	NO2 (0–2 Y)	OR=1.13 (1.01–1.27)
	NO2 (0–1 Y)	OR=1.11 (0.99–1.25)
	PM2.5 (0–1Y)	OR=1.03 (0.87–1.21)
	PM2.5 (0–2Y)	OR=1.03 (0.87–1.21)

Abbreviations: CI: Confidence Interval, NO2: Nitrogen Dioxide, OR: Odds Ratio, PM2.5: Particulate Matter 2.5, PM10: Particulate Matter 10, RRR: Relative Risk Ratio, 0–1 Y: 0–1 year lag, 0–2 Y: 0–2 years lag.

8.4. Association of air pollution and OSA severity

The association between air pollution and the severity of OSA has been the focus of various studies, each contributing unique insights into how different pollutants affect sleep apnea parameters. Bai et al. (2023) highlighted the impact of PM2.5 and relative humidity on OSA severity. They found that a 1-μg/mˆ3 increase in average PM2.5 levels led to a 1.04–1.08-fold increase in the OR for the AHI in both mild-to-moderate and severe OSA cases over periods of 1, 7, and 30 days. Moreover, a 1 % rise in mean Relative Humidity (RH) was linked to a similar increase in OR for AHI across the same patient groups and periods. Daily variations in ambient RH, temperature, and PM2.5 also showed associations with AHI in OSA patients, underlining the influence of short-term environmental changes on sleep apnea severity. He et al. (2022) focused on the effects of NO2 on sleep apnea parameters. Their study indicated that an interquartile range increase in the 2-year average of NO2 was associated with notable increases in AHI and Oxygen Desaturation Index (ODI), particularly in men and younger patients. The study also found a significant correlation between NO2 exposure and the risk of mild OSA, whereas PM2.5 exposure was linked to increases in ODI but not significantly to AHI. Wang et al. (2022) explored how various air pollutants, including PM2.5, NO2, O3, and CO, affect Sleep Disordered Breathing (SDB) parameters in OSA patients. Their findings showed that increases in the levels of these pollutants were associated with increases in AHI, Hypopnea Index (HI), and ODI. The impact of these pollutants varied across different OSA severity levels, suggesting a complex relationship between air quality and sleep apnea severity. Yıldız Gülhan et al. (2020) observed a significant positive correlation between REM-related AHI and relative humidity. They also noted seasonal variations in AHI and total sleep duration, with higher values in winter, which is typically associated with elevated PM10 levels. Cassol et al. (2012) employed bivariate nonparametric correlation analyses to study the relationship between AHI and atmospheric conditions. They found an inverse correlation between AHI and ambient temperature and a positive correlation with atmospheric pressure, relative air humidity, and carbon monoxide levels. In their multivariate cosinor model analysis, relative air humidity emerged as a significant factor affecting AHI. Cheng et al. discovered significant associations between PM10, ozone, sulfur dioxide (SO2), and relative humidity with the AHI in patients who had severe

OSA. Specifically, they noted that ozone and relative humidity were linked to AHI in females but not in males. Furthermore, within the group suffering from severe OSA, these researchers observed that PM10, ozone, SO2, and relative humidity were significantly correlated with AHI during non-rapid eye movement (NREM) sleep, but these correlations did not extend to AHI during rapid eye movement (REM) sleep. Billings et al. (2019) reported that a 10 ppb increase in NO2 was linked to a significantly higher odds of OSA. However, this association was not significant when considering the 4 % desaturation criterion for hypopneas (CMS definition) for AHI. Laratta et al. (2017) study did not find significant correlations between pollution levels and AHI or OSA severity. They also observed no association between pollution levels and inflammatory biomarkers, suggesting a lack of impact of pollution on sleep apnea severity or associated inflammatory markers within their research framework.

8.5. Meta-analysis

In our meta-analysis examining the association of PM2.5 exposure (lag 0–1 year) with the risk of OSA, we synthesized data from four studies: Billings et al. (2019), Wang et al. (2022), He et al. (2022), and Tsai et al. (2023). The analysis yielded varied results: Billings 2019 suggested a potential increased risk of OSA with an OR of 1.60 (95 % CI: 0.78–2.42). He 2022 and He 2023 reported modest associations with ORs of 1.06 (95 % CI: 0.875–1.245) and 1.03 (95 % CI: 0.860–1.200), respectively. Tsai et al., 2023 (Tsai et al., 2023) indicated a possible protective effect with an OR of 0.83 (95 % CI: 0.680–0.980). The pooled OR of 0.987 (95 % CI: 0.836–1.138) suggested no significant overall effect of PM2.5 exposure on OSA risk. Moderate heterogeneity (I^2 = 57 %, tau^2 = 0.0111, p = 0.07) across these studies points to variability that may stem from study-specific factors. The prediction interval (0.425–1.549) indicates the expected range for future studies, suggests that the current evidence and summarization of the current evidence is still not sufficient to adequately understand this relationship given the prediction interval spans protective to adverse ORs (Fig. 2).

We investigated the relationship between NO2 exposure (lag 0–1 year) and the risk of OSA as reported by four distinct studies. These studies, specifically Billings et al. (2019), Wang et al. (2022), He et al. (2022), and Tsai et al. (2023), provided ORs along with 95 % CIs to indicate the strength and precision of the associations they observed. The pooled OR across these studies was 1.095 (95 % CI: 0.920–1.270), suggesting a non-statistically significant positive association between NO2 exposure and increased risk of OSA. The heterogeneity among the studies was high (I^2 = 73 %, tau^2 = 0.0217, p = 0.01), indicating substantial variability that could be due to differences in study design, populations, or other factors. The prediction interval ranged from 0.353 to 1.837, predicting that future studies will likely report ORs within this range. The forest plot visually represents these findings, indicates the expected range for future studies, suggests that the current evidence and summarization of the current evidence is still not sufficient to adequately understand this relationship given the prediction interval spans protective to adverse ORs (Fig. 3).

9. Discussion

This systematic review and meta-analysis aimed to integrate the existing data on how air pollution may influence both the likelihood and intensity of OSA. It reveals a complex relationship, with evidence suggesting that NO2 might contribute to the severity of OSA. However, the effect of both PM2.5 and NO2 on the risk of developing OSA is ambiguous, as the OR fails to show a definitive statistical significance. Therefore, the relationship between air pollution and OSA risk remains uncertain. The heterogeneity in the studies further indicates this uncertainty of evidence in the current literature. Despite this, there's an indicated association between air pollution exposure and higher AHI scores in numerous studies, suggesting that air pollution might exacerbate OSA severity.

Our findings are in line with the growing body of literature suggesting a biologically plausible impact of air pollution on sleep-disordered breathing (Liu et al., 2020). Proposed pathophysiological mechanisms include pollutant-induced systemic inflammation, oxidative stress, and autonomic imbalance, potentially leading to or worsening upper airway dysfunction during sleep (Wang et al., 2022; Tsai et al., 2023). It is important to note that the effects of air pollutants may vary based on the type of pollutant, duration of exposure, and individual susceptibility factors, including age, gender, and underlying health conditions. Seasonal variations observed in some studies, with higher pollution levels linked to greater OSA severity during colder months, add complexity to these findings. This might reflect not only the direct effects of the pollutants but also the influence of behavioral and environmental changes associated with different seasons, such as changes in indoor heating and air quality. Despite some studies identifying specific pollutants as risk factors for increased OSA risk, our meta-analysis suggests these associations may not be as robust across the broader evidence base. This highlights the need for large-scale, multi-site studies to validate and clarify the relationships observed in smaller studies.

The studies analyzed reveal a complex interaction between certain air pollutants, notably PM2.5 and NO2, and increased severity of OSA, as indicated by markers like AHI and Oxygen Desaturation Index (ODI). These relationships appear to be influenced by demographic factors and exhibit variability with different pollutants and OSA severity levels. Seasonal changes also modulate the relationship between air quality and OSA, suggesting that both the direct effects of pollutants and the indirect consequences of seasonal behavior may impact sleep health. However, findings from studies like Laratta C et al., showing no significant correlation between pollution levels and OSA severity, caution against a straightforward interpretation of these associations and emphasize the need for further research to clarify the underlying mechanisms and inform targeted interventions.

The potential association between air pollution and OSA severity has significant implications for clinical practice. Healthcare providers may need to consider environmental factors in OSA risk assessment and management. In high-pollution areas, clinicians could be advised to monitor patients more closely for OSA symptoms and consider environmental factors in the condition's severity. Public health initiatives

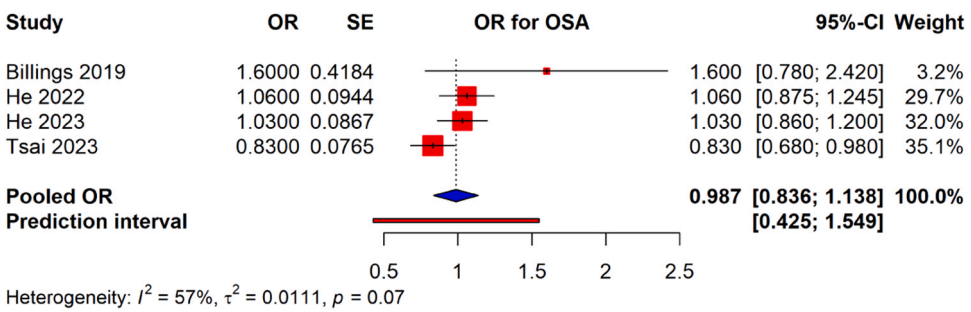

Fig. 2. Association of PM2.5 (0–1Y lag) with risk of OSA.

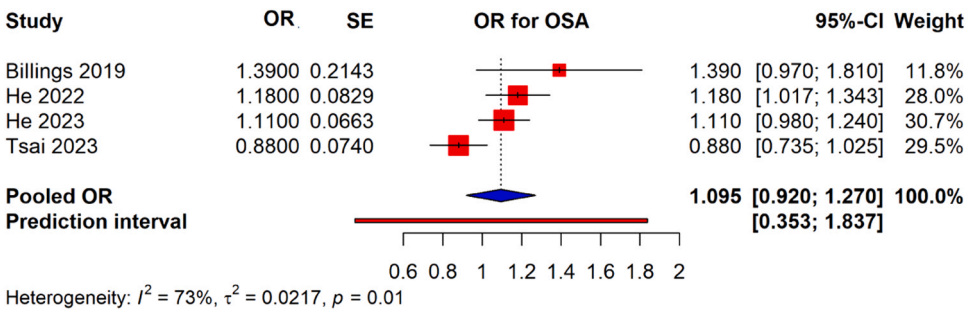

Fig. 3. Association of NO2 (0–1Y lag) with risk of OSA.

aimed at reducing air pollution might also play a role in OSA prevention and management, highlighting the need for multidisciplinary approaches that integrate environmental health into clinical guidelines. For OSA patients, especially those in areas with poor air quality or experiencing seasonal pollution peaks, recommended interventions could include air purifiers, pollution masks, or advice to limit outdoor exercise during high pollution periods. These strategies should be part of comprehensive patient education and self-management programs for OSA.

Our study faces several limitations. The considerable heterogeneity among the included studies in terms of design, methodologies, and populations investigated introduces a moderate to high level of heterogeneity, potentially affecting the clarity of the findings and limiting the conclusions drawn from the pooled data. The methodologies used to measure air pollution exposure varied across studies, leading to possible inconsistencies in exposure assessment. Most studies relied on regional data for air pollution exposure, which may not accurately reflect individual exposure levels, thereby raising the potential for exposure misclassification. The geographic scope of the studies was mostly confined to urban areas or specific regions, which might not reflect the global diversity in pollution patterns or the spectrum of OSA prevalence and severity seen across different populations. The inclusion of cross-sectional studies limits our ability to establish causal relationships between air pollution and OSA. Seasonal variations in pollution levels and their impact on OSA severity were reported by some studies but were not consistently considered across all included research. Our meta-analysis was restricted to just four studies due to limited reports of OR for OSA risk, which might affect the robustness of our conclusions. Despite adjustments for known confounders in many studies, the potential for unmeasured or residual confounding factors remains, which could influence the association between air pollution and OSA. These limitations underscore the need for future research adopting more standardized, accurate, and comprehensive methodologies. Addressing these concerns will strengthen the evidence base and provide clearer guidance for public health policies and clinical strategies aimed at managing and mitigating the risks of OSA associated with air pollution.

10. Conclusion

Our analysis indicates a complex, yet not definitively established, relationship between air pollution and the risk of OSA. A significant association was found between air pollution and the severity of OSA in patients. These findings demonstrate the potential importance of considering environmental factors in OSA management and highlight the need for integrated public health strategies that address both air pollution and sleep health. More studies are required in the future for a better understanding.

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Not applicable.

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CRediT authorship contribution statement

Jeetendra Kumar Gupta: Conceptualization, Funding acquisition, Methodology. **Shilpa Gaidhane:** Writing – review & editing, Writing – original draft, Validation. **Mahalaqua Nazli Khatib:** Writing – original draft, Investigation, Formal analysis. **Sarvesh Rustagi:** Validation, Supervision, Software, Methodology. **Abhay M. Gaidhane:** Software, Methodology, Data curation. **Anas Alkhouri:** Resources, Writing – original draft, Writing – review & editing. **Khalid Al-Mugheed:** Writing – review & editing, Writing – original draft, Visualization. **Bijaya Kumar Padhi:** Investigation, Formal analysis, Conceptualization. **Neelima Kukreti:** Software, Resources, Formal analysis. **Ahmed Mahal:** Investigation, Methodology, Project administration. **Prakasini Satapathy:** Methodology, Formal analysis, Data curation. **Dibyalochan Mohanty:** Data curation, Supervision, Validation. **Tahani Alrahbeni:** Data curation, Conceptualization. **Ladi Alik Kumar:** Conceptualization, Project administration, Resources.

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.

Data availability

The data utilized has been presented in manuscript and supplementary files

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Presentation

None.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neuro.2024.04.005.

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