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REVIEW

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Association Between Maternal Prenatal Exposure to Household Air Pollution and Child Respiratory Health: A Systematic Review and Meta-analysis

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Maternal prenatal exposure to household air pollution (HAP) is a critical public health concern with potential long-term implications for child respiratory health. The objective of this study is to assess the level of association between prenatal household air pollution and child respiratory health, and to identify which HAP pollutants are associated with specific respiratory illnesses or symptoms and to what degree. Relevant studies were retrieved from PubMed databases up to April 27, 2010, and their reference lists were reviewed. Random effects models were applied to estimate summarized relative risks (RRs) and 95% confidence intervals (CIs). The analysis involved 11 studies comprising 387 767 mother-child pairs in total, assessing various respiratory health outcomes in children exposed to maternal prenatal HAP. Children with prenatal exposure to HAP pollutants exhibited a summary RR of 1.26 (95% CI=1.08-1.33) with moderate between-study heterogeneity (I^2=49.22%) for developing respiratory illnesses. Specific associations were found between prenatal exposure to carbon monoxide (CO) (RR=1.11, 95% CI: 1.09-1.13), Nitrogen Oxides (NO_x) (RR=1.46, 95% CI: 1.09-1.60), and particulate matter (PM) (RR=1.26, 95% CI: 1.2186-1.3152) and child respiratory illnesses (all had I^2 close to 0%, indicating no heterogeneity). Positive associations with child respiratory illnesses were also found with ultrafine particles (UFP), polycyclic aromatic hydrocarbons (PAH), and ozone (O_3). However, no significant association was observed for prenatal exposure to sulfur dioxide (SO_2). In summary, maternal prenatal exposure to HAP may contribute to a higher risk of child respiratory health issues, emphasizing the need for interventions to reduce this exposure during pregnancy. Targeted public health strategies such as improved ventilation, cleaner cooking technologies, and awareness campaigns should be implemented to minimize adverse respiratory effects on children.

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Abbreviations: HAP, Household Air Pollution; RR, Relative Risk; CIs, Confidence Intervals; CO, Carbon Monoxide; NO_x, Nitrogen Oxides; O_3, Ozone; SO_2, Sulfur Dioxide; PM, Particulate Matter; UFP, Ultrafine particles; VOCs, Volatile Organic Compounds; PAH, Polycyclic Aromatic Hydrocarbons; FEV1, Forced Expiratory Volume in one second; FVC, Forced Vital Capacity; PRISMA, Preferred Reporting Items for Systemic Reviews and Meta Analyses; MeSH, Medical Subject Heading; HR, Hazard Ration; OR, Odds Ratio; RDS, Respiratory Distress Syndrome; PNA, Physician assessed Pneumonia; SPNA, Severe physician assessed Pneumonia; TTN, Transient Tachypnea.

Keywords: Maternal exposure, Household Air Pollution (HAP), Child Respiratory Health, Prenatal Exposure, Pregnancy Health, Pregnancy Exposure, Child Development, Carbon Monoxide, Nitrogen Oxides, Particulate Matter, Lung Function, Respiratory Illnesses

Author Contributions: This systematic review and meta-analysis was conducted by Krrishika Saxena (KS), a senior at Eleanor Roosevelt High School. It was critically edited and reviewed by Illisha Raj (IR), a candidate with a bachelor's degree in biology from UCLA and an incoming UCLA medical student, ensuring thorough refinement of the manuscript.

BACKGROUND

According to the World Health Organization (WHO), approximately 2.4 billion people worldwide (around a third of the global population) cook using open fires or inefficient stoves fueled by kerosene, biomass (wood, animal dung, and crop waste), and coal, which generates harmful household air pollution [1]. In recent decades, there has been growing concern about the adverse effects of household air pollution (HAP) on human health, particularly in low- and middle-income countries where solid fuel combustion for cooking and heating remains prevalent. Among the vulnerable population, women and children disproportionately bear the greatest health burden from polluting fuels and technologies in homes. This is because women often shoulder the responsibility of household chores such as cooking and collecting firewood, and as a result, they spend more time exposed to harmful smoke from polluting stoves, fuels, combustion of biomass, and other indoor pollutants. Pregnant women and their unborn children are of particular concern due to the potential long-lasting consequences of prenatal exposure to HAP.

These emissions include pollutants such as particulate matter (PM), carbon monoxide (CO), nitrogen oxides (NO_x), sulfur oxides (SO_2), volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons (PAHs), and other toxic substances [2]. These pollutants can penetrate indoor environments, leading to high levels of exposure among household members, particularly pregnant women who spend considerable time indoors.

The primary respiratory diseases observed in children because of prenatal HAP exposure are as follows: pneumonia, tachypnea, apnea, respiratory distress, asthma, allergic rhinitis, wheezing, conjunctivitis, eczema, and lower respiratory tract infections. CO and NO_x exposure during pregnancy are associated with heightened susceptibility to respiratory infections such as pneumonia in children. CO interferes with immune responses, compromising the defense against respiratory pathogens. Prenatal exposure to NO_x also increases the risk of childhood asthma through inflammatory mechanisms, involving airway inflammation and bronchoconstriction. Additionally, PAHs contribute to asthma exacerbation by promoting inflammation through the activation of inflammatory pathways. Fine PM carries allergens, exacerbating allergic rhinitis, by delivering allergenic particles deep into the respiratory system. Ultrafine particles (UFPs) heighten the risk of lower respiratory infections through their ability to penetrate deeply into the lungs and potentially compromise immune defenses. Finally, VOCs play a role in eye irritation leading to conjunctivitis and can contribute to skin irritation in eczema, acting as irritants and triggering inflammatory responses in the eyes and skin.

There are very few comprehensive epidemiological studies that have investigated the variety of negative respiratory effects of the different types of HAP exposure on children, emphasizing the importance of understanding the long-term consequences of maternal prenatal exposure. For instance, Veras et al. conducted a review that concluded that gestational and early life exposure to air pollutants is linked to alterations in lung development and function and to other negative respiratory conditions in childhood (wheezing, asthma) that may last into adulthood [3]. Similarly, Aithal et al. concluded that the use of solid fuels may lower the lung volumes and flow rates in children (Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), Forced mid-expiratory flow (FEF25–75)—all measurements of lung volume and airflow rates) [4]. A study by Hsu et al. also found significant associations for O_3, ammonium (NH_4^+), and OC with decreased FEV1/FVC, FEV1, and FEF25-75, respectively [5]. However, some other studies have also shown that there is not a strong association between prenatal exposure to HAP and child respiratory health. For example, a study by Rana et al. did not find a direct association between HAP exposure and children's mortality due to lower respiratory tract infection diseases [6]. Similarly, a study by Dherani et al. reported no significant relation between prenatal HAP exposure and raspatory syncytial virus [7].

To address the inconsistent findings in existing research and clarify what HAP pollutants are linked to what respiratory illness in children from prenatal exposure, an updated and comprehensive systematic review and meta-analysis are necessary to identify consistent patterns and provide a more robust assessment of the relationship between HAP and respiratory diseases. Additionally, previous studies focused on all HAP in general or only examined one specific one, making it both unclear which pollutants are associated with what respiratory illnesses and symptoms and to what extent as well as a need for a study on all the pollutants together, and not just specific ones, to get a clearer picture. Therefore, this meta-analysis will examine the primary HAP individually to determine their degree of association with respiratory diseases in infants and identify the specific illnesses to which they are most linked. This also sheds light on which are most hazardous as well as discuss the primary sources of each pollutant in the house, enabling more targeted interventions. By emphasizing the need for additional research, we can raise awareness and advocate for the allocation of resources to support studies exploring the complex relationship between HAP and maternal and fetal health. Expanding the knowledge base through rigorous scientific investigations will yield valuable insights to inform evidence-based interventions, ultimately leading to improved health outcomes for pregnant women and their

Table 1. The Search Strategy of the Association Between Prenatal Exposure to Household Air Pollution and Child Respiratory Health Incidence

#1	Search "Air Pollution"[MeSH]
#2	(air pollution[MeSH Terms] OR pollution[MeSH Terms] OR "indoor air pollution"[MeSH Terms] OR "household air pollution"[MeSH Terms] OR HAP) OR ("volatile organic compounds"[MeSH Terms] OR VOCs) OR ("particulate matter"[MeSH Terms] OR PM2.5 OR PM10) OR ("carbon monoxide"[MeSH Terms] OR CO) OR ("nitrogen dioxide"[MeSH Terms] OR NO2) OR ("sulfur dioxide"[MeSH Terms] OR SO2) OR (benzene[MeSH Terms] OR formaldehyde[MeSH Terms] OR toluene[MeSH Terms]) OR ("polycyclic aromatic hydrocarbons"[MeSH Terms] OR PAHs)
#3	#1 OR #2
#4	Search "Maternal Exposure"[MeSH]
#5	(maternal exposure[MeSH Terms] OR prenatal exposure[MeSH Terms] OR maternal exposure OR pregnancy exposure OR pregnancy)
#6	#4 OR #5
#7	Search "Child"[MeSH]
#8	(child[MeSH Terms] OR pediatric[MeSH Terms] OR infant[MeSH Terms] OR baby[MeSH Terms] OR newborn[MeSH Terms] OR neonate[MeSH Terms])
#9	#7 OR #8
#10	Search "Respiratory health"
#11	(respiratory health[MeSH Terms] OR lung function[MeSH Terms] OR respiratory symptoms[MeSH Terms] OR respiratory infections[MeSH Terms] OR asthma[MeSH Terms] OR chronic obstructive pulmonary disease[MeSH Terms] OR COPD OR bronchitis[MeSH Terms] OR wheezing[MeSH Terms] OR pneumonia[MeSH Terms] OR respiratory diseases[MeSH Terms])
#12	#10 OR #11
#13	#3 AND #6 AND #9 AND #12

unborn children.

MATERIAL AND METHODS

Search Strategy

Following the development of the research question, a systematic review and meta-analysis were carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [8]. Medical Subject Heading (MeSH) terms and keywords used in similar papers were also used to help with the search. The studies were filtered and selected from PubMed, ensuring that their publishing dates were after 2010. Table 1 shows a detailed database search technique that was used. Additional papers were discovered by manually reviewing the reference lists of primary research and review articles.

Study Selection

Eligible studies for the present meta-analysis were required to meet the following criteria: (i) observational designs (eg, cohort, cross-sectional) examining the relationship between maternal prenatal exposure to household air pollution and respiratory health outcomes in children; (ii) participants consisting of pregnant women were known to be exposed to a type of household air pollutant, including CO, NO_x, SO_2, PM, and PAH, for at least a trimester and their children, aged 0-12 years, as the target population; (iii) accurately measured respiratory specific illnesses, function, and symptoms including pneumonia, asthma, allergic rhinitis, eczema, wheezing, tachypnea, apnea, respiratory distress, and lower respiratory tract illnesses in children exposed to prenatal HAP; (iv) reporting of relative risk (RR), hazard ratio (HR), odds ratio (OR), or necessary data for calculating these measures, accompanied by a 95% confidence interval (95% CI); and (v) exclusion of review articles, case reports, commentaries, and conference abstracts.

Out of the 9839 results that came up from the search, 9814 were excluded as they only had the mentioned keywords and did not focus on the data collection of prenatal HAP exposure to their child respiratory outcomes. An additional 14 articles were screened out as they did not include RR, OR, or HR as a means of presenting results, focused on other factors like sex, race, or heavy metal exposure, and other narrative and systematic reviews were filtered out. In cases where data were duplicated, the study with the largest number of cases was prioritized to avoid redundancy. Through these rigorous criteria, the meta-analysis aimed to incorporate studies that provided robust evidence regarding the association between mater-

nal prenatal exposure to household air pollution and respiratory health outcomes in children, ensuring reliability and minimizing bias in the analysis.

Data Extraction and Quality Assessment

The data from each of the included studies were extracted carefully by two independent reviewers (KS and IR). The recorded information consisted of essential elements such as the first author's name, publication year, country of origin, study design, number of cases/participants, type of HAP and the monitoring method employed, timeframe of HAP exposure in mothers, methodology for diagnosing respiratory conditions in children, frequency of assessments, specific respiratory illnesses examined, and corresponding risk estimates with their corresponding 95% CI. To assess the risk of bias in the observational studies included the Newcastle-Ottawa quality assessment scale [9] was used by the two independent reviewers. This scale evaluates the risk of bias in three categories: selection, comparability, and outcome assessment. Studies that achieved a literature quality score of at least 5 were considered to have a minimal risk of bias.

Statistical Analysis

The study employed data synthesis and meta-analysis to investigate the impact of maternal prenatal exposure to HAP on child respiratory health outcomes. The main objective was to calculate the pooled or summary RR of respiratory illnesses incident in children exposed to HAP. Effect sizes from individual studies, including OR, risk ratios, or mean differences (MD), along with their corresponding 95% CI, were collected and combined using a random-effects model.

To calculate the standard error (SE) for each study, the provided CI data, and a confidence level of 95% were utilized. The weight for each study was then calculated to account for its influence on the overall summary RR. The summary RR was subsequently determined by combining the effect sizes of all 11 studies with their respective weights.

To assess heterogeneity among the included studies, Cochran's Q statistic was computed, and the I^2 statistic indicated the proportion of variation in effect sizes due to heterogeneity. A significant p-value for Cochran's Q statistic ($p < 0.001$) indicated a genuine association between HAP exposure and child respiratory illness.

The same methodology was applied in individual forest plots analyses to explore specific relationships between prenatal exposure to common HAP pollutants (CO, PM, and NO_x) and child respiratory health outcomes. Studies were grouped based on similar HAP pollutant exposure to estimate the relationship.

Publication bias was evaluated using funnel plots and formal statistical tests such as Egger's regression test or Begg's rank correlation test ($p < 0.001$). Sensitivity analyses were conducted by excluding studies with a high risk of bias or small sample sizes to assess the robustness of the results.

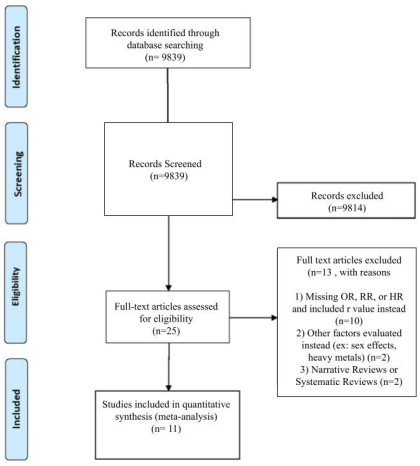

Figure 1. **Flow chart for screening of relevant literature**. Selection of studies for inclusions in the present meta-analysis.

All data analyses were performed using STATA software (StataCorp. 2023. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC), and the significance level was set at $p < 0.001$. The statistical analysis framework aimed to synthesize evidence from the included studies, identify sources of heterogeneity, and assess publication bias, providing valuable insights into the association between maternal prenatal HAP exposure and child respiratory health outcomes.

RESULTS

Characteristics of the Retrieved Studies

Of the 9839 retrieved studies remaining after the removal of duplicates, 9814 (99.0%) were excluded after screening the titles and abstracts as depicted in Figure 1. After a full-text review of the remaining 25 (0.25%) studies, two analyzed factors other than respiratory illnesses or prenatal HAP, such as sex effects or heavy metals, two were narrative or systematic reviews, and 10 lacked OR and 95% CI values. All the 11 studies included at least one type of HAP pollutant and how it is or is not associated with some type of respiratory illnesses or symptoms in children.

The characteristics of the 11 studies included for analysis, comprising ten cohort studies and one cross-sectional study, are summarized in Table 2. Importantly, each study was published between 2010 and 2022. The number of mother-child pairs and their controls ranged from 332 to 223 375 in each research. The included studies

utilized various methods to measure HAP exposure, such as CO monitoring, Lascar EL-CO-USB, Community Multi Scale Air Quality, Aerodynamic Diameter, Personal Exposure Monitor, Satellite-based thyroid monitor, spatial-temporal air quality monitoring stations, land-use regressions, and satellite-based spatial temporal models. The child respiratory diagnoses were assessed using whistler lung function measurement instrument (LFMi), fieldworkers' recording, newborn ERMs, summary discharge data, reports by mothers, and direct doctor diagnosis. The frequency of respiratory disease recording varied, including weekly home visits during the first year, assessments at birth and once throughout the children's school years, assessments every 2 months for the first 2 years, and assessment of 4-month intervals from birth to 30 months (about 2 and a half years).

These studies were conducted in the US (n=2), China, specifically in Shanghai and Wuhan (n=3), Ghana, West Africa (n=2), Taichung, Taiwan (n=1), Mexico City, Mexico (n=1), Oslo and Bergen, Norway (n=1), and Poland, Krakow (n=1). They were adjusted for potentially important confounders, such as gestational age, birth weight, maternal age, race, smoking or alcohol presence during pregnancy, education, obesity, sex, and more as depicted in Table 2. Based on the Newcastle–Ottawa quality assessment scale, all studies were judged to have a low risk of bias (Table 3).

The forest plots in Figure 2 show the summarized results for the association between maternal prenatal exposure to household air pollution and child respiratory health, involving 387 767 pairs of mother-child pairs. Women with HAP exposure were 1.26 or 26% times more likely to have a child with respiratory illness (summarized RR=1.26; 95% CI=1.08-1.33). Moderate heterogeneity was observed ($I^2=49.2\%, p < 0.001$).

The investigation also aimed to explore the level of association between maternal prenatal exposure to specific HAPs and child respiratory health. The findings revealed that there was no heterogeneity observed among the studies assessing the association between each HAP and child respiratory diseases, as indicated by an I^2 of 0%. This lack of heterogeneity suggests that the effect size estimate obtained from these studies is likely to be more precise and reliable since all the studies demonstrated consistent results. However, it is essential to consider that the absence of heterogeneity might be influenced by the relatively smaller size of the specific association studies, which contributes to the homogeneity observed.

The summary RR and forest plots indicated positive associations between prenatal exposure to certain HAPs and child respiratory health issues (Figure 3). Specifically, maternal exposure to CO was associated with a 1.11 times higher risk of child respiratory health issues, including physician-assessed pneumonia, severe physician-assessed pneumonia, and transient tachypnea (95% CI: 1.09-1.13) as supported by studies by Seeni, Kinney, and Lee [10-12].

Likewise, prenatal exposure to NO_x was associated with a 1.46 times higher risk of child respiratory health issues, such as respiratory tract infections, allergic diseases, allergic rhinitis, asthma, and hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX), with a summary RR of 1.46 (95% CI: 1.09-1.60) as supported by studies by Madsen, Guo, Liu, and Seeni [10,13-15].

On the other hand, prenatal exposure to particulate matter as a whole was associated with 1.26 times more likely of child respiratory health issues, such as asthma, wheeze, allergic diseases, apnea, and transient tachypnea, with a summary RR of 1.27 (95% CI: 1.2186-1.3152) as supported by studies by Zhang, Rivera, Guo, Lin, Jedrychowski, and Seeni [13,14,16-19,]. It should be noted that no significant association was found between PM10, particulate matter of 10 micrometers, and asthma and allergic rhinitis, as reported in the Liu study [15].

Moreover, SO_2 showed no significant association with any of the respiratory illnesses studied, as evidenced across multiple studies, including those conducted by Guo, Liu, and Seeni [10,14,15].

In contrast, O_3, PAH, and UFP were associated with respiratory distress syndrome (RDS), wheezing, and asthma, respectively, as summarized by Wright, Seeni, and Jedrychowski [10,19,20]. However, a forest plot and summarized RR was not constructed for these particular HAPs due to a limited number of studies available for a more comprehensive analysis.

Funnel plots, as well as the Egger's and Begg's tests (p=0.789 and 0.537, respectively), revealed minor evidence of differences in terms of experimental population characteristics (Figure 4), as indicated by the two outliers: Wright et al. and Rivera et al. Upon recalculating the summary risk ratios and excluding these outliers, the observed change was a decrease in the I^2 statistic from 49.22% to 32.12%; however, their influence does not markedly alter the direction or magnitude of the pooled result as they still fall within the moderate zone of heterogeneity.

DISCUSSION

This systematic review and meta-analysis of 11 observational studies revealed a positive association between maternal prenatal exposure to household air pollution, specifically CO, NO_x, PM, and child respiratory health. The results showed that children exposed to these pollutants during pregnancy had a 26% higher likelihood of respiratory issues compared to those not exposed. This finding underscores the critical importance for pregnant women to take measures to reduce the risk of pollutant

Table 2. Characteristics and Adjusted Cofounders of Studies Included in the Meta-Analysis

First Author, (Ref), Year, Country	Study Design	Study size (Mother-Child Pairs)	Type of HAP + Monitoring Type	Mother Time of Exposure Recording	Child Respiratory Diagnosis Method	Child Age/ Frequency of Diseases Recording	Child Respiratory Illness Assessed	Matched or Adjusted Factors	Risk Estimates (95% CI)
Lee et al. [12], 2019, Ghana, West Africa	Prospective Cohort Study	404	CO + CO monitoring (Lascar EL-CO-USB Data Logger)	(24 weeks) Third Trimester Pregnancy	Doctor diagnosed at Kintampo Municipal Hospital	Weekly home visits first year	Physician-assessed pneumonia (PNA) and Severe PNA (SPNA)	Birth weight and Gestational age	Physician- assessed (PNA) 1.02 (1.00-1/04) and PNA 1.04 (1.00-1.04)
Kinney et al. [11], 2021, Ghana, West Africa	Cohort Study	1141	CO +Lascar EL-CO-USB	(24 Weeks) Third Trimester Pregnancy	Fieldworkers performed	Weekly home visits first year	Physician-assessed pneumonia (PNA) and Severe PNA (SPNA)	All covariates adjusted as stated: not specified what the covariates were	Pneumonia 1.10 (1.04-1.16) Severe Pneumonia 1.06 (0.99-1.13)
Seeni et al. [10], 2018, US	Cohort Study	223,375	CO NO_x, O_3, Pm10, PM 2.5, SO_2 + Community Multiscale Air Quality	All trimesters	Newborn ERMs + Summary Discharge	Neonate, one time	Transient Tachypnea, Asphyxia, Respiratory distress	Gestational age, maternal age, race, smoking or alcohol use during pregnancy	TTN from CO: 1.1 (1-1.2) RDS from NO_x: 1.03 (-0.95-1.1) RDS from O_3: 0.98 (.92-1.04) TTN PM10: 1.02 (0.96-1.1) Asphyxia from PM 2.5: 1.2 (1.1-1.3) No significant association from SO2: 0.72 (0.65-0.79)
Liu et al. [15], 2016, Shanghai, China	Cross-Sectional Study	3358	NO_2, SO_2, PM10, + Aerodynamic Diameter	All gestation periods	Doctor-Diagnosed	First 2-3 years, once	Asthma, Allergic Rhinitis	All covariates adjusted as stated: not specified what the covariates were	Asthma from NO_2: 1.77 (1.29-2.43) Allergic Rhinitis from NO_2: 1.67 (1.07-2.61) No association from SO_2 and PM10

Jedrychowski et al. [19], 2010, Krakow, Poland	Cohort Study	339	PAH, PM 2.5 + Personal Exposure Monitor	First or Second Trimester	Reported by Mothers	First 2 years of Child, every 2 months	Wheezing Days	Environmental tobacco smoke (ETS), gender of child, maternal characteristics (age, education and atopy), parity, and mold/dampness in the home	PAH 1.69 (1.52-1.88) PM 2.5 1.38 (1.25-1.51)
Lin et al. [18], 2021, Taichung, Taiwan	Cohort Study	140,911	PM 2.5 + Satellite-based hybrid model	30 gestational weeks - birth	Hospital Records	2.97 +/ 1.78 years, once	Allergic Rhinitis	All covariates adjusted as stated: not specified what the covariates were	1.025 (1.00 -1.05)
Wright et al. [20], 2021, US	Longitudinal cohort study	376	UFP + spatiotemporally	37 weeks	Maternal Reports	4 month intervals from birth to 30 months	Asthma	Maternal age, education, race, and obesity; child sex; nitrogen dioxide (NO_2) and temperature averaged over gestation	4.28 (1.41-15.7)
Guo et al. [14], 2020 Wuhan, China	Observational Cohort Study	332	SO_2, NO_2, PM10, PM2.5 + Air quality Monitoring stations	Second Trimester	Parents Reported	Not Specified	Allergic Diseases: Asthma, Allergic Rhinitis, Allergic Conjunctivitis or/and eczema	All covariates adjusted as stated: not specified what the covariates were	Mentioned diseases from NO_2 1.292 (1.005,1.662) Mentioned diseases from PM10 1.210 (1.042-1.405) Mentioned diseases from PM2.5 1.270 (1.004,1.606) No significant association from SO_2
Madsen et al. [13], 2017, Oslo and Bergen, Norway	Cohort Study	17,533	NO_2 + Lan Ude Regression	All trimesters	Maternal Surveys	0-6 Months, once	Lower Respiratory Tract Infections (syncytial virus, bronchiolitis, bronchitis and pneumonia) and Wheezing	Age at delivery, maternal marital status, maternal education, sex of child, maternal pre-pregnancy BMI, parity, year of birth, smoking during pregnancy, maternal atopy and area	0.99 (.84-1.17)

Rivera et al. [17], 2022, Mexico City, Mexico	Observational Cohort Study	535	PM 2.5 _ Satellite-based-spatio-temporal model	14 weeks - birth	Maternal Reports	6-8 years, once	Wheeze	Child sex, birth weight for gestational age z-score, maternal asthma, educational attainment at enrollment (<high school, some high school or high school graduate, >high school)	3.76 (1.41, 10)
Zhang et al. [16], 2021, Central China	Cross-sectional Questionnaire	5788	PM 1 Spatiotemporal Models	All trimester	Maternal Report	3-5 years, once	Asthma + Wheezing	Maternal smoking status, age at delivery, breast-feeding duration, birth weight, gestational week, family history, maternal education	1.618 (1.159-2.258) 1.543 (0.822-2.896)

exposure and safeguard the respiratory health of their children.

Regarding HAP prenatal exposure and child respiratory health, the inconsistent findings of previous studies might be attributed to different experimental outcome measures, geographical location, and more. For instance, the study investigating the association between HAP from solid fuel use (SFU) and child mortality in Myanmar [6] has some potential sources of inconsistency and limitations. Firstly, the use of proxies (fuel types and levels of SFU exposure) for HAP exposure might not fully capture the actual variability in different HAP concentrations among households, leading to imprecise exposure assessments. Additionally, it is important to note that this study focused on accounting for mortality resulting from respiratory infections rather than the occurrence of the respiratory infections themselves. Consequently, there might be cases where individuals experienced respiratory illnesses but did not have mortality related to them. There is a significant difference between morbidity and mortality concerning HAP prenatal exposure. For instance, the Ghana Randomized Prenatal and Postnatal Air Pollution and Health Study mentioned how HAP exposure can be associated with 18.5 million morbidities due to repository infections but only 210,000 deaths [11]. Similarly, the 2008 study by Derani might have employed a retrospective approach that might have limitations due to its reliance on previously collected data, heterogeneity, potential publication bias, and varying methodologies across studies [7].

The findings of the current study raise questions about the potential mechanisms underlying the increased risk of child respiratory illnesses due to each prenatal HAP exposure. First, the inhalation of fine particulate matter originating from HAP introduces many toxic substances, including metals, organic compounds, and combustion byproducts. PM2.5 and PM10 particles can penetrate deeply into the respiratory tract, triggering inflammation and oxidative stress. These processes disrupt lung development by impairing branching morphogenesis, alveolarization, and cellular differentiation, leading to altered lung structure and reduced functional capacity [21]. Additionally, the incomplete combustion of solid fuels releases CO which readily binds to hemoglobin, limiting oxygen transport and potentially affecting the oxygen-dependent processes crucial for lung maturation [22]. Volatile organic compounds such as benzene, formaldehyde, and toluene can cause airway irritation, inflammation, and cellular damage, disrupting normal lung function and increasing susceptibility to respiratory illnesses [23]. PAHs formed during incomplete combustion exert toxic effects on the developing respiratory system by interfering with critical signaling pathways and transcriptional regulators involved in lung cell differenti-

Table 3. Methodological Quality of Observational Studies Included in the Meta-Analysis

First Author, (Ref), Year, Country	Selection			Compatibility		Outcome			Quality Score (Out of 8)
	Representativeness of the exposed cohort	Selection of non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Lee et al. [12], 2019, Ghana , West Africa	✓		✓	✓	✓	✓	✓	✓	7
Kinney et al. [11], 2021, Ghana , West Africa	✓		✓	✓	✓	✓	✓	✓	7
Seeni et al. [10], 2018, US	✓		✓	✓	✓				5
Liu et al. [15], 2016, Shanghai, China	✓		✓	✓	✓	✓			6
Jedrychowski et al. [19], 2010, Krawkow, Poland	✓		✓	✓	✓	✓	✓	✓	7
Lin et al. [18], 2021, Taichung, Taiwan	✓		✓	✓	✓	✓			6
Wright et al. [20], 2021, US	✓			✓	✓	✓	✓	✓	7
Guo et al. [14], 2020, Wuhan, China	✓		✓	✓	✓	✓	✓	✓	7
Madsen et al. [13], 2017, Olso and Bergen, Norway	✓		✓	✓	✓	✓	✓	✓	7
Rivera et al. [17], 2022, Mexico City, Mexico	✓	✓	✓	✓	✓	✓	✓	✓	7
Zhang et al. [16], 2021, Central China	✓	✓		✓	✓	✓	✓	✓	7

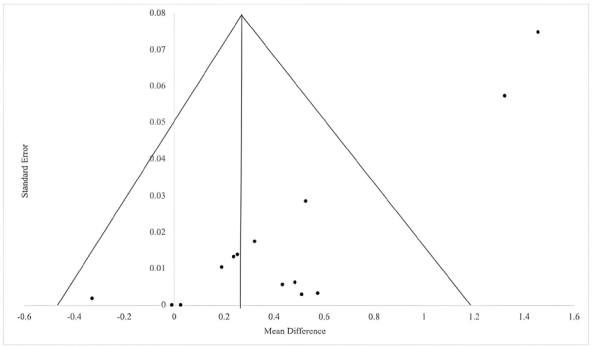

Figure 2. **Forest Plot of prenatal HAP exposure and child respiratory illness incident**.

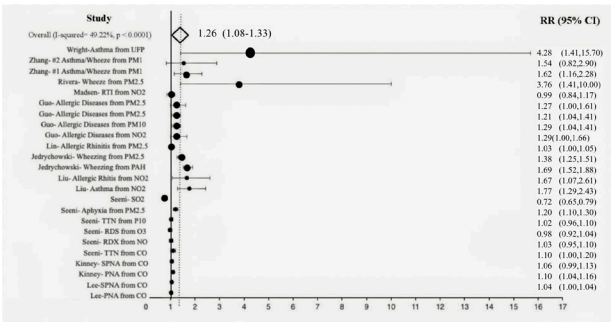

Figure 3. **Forest plots of prenatal exposure to specific pollutants (CO, NO_x, and PM) and child respiratory illness incident**.

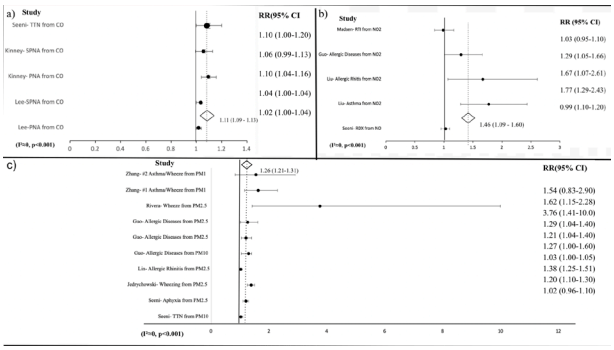

Figure 4. **Funnel plot corresponding to the random-effects meta-analysis of the relationship between prenatal HAP exposure and child respiratory illness incident**.

ation, proliferation, and repair mechanisms [24]. NO_x and SO_2, emitted during solid fuel combustion, can further exacerbate respiratory problems by inducing airway inflammation and damaging lung tissue [25]. The complex interplay of these pollutants with intricate developmental processes and delicate cellular interactions underscores the significance of understanding the intricate mechanisms by which maternal prenatal exposure to HAP impacts child respiratory health.

The strengths of the present meta-analysis lie in its quantitative analysis of the association of prenatal HAP exposure and child respiratory health using a large number of mother and child pairs (n=387 767). The large sample size of this meta-analysis provides strong power for the main analyses and the conclusions derived. Furthermore, numerous sensitivity analyses showed that the main findings were reliable. Quality assessment showed that all the studies included were at a low risk of bias. Also, although 10 studies were excluded due to the lack of risk estimates, results of these studies further support the link between prenatal exposure to HAP and child respiratory health incidents.

However, findings from the present meta-analysis should still be interpreted logically due to some limitations. First, the meta-analysis was prone to inherent recall and selection bias due to the inclusion of original observational studies. Furthermore, since almost half of the included studies measured respiratory illness presence with the use of questionnaires, self-report, they may not be fully accurate. Importantly, the statistical power of our meta-analysis was assessed to determine its ability to identify significant associations between maternal prenatal HAP exposure and child respiratory health outcomes. Based on the calculated statistical power values for each individual study, our meta-analysis demonstrated a statistical power of over 71.6%. This high level of statistical power was achieved for a range of effect sizes, with minimum OR values of 1.02 and maximum values of 4.28. Therefore, our meta-analysis exhibited the ability to detect meaningful associations even for modest effect sizes. Notably, the comprehensive data set and large sample sizes involved in our analysis contributed to the attainment of this considerable statistical power. It is worth mentioning that while our main analysis demonstrated strong statistical power, the limited available studies in certain subgroups (specifically looking at the individual relation of prenatal exposure to UFP, PAH, O_3, and SO_2 and child respiratory illness and symptoms) restricted the feasibility of performing a more detailed subgroup analysis.

These findings underscore the imperative for reducing household air pollution exposure and improving respiratory health. This necessitates the implementation of precisely tailored solutions and the development of specific products that cater to the unique requirements of local communities. To address CO, households can utilize affordable carbon monoxide detectors for early detection, along with improved chimney construction to channel CO outside the house [26]. For NO_x reduction, promoting the use of low-cost, improved cookstoves that burn solid fuels more efficiently can be effective, and encouraging clean energy alternatives like biogas or LPG (Liquefied

Petroleum Gas) can further lower NO_x emissions [27]. To tackle PM, households can switch to affordable, improved cookstoves with better combustion efficiency and consider low-cost ventilation solutions, such as adding mesh screens or exhaust fans to improve air circulation [28]. For PAH, promoting cleaner cooking fuels like LPG or biogas, as well as using low-cost improved cookstoves, can significantly reduce PAH emissions [28]. To address O_3 and UFP, introducing affordable air purifiers with appropriate filters and improving ventilation through measures like exhaust fans or window openings can help improve indoor air quality [29]. For overall indoor air quality, community-based programs can offer affordable or subsidized air quality interventions, and educational campaigns can raise awareness about HAP's health impacts and cleaner cooking practices. By adopting these specific solutions and products, communities can make significant strides in reducing HAP exposure and promoting better respiratory health for vulnerable populations.

CONCLUSIONS

The results of this meta-analysis provide insights into the association of prenatal HAP exposure with an increased risk of children's respiratory illnesses. These findings may help researchers to identify children at risk of respiratory illnesses early during pregnancy to provide targeted interventions.

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