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Ambient air pollution and Children's health: An umbrella review

Keshuo Liu[a,b], Huanhuan Zhang[b], Yacong Bo[b], Yao Chen[a], Panpan Zhang[a], Cunrui Huang[c], Zengli Yu[b,*], Zhan Gao[a,**]

[a] The Fifth Affiliated Hospital of Zhengzhou University, Zhengzhou, China
[b] School of Public Health, Zhengzhou University, Zhengzhou, China
[c] Vanke School of Public Health, Tsinghua University, Beijing, China

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ABSTRACT

The amount of data that is currently accessible on ambient air pollution and children's health has significantly increased. Although numerous systematic reviews and meta-analyses have evaluated the effect of air pollution on children's health, the results are mixed, including positive, negative, or null associations. The objective of this umbrella review is to thoroughly evaluate the validity of existing research on the connection between air pollution and children's health. We identified 33 systematic reviews of observational studies in which a diversity of health outcomes for children were reviewed, including mortality, respiratory diseases, hypertension, etc. According to our review's findings, being exposed to air pollution increases the chance of developing leukemia among children, as well as autism spectrum disorders, hypertension, otitis media, obesity, pneumonia, asthma, respiratory diseases, eczema, and allergic rhinitis. Additionally, there was a sizable positive association between air pollution and child mortality. The findings of this extensive umbrella review provide convincing proof that exposing children to air pollution increases the risk of developing multiple diseases. Our results have implications for strengthening childhood health care, reducing air pollution, and improving intergenerational equity.

1. Introduction

According to statistics, almost all people (99%) were exposed to concentrations higher than the WHO recommendation (5 μg/m^3 annual mean) (WHO, 2022), and 93% of children under 15 years of age breathe polluted air (WHO, 2018). 4.2 million premature deaths were brought on by ambient air pollution in 2016, with nearly 300,000 of those fatalities occurring in children under the age of five (Adair-Rohani, 2018). Due to their developing bodies and underdeveloped immunological and respiratory systems, children are especially vulnerable to the impact of air pollution (Lin et al., 2021a,b). A serious public threat to the health and welfare of people is air pollution. It has become the fourth leading risk factor for death after high blood pressure, tobacco use and poor diet. In the past, 40% of chronic obstructive pulmonary disease (COPD) and 192 million years of life lost (YLL) were associated with air pollution (IHME, 2023).

According to the studies we included, both developing and developed regions or countries are suffering from air pollution (Karimi and Shokrinezhad, 2020). The effects of toxic substances can begin before birth and continue into later life, in which the structural and functional development of certain organs is affected (Miller and Marty, 2010). Previous research has revealed that air pollution exposure can have an impact on the blood system (Gong et al., 2019), mortality (Karimi and Shokrinezhad, 2020), respiratory system (Orellano et al., 2018), nervous system (Liu et al., 2023), and circulatory system (Yan et al., 2021). It is also linked to metabolic disorders (Huang et al., 2022), allergic disease (Yue et al., 2022), and infectious disease (Lee et al., 2020), etc. In China, studies have shown that air pollution may increase the risk of death among children (He et al., 2022). In terms of the respiratory system, exposure to coarse particulate matter in infants (Lu et al., 2023a,b,c,d) and young children (Lu et al., 2022) may increase the risk of asthma, and allergic rhinitis (Lu et al., 2023a,b,c,d) and pneumonia (Lu et al., 2023a,b,c,d) in infants are also closely related to it. In addition, exposure to air pollution has been associated with autism spectrum disorders (Geng et al., 2019), elevated blood pressure (Zhang et al., 2020), allergies (Liu et al., 2020), and otitis media (Lu et al., 2023a,b,c,d) in children.

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* Corresponding author.
** Corresponding author.
E-mail addresses: zly@zzu.edu.cn (Z. Yu), 1657991676@qq.com (Z. Gao).

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Before this study, hundreds of epidemiological studies explored the effects of air pollution on children's health and conducted many systematic reviews and meta-analyses to synthesize these results; however, the conclusions are mixed. In addition, the majority of the previous studies focused only on one aspect of health outcomes. Since air pollution exposure is proposed to be linked to numerous health outcomes, the overall picture of air pollution exposure and health outcomes remains unclear from the available evidence, which may hinder the guide on children's care for clinicians and public health workers.

To provide researchers and public health professionals with more comprehensive and higher-quality evidence relating air pollution exposure to children's health, we conducted this umbrella review, detailing these links and synthesizing the available evidence to help children understand and prepare for air pollution. This work will protect children today and those who will come after them.

2. Methods

During the whole research process, the PRISMA statement (Table S1) (Page et al., 2021), the preferred reporting items for review overview (Table S2) (Gates et al., 2022), and the umbrella review guidelines (Aromataris et al., 2015) were followed. The protocol has been registered on PROSPERO (CRD42022371501).

2.1. Search strategy

PubMed, Scopus, Medline, Embase, the Web of Science, and the Cochrane Library were used as the main search engines for studies published up to October 8, 2022, and confined to studies published in English. During the literature search, we followed the PRISMA standards and the PRIOR (Preferred Reporting Items for Overviews of Reviews) statement. Supplementary materials provide a complete search strategy. (Table S3).

2.2. Eligibility criteria

PECOS(Participants, Exposure, Comparators, Outcomes, and Study design) was used as eligibility criteria. Children as "Participants", air pollution as "Exposure", "Comparator" stands for risk ratio (RR), odds ratio (OR), or hazard ratio (HR), "Outcome" refers to the various health outcomes of children exposed to air pollution, and "Design" means a review with or without meta-analysis (the focus is on reviews for which a meta-analysis has been performed). Exclusion criteria were as follows: narrative reviews, letters, conference abstracts, grey literature, and research protocols; genetic or experimental studies examining animals; or focused on non-general populations, such as occupational groups. The details are shown in Table 1.

Table 1
Eligibility criteria for this comprehensive review of the relationship between ambient air pollution and child health outcomes.

Element	Inclusion criteria	Exclusion criteria
Population	Children	Adult
Exposures	Outdoor air pollution	Indoor air pollution
Outcomes	Adverse health outcome	Adverse health outcomes not caused by exposure to air pollution
Review Design	Reviews of relevant quantitative observational epidemiologic research, including cohort, case-control, and cross-sectional studies, with or without the utilization of meta-analysis (the focus is on reviews for which a meta-analysis has been performed)	Narrative review Grey literature
Language	English	Non-English

2.3. Study selection

All identified records were imported into Endnote X9, and two researchers (KL and HC) worked alone to screen the title, abstract, and full text of the article and remove duplicate records. Disputes were resolved by consensus with the third author (ZY).

2.4. Data extraction

Information was collected separately by two authors (KL and HC), with inconsistencies resolved by a third researcher (ZY). For each eligible article, we extracted information as shown in Table S4. For each meta-analysis, the key information extracted was shown in Table S7.

2.5. Evaluation of the quality of methodology and evidence

After screening studies, the more specific and sensitive AMSTAR 2 was used instead of JBI to analyze study quality (Ferguson et al., 2022). Quality and credibility were also assessed using AMSTAR 2 (Shea et al., 2017). Detailed scoring items for AMSTAR 2 can be found in Table S5. In this review, we used the concept of recommendation grading, assessment, formulation, and evaluation (GRADE) to evaluate the evidence (Brozek et al., 2021). There are five deterioration criteria (limitation of research method, inconsistencies, impreciseness, possibility of publication bias, indirect) and three upgrade factors (large effect, dose effect, and confounding) in the GRADE system (Guyatt et al., 2011).

2.6. Data synthesis

Given associations of interest, they may be assessed in two or more reviews with overlapping results, which could bias findings and estimates. Therefore, we calculated the level of overlap between component studies using a citation matrix with a method name as the corrected covered area (CCA) (Nyadanu et al., 2022). The CCA was calculated using the following formula, where N is the sum of the number of included primary studies in the umbrella review, r again for the number of rows, and c for the number of columns. CCA >15% indicates a very high degree of overlap, 11–15% indicates high, 6–10% indicates moderate, and less than 5% is slight (Pieper et al., 2014).

$$\text{CCA}\ (\%) = \frac{N - r}{rc - r}$$

Systematic reviews without meta-analysis were narratively synthesized. Pooled estimates (e.g., number of primary studies, OR, and I^2 statistics, etc.) for the meta-analysis review were derived from the preliminary measurements provided. The reviews that underwent meta-analysis used forest plots for combined effect estimation.

3. Results

3.1. Literature search

Six databases yielded 15,502 records (Fig. 1). There were 5121 articles excluded due to duplication. After the initial screening, 91 articles proceeded to the full-text review stage. After further reading, 58 articles were eliminated for the following reasons: articles that were not written in English (n = 15); no systematic review or meta-analysis (n = 14); non-child health (n = 10); conference abstract (n = 13); no clear result (n = 6). In summary, 33 articles were identified as eligible for this umbrella review (30 with meta-analyses and 3 without meta-analyses). Three of these articles were on the blood system, two on mortality, two on the nervous system, fifteen on the respiratory system, three on the circulatory system, one on infectious diseases, three on metabolic systems, and four on allergic diseases.

The selected characteristics of the contained reviews were described in Fig. 2. A total of 526 primary studies from 51 countries were all

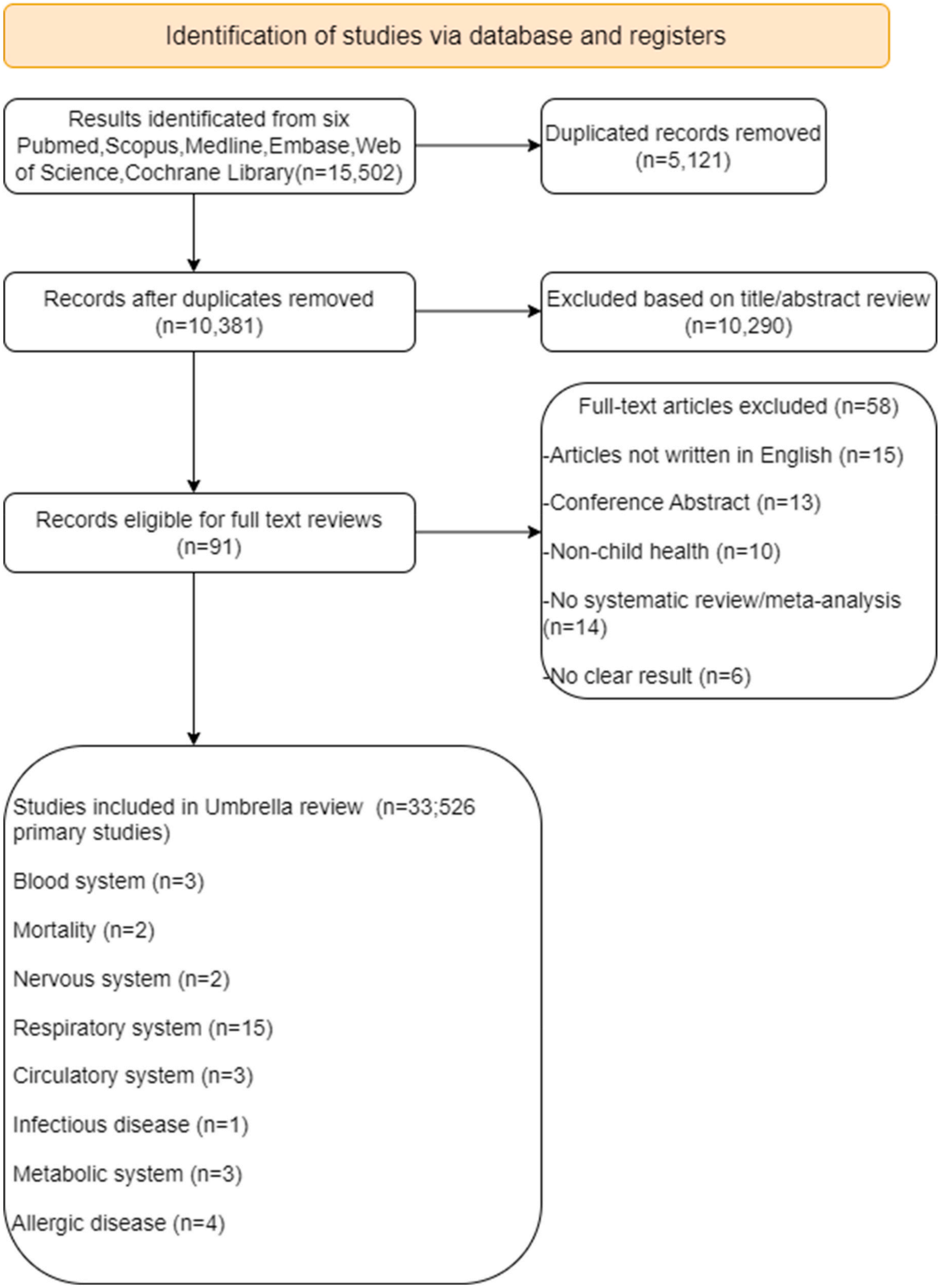

Fig. 1. Flowchart of the systematic search and selection process.

published after 2010, with a focus on the period from 2020 to 2022, including the United States (125), China (107), and Canada (35), among others (Table S8). There were 5–46 primary studies included within every meta-analysis, with an average of 16.

3.2. Risk of bias

The AMSTAR 2 scores of the 33 included articles were as follows: 6 (18.2%) were rated as high quality, 4 (12.1%) as moderate quality, 13 (39.4%) as low quality, and 10 (12.2%) as very low quality. According to

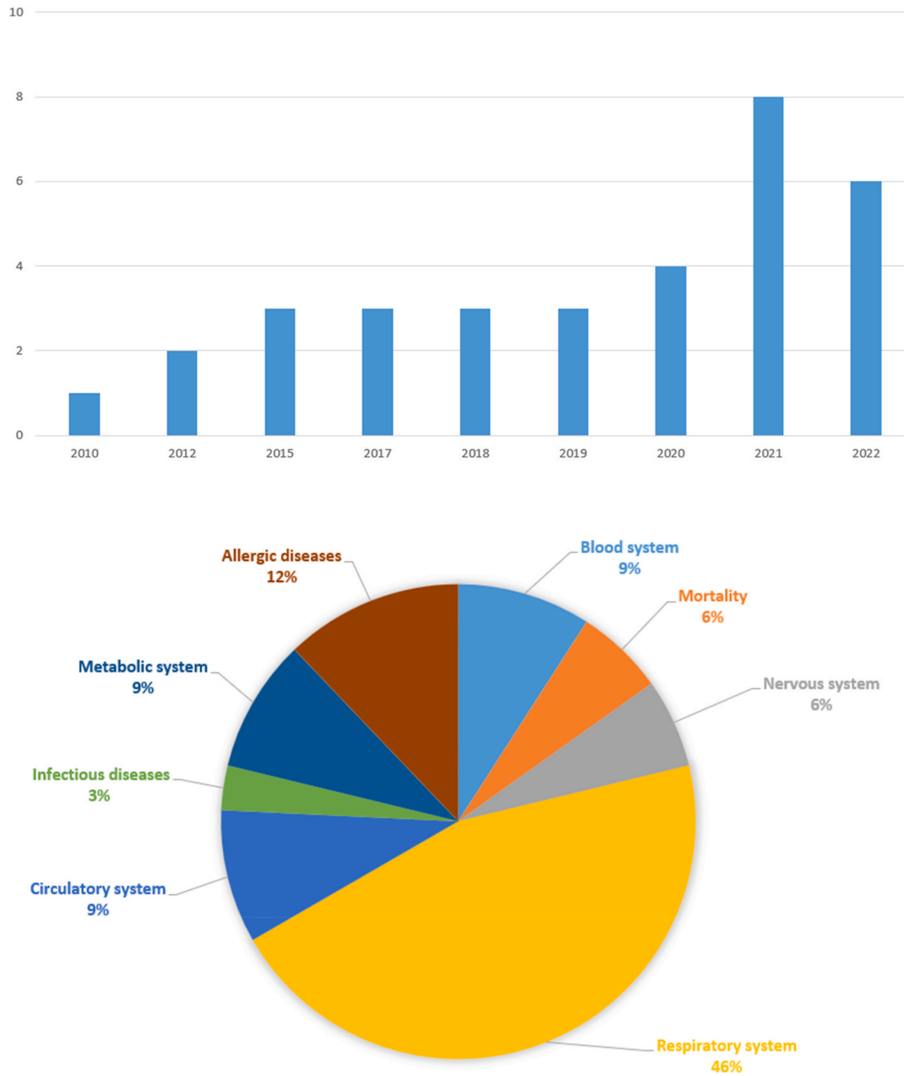

Fig. 2. Essential features of the studies included in this umbrella review. Date of publication of all included studies; Proportion of each health outcome.

GRADE criteria, each estimate was assessed for its quality of evidence. Six studies (18.2%) were evaluated as moderate, ten (30.3%) as low, and seventeen (51.6%) as very low among the 33 studies considered (Table S5).

3.3. Study overlap

The 33 eligible systematic reviews included 771 component studies, including 245 duplicates, of which 526 were unique component studies. The CCA was 1.23%, indicating a slight overlap.

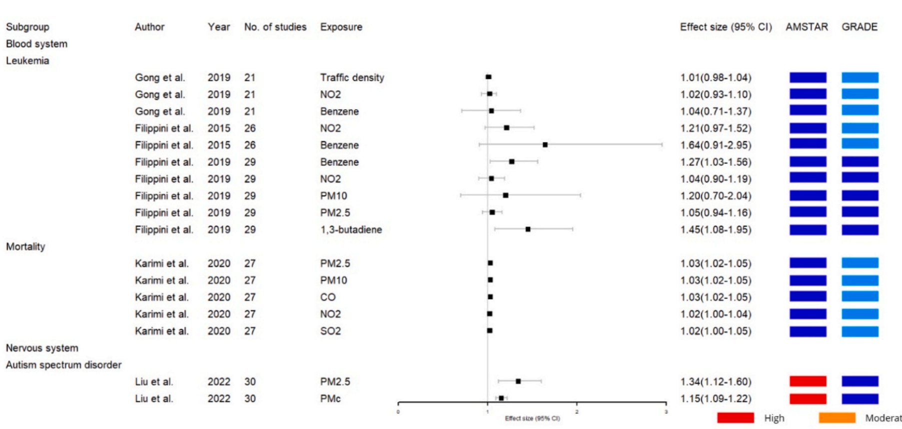

Fig. 3. Association between air pollution and the blood system, mortality, and nervous system.

3.4. Blood system

Three systematic reviews assessed the effect of air pollution on childhood leukemia (Gong et al., 2019; Filippini et al., 2015, 2019). Details of systematic reviews were shown in Table S4. As shown in Fig. 3, traffic density, NO_2, benzene, PM_{10}, $PM_{2.5}$, and 1,3-butadiene were found to increase childhood leukemia risk. Although all three studies found an association between air pollution and leukemia, only benzene (RR = 1.27 (95%CI:1.03, 1.56)) and 1, 3-butadiene (RR = 1.45 (95%CI:1.08, 1.95)) were significantly associated with the increased risk of leukemia (Filippini et al., 2019). There is moderate heterogeneity, as the heterogeneity test showed in most of the studies. Only a few research showed publication bias in their studies. According to the AMSTAR 2, all studies were graded low in terms of quality. On the other hand, when using GRADE, all studies were found to be assessed as low or very low.

3.5. Mortality

Based on the results of a meta-analysis (Karimi and Shokrinezhad, 2020) and a systematic review (Ibrahim et al., 2021), exposure to $PM_{2.5}$ (RR = 1.03 (95%CI:1.02, 1.05)), PM_{10} (RR = 1.03 (95%CI:1.02, 1.05)), CO (RR = 1.03 (95%CI:1.02, 1.05)), NO_2 (RR = 1.02 (95%CI:1.00, 1.04)), and SO_2 (RR = 1.02 (95%CI:1.00, 1.05)) was associated with a higher risk of child mortality (Fig. 3). According to AMSTAR 2, one study was graded as moderate and one study was graded as low. On the other hand, GRADE showed two studies rated as low or very low.

3.6. Nervous system

The relationship between air pollution and child autism spectrum disorder was studied in two meta-analyses (Lin et al., 2021a,b; Liu et al., 2023). Studies with high AMSTAR 2 scores indicate that exposure to $PM_{2.5}$ (RR = 1.34 (95%CI:1.12, 1.60)) and PM_{coarse} (PM_c, PM with an aerodynamic diameter between 2.5 and 10 μm) (RR = 1.15 (95% CI:1.09, 1.22)) was associated with an increased risk of autism spectrum disorder in children (Fig. 3). In addition, one study found that $PM_{2.5}$ exposure–response phenomenon, different concentrations of $PM_{2.5}$ have different effects on autism spectrum disorders. According to AMSTAR 2, one study was graded high and one study was graded low. On the other hand, GRADE showed two studies rated as low or very low.

3.7. Circulatory system

This research included three meta-analyses related to hypertension (Yan et al., 2021; Huang et al., 2021; Qin et al., 2021). Existing evidence shows that long-term exposure to PM_{10} (RR = 1.17 (95%CI:1.13, 1.21)) can raise blood pressure in children and affect the prevalence of hypertension. Three studies had sufficient evidence for long-term exposure, but there was relatively little evidence for short-term exposure. The AMSTAR 2 results showed that one study was rated high and two others were rated low or very low. When GRADE was used to grade the evidence for the included articles, one study was rated moderate, and the other two were rated very low.

3.8. Infectious disease

Included a study on the association of particulate matter with otitis media in children (Lee et al., 2020). Children were more likely to develop otitis media in environments with higher particulate matter concentrations. Compared with the increase of PM_{10} (RR = 1.01 (95% CI:1.01, 1.02)) concentration, the increase of $PM_{2.5}$ (RR = 1.03 (95% CI:1.01, 1.06)) concentration has a greater impact on otitis media (Lee et al., 2020). The level of evidence in this study was low according to AMSTAR 2 and GRADE standards.

3.9. Metabolic system

Three meta-analyses (Parasin et al., 2021; Huang et al., 2022; Bahreynian et al., 2019) showed that air pollution exposure, particularly particulate matter exposure, affects children's weight status and increases the risk of obesity. Among the studies with high AMSTAR 2 and moderate GRADE scores, PM_{10} (RR = 1.12 (95% CI: 1.06, 1.18)), $PM_{2.5}$ (RR = 1.28 (95% CI: 1.13, 1.45)), PM_1 (RR = 1.41 (95% CI: 1.3, 1.53)) and NO_2 (RR = 1.11 (95%CI:1.06, 1.18)) were significantly associated with obesity. The results of the heterogeneity test showed that most of the studies had high inter-study heterogeneity. Two studies were rated high by AMSTAR 2 and moderate by GRADE. The other study had low AMSTAR 2 and GRADE scores.

3.10. Respiratory system

Fifteen systematic reviews have shown that exposure to air pollution has a negative impact on children's respiratory health. (Fig. 4, Fig. 5, Fig. 6). The results of the heterogeneity test showed that most of the studies had high inter-study heterogeneity. Publication bias had only been revealed by a few studies. At least half of the studies in terms of quality were rated low or moderate by AMSTAR 2. On the other hand, GRADE considered the evidence from most of the included studies to be low or very low.

3.10.1. Respiratory diseases

Based on the results of two systematic reviews (King et al., 2018; Rodriguez-Villamizar et al., 2015) and two meta-analyses (Ziou et al., 2022; Zhang et al., 2022), a study with high AMSTAR 2 scores and moderate GRADE scores showed that children and adolescents were exposed to $PM_{2.5}$ (RR = 1.01 (95%CI: 1.00, 1.01)) and PM_{10} (RR = 1.02 (95%CI: 1.01, 1.02)), which may cause upper respiratory tract infection. Boys are more susceptible to short-term exposure to $PM_{2.5}$ than girls (Zhang et al., 2022). In addition, several remaining studies with low or very low AMSTAR 2 and GRADE ratings found an association between air pollutants and bronchiolitis hospitalizations and adverse effects on lung function.

3.10.2. Pneumonia

A meta-analysis found that PM_{10} (RR = 1.02 (95%CI: 1.01, 1.02)), $PM_{2.5}$ (RR = 1.02 (95%CI: 1.01, 1.03)), NO_2 (RR = 1.01 (95%CI: 1.01, 1.03)) 1.00, 1.02)), O_3 (RR = 1.02 (95%CI: 1.01, 1.03)) and SO_2 (RR = 1.03 (95%CI: 1.00, 1.05)) increased the short-term hospitalization for pneumonia in children. Even at low levels, PM2.5 pollution is still associated with pneumonia in children. Both AMSTAR 2 and GRADE scores were very low (Nhung et al., 2017).

3.10.3. Asthma

The results of 10 meta-analyses (Orellano et al., 2018; Orellano et al., 2017; Luong et al., 2019; Takenoue et al., 2012; Gasana et al., 2012; Weinmayr et al., 2010; Zhang et al., 2022; Yan et al., 2020; Bowatte et al., 2015; Han et al., 2021) show that both prenatal maternal exposure and early childhood exposure to air pollution are associated with child asthma incidence and prevalence, as well as asthma development and exacerbation. Studies with high AMSTAR 2 scores and moderate GRADE scores showed that $PM_{2.5}$ (RR = 1.07 (95%CI: 1.00, 1.13)), NO_2 (RR = 1.21 (95%CI: 1.12, 1.31)), benzene (RR = 1.11 (95%CI: 1.06, 1.17) and total volatile organic pollutants (RR = 1.06 (95%CI: 1.03, 1.1)) were significantly associated with the risk of asthma. The effects of $PM_{2.5}$ and NO_2 on asthma in Asia were higher than those in Europe and North America (Han et al., 2021). In addition, the degree of association between $PM_{2.5}$ and asthma increased with age (Bowatte et al., 2015).

3.11. Allergic disease

The effect of air pollution on allergic disease was examined in 4

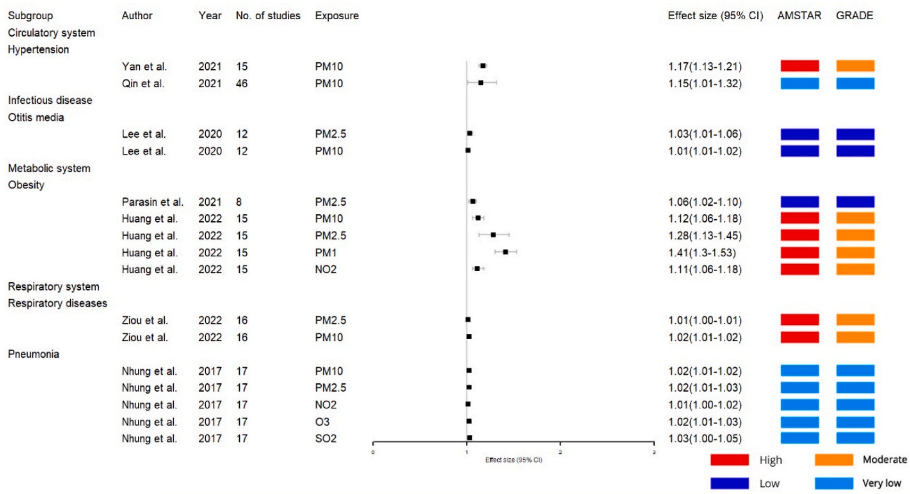

Fig. 4. Association between air pollution and the circulatory system, infectious diseases, metabolic system, and respiratory system.

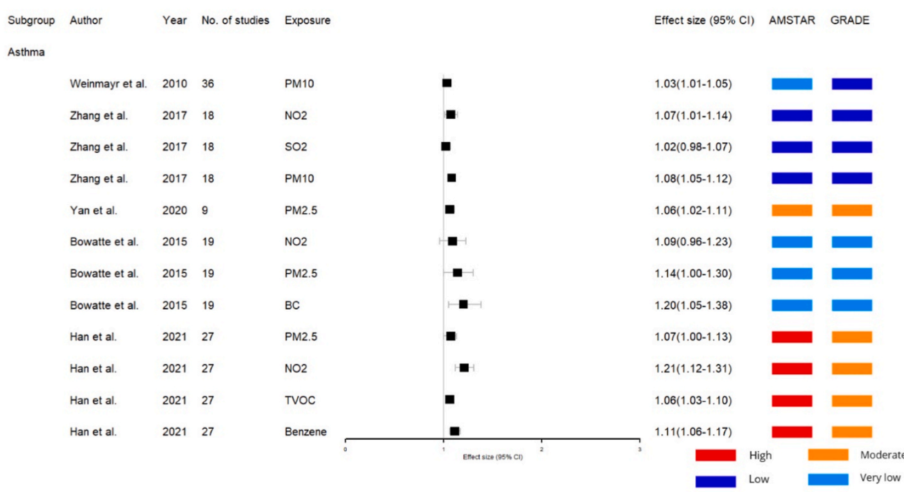

Fig. 5. Association between air pollution and the respiratory system.

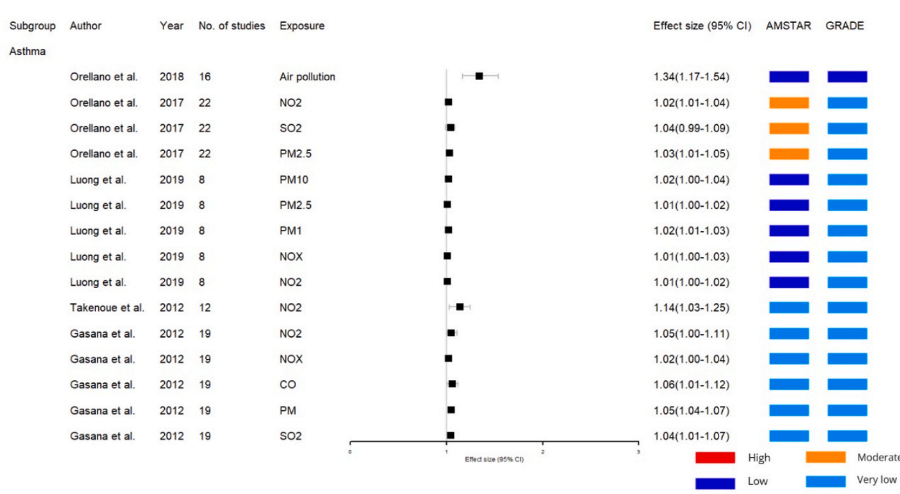

Fig. 6. Association between air pollution and the respiratory system.

systematic reviews (Fig. 7).

3.11.1. *Eczema*

Children's eczema risk was significantly associated with maternal prenatal exposure to nitrogen dioxide (RR = 1.13 (95%CI: 1.06, 1.19)),

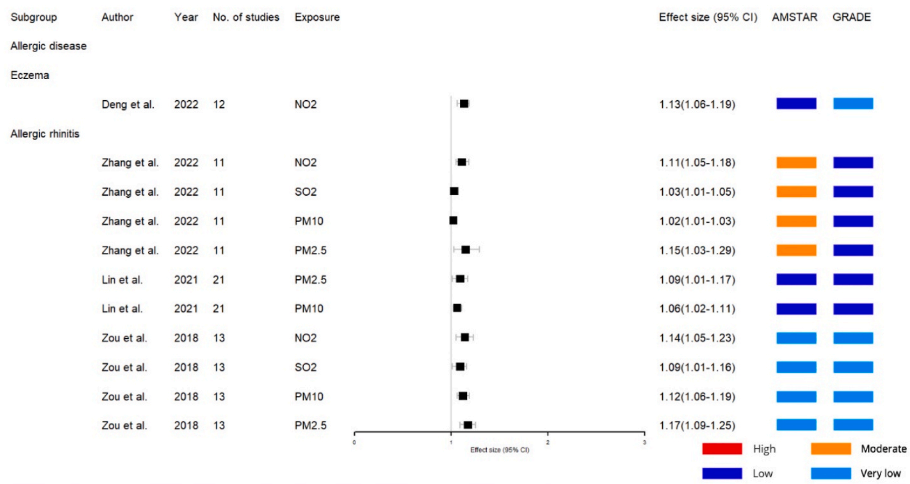

Fig. 7. Association between air pollution and allergic diseases.

particularly during the first and second trimesters (Yue et al., 2022). The study was rated low by AMSTAR 2 and very low by GRADE.

3.11.2. Allergic rhinitis

The results of three meta-analyses (Zhang et al., 2022; Lin et al., 2021a,b; Zou et al., 2018) suggest that exposure to NO_2 (RR = 1.11 (95% CI: 1.05, 1.18)), SO_2 (RR = 1.03 (95%CI: 1.01, 1.05)), PM_{10} (RR = 1.02 (95%CI: 1.01, 1.03)), and $PM_{2.5}$ (RR = 1.15 (95%CI: 1.03, 1.29)) may increase the risk of allergic rhinitis in children. Furthermore, particulate matter poses a greater threat than gaseous pollutants, and $PM_{2.5}$ is more likely to affect developing countries and regions, especially China. PM_{10} is more likely to have an impact on developed countries and regions. The AMSTAR 2 scores for the three studies were moderate, low, and very low, and the GRADE scores were low and very low, respectively.

4. Discussion

4.1. Main findings

A total of 33 systematic reviews were identified in this review (30 meta-analyses were performed and 3 were not performed), including 3 on the blood system, 2 on mortality, 2 on the nervous system, 3 on the circulatory system, 1 on infectious diseases, 3 on the metabolic system, 15 on the respiratory system, and 4 on allergic disease. Overall, we observed that air pollution exposure can increase the risk of leukemia, autism spectrum disorders, hypertension, otitis media, obesity, pneumonia, asthma, other respiratory diseases, allergic rhinitis, eczema, and childhood mortality.

This umbrella review had a slight overlap (1.23% CCA). So far, no other umbrella reviews that have been written and published that may be compared with this have been found. While it is widely recognized that different pollution levels can have differing toxic and health effects, low-level exposure to air pollution is often underestimated. Certain diseases have been linked to even relatively low concentrations of ambient air pollution (Nhung et al., 2017). The association was more significant for particulate matter than gaseous pollutants for increased risk of childhood death (Karimi and Shokrinezhad, 2020). Among particulate matter, $PM_{2.5}$ is more harmful to allergic rhinitis in children than PM_{10}, possibly because its aerodynamic equivalent diameter is smaller and it can enter deeper airways (Lin et al., 2021a,b). Further, air pollution exposure and physical health are more closely related for boys than for girls because boys tend to spend more time outdoors than girls (Zhang et al., 2022). Assessment of ambient air pollution exposure may be an important source of heterogeneity, and there are many assessment methods, such as air station monitoring data, temporal and spatial-temporal models, etc. Some used the spatial-temporal variation, while others didn't (Yan et al., 2021).

Air pollution is composed of a variety of pollutants, but particulate matter is the most representative and harmful to human health (Lin et al., 2021a,b), among which fine particles are more dangerous than coarse particles. Therefore, this paper summarizes the effects of $PM_{2.5}$ on children's health. PM2.5 affects the neurodevelopment of early children and is significantly associated with autism spectrum disorders (Lin et al., 2021a,b). PM2.5 is associated with increased systolic and diastolic blood pressure and can affect the cardiovascular system through various mechanisms (Huang et al., 2021). Short-term increases in PM2.5 concentration may be associated with the development of otitis media (Lee et al., 2020). PM2.5 can not only affect body weight through direct mechanisms, but also lead to obesity through some indirect forms, such as affecting sleep and leading to weight gain (Parasin et al., 2021). There is some association between long-term exposure to PM2.5 and hospitalization for bronchiolitis, but the results are not very consistent among studies (King et al., 2018). However, short-term or long-term exposure to PM2.5 can significantly reduce lung function (Zhang et al., 2022). It is also associated with hospitalization for pneumonia in children (Nhung et al., 2017). PM2.5 is not only associated with wheezing related diseases in children (Orellano et al., 2017), but also can aggravate asthma (Luong et al., 2019). In addition, exposure to PM2.5 is also associated with allergic rhinitis in children (Zhang et al., 2022; Lin et al., 2021a,b; Zou et al., 2018). It is also because of the association of PM2.5 with multi-system diseases that it is further associated with child mortality (Karimi and Shokrinezhad, 2020).

The majority of studies were from the United States and China (44.11%, Table S8). With relatively few studies from developing regions and a lack of data on high pollution levels or vulnerable populations, the call for an investigation in LMICs cannot be overemphasized in the future.

4.2. Biological plausibility

Air pollution and childhood leukemia are associated primarily with benzene, according to biological evidence. Benzene metabolites can cause DNA damage through a variety of mechanisms, and benzene is therefore considered to be a hemotoxic substance and a leukemic progenitor (Whysner et al., 2004). The underlying mechanism by which air pollution contributes to child deaths has not been elucidated, but the process should be related to children's immature immune system and respiratory system (Karimi and Shokrinezhad, 2020). At present, the mechanism of allergic rhinitis caused by particulate matter is not clear. For asthma, common air pollutants may cause or aggravate asthma through different mechanisms. Exposure to particulate matter may trigger airway inflammation and oxidative stress and may further cause asthma (Orellano et al., 2018). The mechanism by which particulate matter causes autism spectrum disorders in children has not been clarified. Although the specific mechanism of particulate matter causing hypertension is not clear, it is believed to be related to oxidative stress and inflammation caused by exposure to particulate matter. In addition, particulate matter can cause endothelial dysfunction and an imbalance of vascular homeostatic responses, which may result in an increase in blood pressure (Brook and Rajagopalan, 2009). The exact role that particulate matter plays in the development of children's otitis media is unknown. However, particulate matter can affect the occurrence and development of otitis media by promoting cell apoptosis (Song et al., 2012). The mechanisms that link air pollution exposure to childhood obesity are unclear. But it has been linked to oxidative stress, inflammation, and insulin resistance caused by air pollution. In addition, air pollution may reduce people's desire for outdoor activities (Huang et al., 2022; Bahreynian et al., 2019). Air pollution during pregnancy may increase the risk of childhood eczema and allergies through an unknown mechanism. Oxidative stress can also damage the skin barrier (Yue et al., 2022; Ahn, 2014).

4.3. Strengths and limitations

This evaluation of the umbrella provides a number of benefits. First, this umbrella review provides a comprehensive overview of the effects of air pollution on children's health. We conducted a comprehensive literature search and included a large number of studies, including 33 systematic reviews and 526 primary studies covering health outcomes for 7 to 25,704,288 participants in 9 different systems or organs. Second, the PRISMA guidelines and the PRIOR statement were used to achieve this review of methodological rigor. Third, this study achieved visual presentation and comparative analysis of the results of each review, which can assist and guide the work of healthcare decision makers. Fourth, the results of CCA calculations indicate a slight degree of overlap. Several limitations should be considered. First, our study is restricted to English publications, which may limit the general applicability of the research results; however, it appears to have little effect on the conclusions (Dobrescu et al., 2021; Morrison et al., 2012). Second, there were more studies in the United States (125/526) and fewer studies in areas with less developed economies or high pollution levels, which may have led to selection bias. However, this umbrella review included component studies in both highly polluted (China) and less polluted (USA) settings. Third, common child health outcomes have been more intensively studied than others. Based on such studies with small sample size or few cases, the results of observational studies are inevitably biased. In addition, children often face the common harm of multiple pollutants, and it is difficult to distinguish the separate effects of a pollutant and the combined effects of multiple pollutants. Fourth, primary studies with prospective or retrospective designs can lead to bias and confounding. Although the most important confounding factors were controlled in most of the preliminary studies (65.02% for the gender of the child and 42.59% for the age of the child), residual confounding could not be completely excluded. Fifth, the unavoidable high heterogeneity. This might be due to regional variations in exposure levels, illness definitions, and exposure evaluation approaches. Conclusions should be interpreted and applied with full consideration of the strengths and limitations of this umbrella analysis.

4.4. Implications for research and public health

Children of various ages were included in the original studies since the great majority of them did not limit the age of the children. For children, who grow and develop at a faster rate, the effects of air pollution may be different at different ages. Therefore, future researchers should take the age of the children into account and try to include studies where the children are close in age. This will also allow for a more precise implementation of conservation measures.

There is an old saying in China: better safe than sorry. Given the possibility of epidemiological evidence that may link exposure to ambient air pollution in children to poor health, the precautionary principle needs to be considered, which states that "Precautions should be taken when an activity presents hazards to the environment or human health, despite the fact that certain cause-and-effect relationships are not fully established by science" (Hooper and She, 2003). The preventive measures to reduce threats are significant for air pollution since it frequently exhibits persistent positive connections with adverse health outcomes, notwithstanding the difficulties in proving causation with certainty. Healthcare professionals are better placed to inform children and their parents about the potential hazards of exposure to ambient air pollution and the need for targeted preventive action, such as reducing outside activities, wearing particle filters or masks in places with low air quality, and adopting air quality when choosing a residential location. Despite the fact that WHO air quality guidelines have established maximum levels for air pollutants, it does not appear that these levels are sufficient to ensure that infants are protected from air pollutants, so it is of benefit to present and future generations to reduce the maximum levels in the future.

5. Conclusions

This comprehensive umbrella review shows that children who are exposed to air pollution are at greater risk of developing leukemia, allergic rhinitis, pneumonia, asthma, and autism spectrum disorders, as well as significant associations with child mortality, hypertension, otitis media, obesity, and eczema. This comprehensive umbrella review highlights the development and implementation of preventive measures to reduce global air pollution alert levels. Future studies should consider the health effects of exposure to air pollution in children at different ages.

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Data availability

Data will be made available on request.

CRediT authorship contribution statement

Keshuo Liu: Writing – original draft, Conceptualization, Funding acquisition, Visualization, Validation. **Huanhuan Zhang:** Visualization, Methodology, Data curation, Writing – review & editing. **Yacong Bo:** Methodology, Data curation. **Yao Chen:** Investigation, Resources, Methodology, Data curation. **Panpan Zhang:** Writing – review & editing, Funding acquisition. **Cunrui Huang:** Conceptualization, Writing – review & editing, Data curation. **Zengli Yu:** Conceptualization, Validation, Investigation, Data curation, Writing – review & editing. **Zhan Gao:** Validation, Investigation, Writing – review & editing.

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.2024.102108.

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