Short-term and long-term effects of air pollution on acute lower respiratory infections incidence and mortality: an overview and critical appraisal of systematic reviews

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Shareable abstract (@ERSpublications)
Air pollution, especially from $PM_{2.5}$ and NO_2, is linked to higher risk of acute lower respiratory infections mortality and incidence. Rigorous systematic reviews are needed to better assess short-term effects and support public health policies. https://bit.ly/46URsls

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Abstract

Background Acute lower respiratory infections (ALRIs) are a significant health concern, particularly affecting children and older adults. Air pollution is a known risk factor. Despite numerous systematic reviews exploring this relationship, varying methodological quality hinders the derivation of reliable concentration–response functions essential for health risk assessment.

Methods We critically appraised systematic reviews investigating the association between air pollution and ALRI incidence and mortality, evaluating both short-term and long-term effects across age groups. Comprehensive searches were conducted in PubMed and Embase (up to November 2024). Included systematic reviews were evaluated using AMSTAR2-EH (A MeaSurement Tool to Assess systematic Reviews-Environmental Health), assessing methodological quality specific to environmental epidemiology.

Results Among 330 unique systematic reviews, 15 met inclusion criteria. Short-term systematic reviews did not meet methodological appraisal standards. Studies on other pollutants, like ozone (O_3) and sulfur dioxide (SO_2), lacked conclusive methodologically high-quality evidence. Long-term systematic reviews generally demonstrated methodological rigour, linking nitrogen dioxide (NO_2) exposure to ALRI incidence in children (relative risk 1.09, 95% CI 1.03–1.16) and ALRI mortality in adults (relative risk 1.06, 95% CI 1.02–1.10 and 1.08, 95% CI 1.04–1.12 for NO_2; relative risk 1.204, 95% CI 1.095–1.325 for particulate matter with a 50% cut-off aerodynamic diameter of 2.5 µm ($PM_{2.5}$)).

Conclusions This overview systematically assessed systematic reviews using AMSTAR2-EH, highlighting methodological gaps, particularly in short-term studies, bias assessment and protocol registration. Overall, the evidence suggests a mild but significant association between short-term exposure to air pollutants and pneumonia incidence, and a stronger, more consistent association between long-term exposure and ALRI

incidence and mortality, especially for NO_2 and $PM_{2.5}$. These findings can inform public health policies and environmental regulations aimed at reducing respiratory disease burden due to air pollution.

Introduction

Acute lower respiratory infections (ALRIs) represent a persistent and widespread public health challenge. This term encompasses a range of infections, including pneumonia, acute bronchitis and bronchiolitis, which are prevalent and potentially fatal diseases, particularly affecting children and older adults [1]. ALRIs are a leading cause of mortality worldwide [2], with approximately 488.9 million incident cases and 2.4 million deaths attributable to lower respiratory tract infections in 2019 [1]. Although global incidence and mortality have declined over the past three decades, the health and economic impacts of ALRIs remain remarkable [2, 3].

Beyond their impact on mortality, ALRIs contribute to considerable healthcare and social costs worldwide. Hospitalisations, prolonged treatment and complications such as respiratory failure contribute to substantial medical costs and resource consumption [4, 5]. Additionally, indirect costs, including long-term disability [6] and an increased risk of severe complications such as myocardial infarction [7, 8], stroke [7, 8] and heart failure [9], further underscore the socioeconomic impact of these infections, particularly in low-income and middle-income countries, where access to healthcare and preventive measures may be limited [10–12].

Air pollution is a global concern and is recognised as one of the major environmental risk factors for mortality [13], the leading cause of morbidity [14] and the main risk factor contributing to disability-adjusted life years (DALYs) [15]. Although air quality has improved in some countries [16, 17], 99% of the world's population still lives in areas where pollution levels exceed World Health Organization (WHO) guideline limits [18]. In 2019, ambient outdoor air pollution was responsible for approximately 4.2 million premature deaths worldwide, primarily due to exposure to fine particulate matter (PM), a major contributor to cardiovascular and respiratory diseases as well as cancer [19].

Among the various diseases associated with air pollution, ALRIs contribute significantly to its health burden. According to WHO estimates, 14% of air pollution-related deaths result from ALRIs [19], while the Global Burden of Disease Study 2019 highlighted that 14% of DALYs due to lower respiratory tract infections were attributable to ambient PM [1]. Several biological mechanisms may explain this association, including increased airway inflammation, impairment of macrophage function leading to reduced pathogen clearance, altered expression of cellular receptors facilitating infection and disruptions in the lung microbiome [20].

Extensive research has explored the relationship between air pollution and ALRIs, assessing both short-term and long-term effects on morbidity and mortality in different populations. However, for an accurate health risk assessment (HRA), including calculation of the burden attributable to air pollution, it is essential that robust concentration–response functions (CRFs) derived from systematic reviews and meta-analyses are available. CRFs provide statistical estimates of the relationship between pollutant exposure and health outcomes, using pollutant concentrations as proxies for outdoor exposure levels.

A recent study reviewed the existing systematic reviews and meta-analyses to derive CRFs for the long-term effects of air pollution on a range of outcomes, including ALRI incidence [21]. The authors proposed a comprehensive strategy for selecting appropriate CRFs and introduced a novel tool for evaluating the methodological quality of systematic reviews in environmental epidemiology: an adapted version of AMSTAR2, named AMSTAR2-EH (A MeaSurement Tool to Assess systematic Reviews-Environmental Health) [22].

The incidence of ALRIs substantially contributes to the burden on healthcare systems. To date, strong evidence shows causal relationships between exposure to long-term PM with a 50% cut-off aerodynamic diameter of 2.5 µm ($PM_{2.5}$) and mortality from ALRIs [23]. Moreover, consistent findings highlight the short-term impact of air pollution on ALRIs, particularly in children [24, 25], because environmental PM can trigger oxidative stress and inflammation in lung tissues directly and can also enter the bloodstream through the respiratory tract. Building on the approach proposed by Forastiere *et al.* [21], our study specifically focuses on ALRI outcomes and expands the scope of their appraisal by including both incidence and mortality, considering both short-term and long-term exposures. This allows for a more targeted assessment of the available evidence and for the identification of robust CRFs suitable for HRAs specific to ALRIs.

This study aims to bridge a critical gap in the literature by systematically evaluating the methodological quality of existing systematic reviews and meta-analyses on the association between air pollution and ALRI, with a particular focus on both short-term and long-term effects on incidence and mortality in adults and children. By identifying robust CRFs, this research will contribute to improving HRAs and refining estimates of the burden of disease attributable to air pollution. These findings have important implications for public health policies, because more reliable CRFs can enhance air quality guidelines, inform regulatory standards and support targeted interventions to mitigate the impact of air pollution on respiratory health. Moreover, by applying the newly developed AMSTAR2-EH tool, this study will provide insights into the methodological strengths and limitations of current evidence syntheses in environmental epidemiology, potentially guiding future research toward more rigorous and transparent systematic reviews.

Methods

Literature search strategy

Although we did not publish a formal protocol in advance, we formulated a PECOS (Population, Exposure, Comparator, Outcome and Study) question prior to the conduct of the review and followed an internal review protocol, based on a set of rules and procedures that were shared and agreed upon with the expert panel through the process. The PECOS question was: in a general population (P), including subgroups of susceptible individuals, adults and children, what is the increase in the health risk of ALRI incidence and mortality (O) associated with short-term and long-term exposure to ambient air concentrations of PM with a 50% cut-off aerodynamic diameter of 1 µm (PM_1), 2.5 µm ($PM_{2.5}$) and 10 µm (PM_{10}), carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen dioxide (NO_2) and ozone (O_3) (E), compared to individuals exposed to lower levels of the same pollutant (C), as reported in systematic reviews with meta-analysis (S)? The complete formulation of the PECOS question, along with detailed inclusion and exclusion criteria, is available in table 1. In summary, we excluded studies conducted on animals as well as those focusing on occupational, indoor or specific exposures not related to general air pollution. ALRIs are defined as infections of the lower respiratory tract, primarily affecting the bronchi and lungs. In this study, ALRIs included pneumonia, acute bronchitis and bronchiolitis as the representative health outcomes. We included studies that defined ALRI morbidity based on hospital records, questionnaires or physician-diagnosed ALRI. Consistent with the approach adopted by the Health Effects Institute (HEI) panel [26], we considered all ALRI morbidity studies as incidence studies, given the acute nature of these infections and the expected absence of the condition prior to diagnosis or between recurrent episodes in the same individual.

We conducted a comprehensive search of the PubMed database (up to April 2024) and Embase (up to June 2024). The full search strategies are described in supplement 1.1: search strategies. In November

TABLE 1 Inclusion and exclusion criteria for each PECOS domain

	Inclusion criteria	Exclusion criteria
Population	All studies conducted on the general population, including both adults and children, will be considered, with no restrictions based on residence or nationality.	Studies conducted on animals.
Exposure	Both short-term and long-term exposures to PM_1, $PM_{2.5}$, PM_{10}, carbon monoxide, nitrogen dioxide, sulfur dioxide and ozone will be considered. Studies evaluating the health effects of traffic exposure and multi-pollutant studies will also be included.	Occupational exposures, indoor exposures, active and passive smoking, as well as specific exposures other than general air pollution (*e.g.* dust, industrial point sources). Studies that consider only the distance from roads as the exposure.
Comparator	Controls will be defined as individuals exposed to lower levels of air pollution within the same population or a reference population.	Studies that use working populations as a comparison group.
Outcomes	Acute lower respiratory infection, pneumonia, bronchiolitis, bronchiolitides, bronchitis, bronchitides, bronchitis.	COVID-19, chronic bronchitis, bronchiectasis.
Study	Only systematic reviews with meta-analysis will be considered. Studies assessing incidence, mortality, prevalence, *etc*. will be included, difference will be highlighted during data extraction. All studies will be included regardless of the administrative source used (*e.g.* hospital discharge records, emergency department data, mortality records), with sources distinguished during data extraction.	Narrative reviews and non-peer-reviewed articles.

PM_x: particulate matter with a 50% cut-off aerodynamic diameter of x µm.

2024, we updated the search to capture newly published studies by reviewing articles identified through a PubMed automatic alert, which had been set up immediately after the initial search in April 2024 using the same search string reported in supplement 1.1. This approach was implemented to ensure the inclusion of the most recent and relevant evidence prior to manuscript submission. Duplicate records were manually removed prior to screening. Articles published in languages other than English were translated before evaluation.

Studies were initially selected based on their title and abstract, provided they met the selection criteria defined in the PECOS formulation, and shared with the working group. This first screening was conducted by four authors, working independently in pairs, using the online tool CADIMA [27]. Articles meeting the inclusion criteria underwent full-text screening by 13 reviewers, who worked independently in six pairs, according to the selection criteria defined in the PECOS formulation. The authors were invited to reach consensus on inclusion, and any disagreements in either screening phases were resolved by a third reviewer.

Methodological appraisal using the AMSTAR2-EH tool

Articles that passed the second screening phase were critically appraised using the AMSTAR2-EH tool [21], which builds upon the original AMSTAR2 checklist [22] with adaptations specific to environmental epidemiology. Its purpose is to provide a structured framework for critically appraising the methodological quality of systematic reviews in this field. The tool includes 21 items: 12 derived (with minor modifications) from AMSTAR2, and nine new items developed specifically for environmental epidemiology. Five of these are designated as "critical" domains, which are essential for the reliability of a systematic review. According to the proposed criteria by Forastiere *et al*. [21], a systematic review can be considered a credible source of CRFs for HRA only if it satisfies all five critical items. Additionally, it may fail no more than four noncritical criteria, with overall credibility increasing as the number of unmet noncritical criteria decreases. Consistent with this distinction, in our study we adopted the same threshold to define methodologically high-quality systematic reviews.

Additionally, for this review, the working group decided to apply the AMSTAR2-EH tool sequentially. Specifically, the first 12 questions were initially assessed. The remaining nine criteria were evaluated only if the systematic review met critical items Q6 and Q8, and at least four noncritical items among the first 12. This strategy ensured that the extended assessment was conducted only for systematic reviews that met minimum completeness and transparency standards. Moreover, the group established that a positive ("Yes") rating for any item required that all sub-criteria listed under that item be fully satisfied. If relevant information was missing, the item was rated as "No". For item Q6 specifically, a "Yes" required at minimum a flow diagram of the study selection process and a general explanation for excluded studies.

The same pair of reviewers independently completed the appraisal after full-text screening inclusion. They then reached a consensus on each item, with any disagreements resolved by a third reviewer.

Assessing the quality of evidence

Because this study is an overview and critical appraisal of systematic reviews, we did not perform a new certainty assessment using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework [28]. However, we extracted whether each included systematic review applied GRADE to the primary studies, as well as the level of certainty reported.

Data extraction

Data extraction was conducted independently by two authors. In case of disagreement, conflicts were resolved through discussion and consensus. The extracted information included the target population (adults, children or both), outcome, exposure, exposure contrasts, health information sources (*e.g.* mortality records, hospital admissions, emergency department visits or registries), International Classification of Diseases 9th or 10th revision (ICD-9/10), effect duration (short-term or long-term), lag considered for short-term effects, effect type (*e.g.* odds ratio (OR), relative risk, hazard ratio (HR)), effect estimate with its 95% confidence interval (CI), meta-analysis heterogeneity and number of meta-analysed studies.

Where systematic reviews referred to extended reports or companion documents, these were retrieved and consulted. If relevant data were not fully reported in the published systematic review, the missing information was extracted directly from the supplementary material or original reports where available.

Results

The Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) 2020 flowchart describing the study selection process is presented in figure 1. A total of 419 studies were identified through the literature search, included five studies added in November 2024 *via* the automatic PubMed alert. After removal of duplicates, 330 records were screened by title and abstract according to the inclusion and exclusion criteria described in table 1. Of these, 297 studies were excluded based on title and abstract screening (see supplement 2 for a full list of excluded studies) and 33 studies were selected for full-text evaluation.

Following full-text assessment, 18 were excluded for not meeting at least one PECOS component. The reasons for exclusion are summarised in figure 1 and detailed with specific justification in supplement 2. Specifically, one study [29] was excluded for not meeting the criteria for exposure, comparator and outcome; two studies [15, 30] were excluded for not meeting the criteria for comparator, outcome and study type; one study [31] was excluded for not meeting the criteria for comparator and study type; four studies [32–35] were excluded for not meeting the criteria for exposure; two studies [36, 37] were excluded for not meeting the criteria for exposure and comparator; two studies [38, 39] were excluded for not meeting the criteria for exposure, comparator and study type; one study [40] was excluded for not meeting

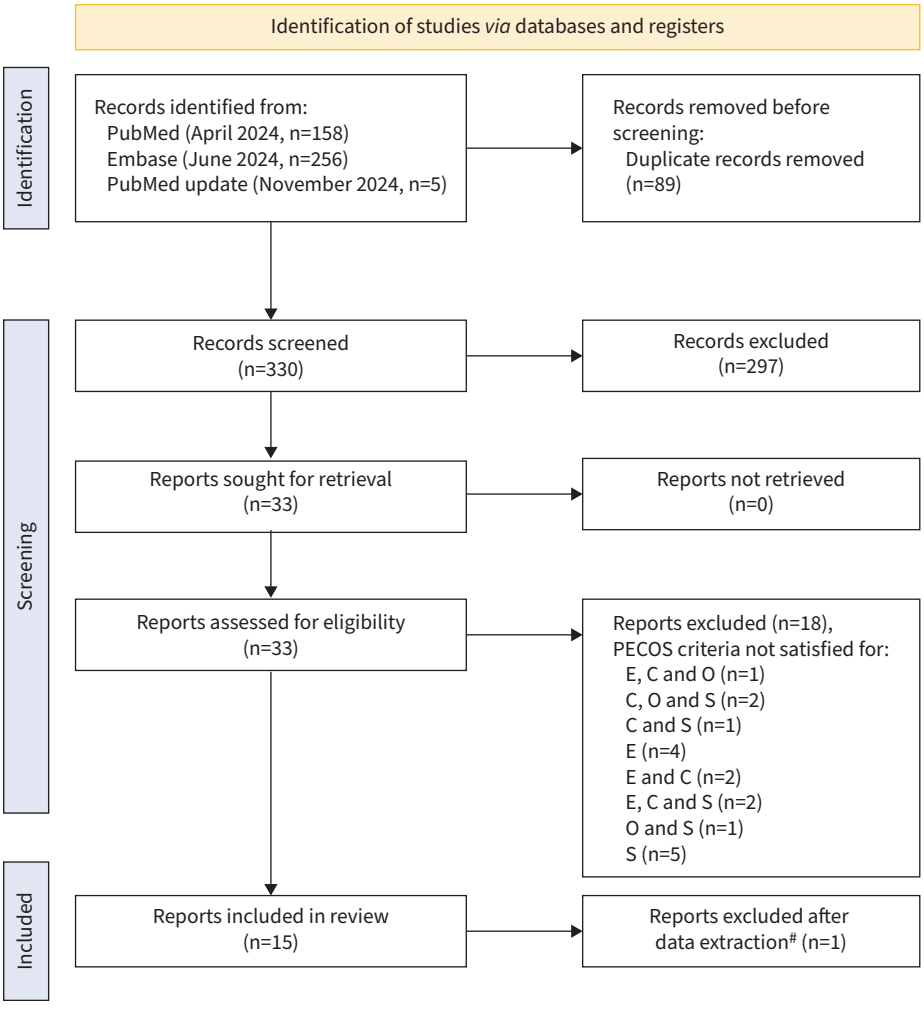

FIGURE 1 Preferred Reporting of Items for Systematic reviews and Meta-analyses (PRISMA) 2020 flowchart of studies through the review process. The number of studies failing to satisfy PECOS criteria are provided, along with the criteria failed. P: population; E: exposure; C: comparator; O: outcome; S: study. #: one study was excluded after data extraction due to its focus on seasonal stratification, which was not aligned with the aims of the present review.

the criteria for outcome and study type; and five studies [41–45] were excluded for not meeting the criterion for study type only.

Ultimately, 15 systematic reviews were included in the analysis. Of these, six investigated the short-term effects [46–51], seven examined long-term effects [52–58], and two addressed both short-term and long-term effects of air pollution on ALRI [48, 59]. One study by Bergmann *et al.* [60] was excluded after data extraction due to its focus on seasonal stratification, which was not aligned with the aims of the present review.

We chose to describe in the text and present in tables 2 and 3 only those systematic reviews with meta-analyses based on more than one primary study. All systematic reviews that passed the full-text screening, independent of their methodological appraisal, are reported in tables 2 and 3. Details on all included systematic reviews and the corresponding extracted data are available in supplement 3.

Short-term effects

Summary of evidence

Eight studies assessed the short-term effects of air pollution on ALRI, of which only four conducted a meta-analysis (table 2). These reviews primarily focused on the impact of air pollution on pneumonia incidence rather than on ALRI incidence as a broader category. Out of the four meta-analyses, three [46–49] investigated the effect on the general population, while one [49] specifically targeted children. None assessed mortality outcomes, and incidence was generally evaluated from hospital admissions and/or emergency department visits. The studies investigated the short-term effects of a wide range of pollutants, with studies focusing on CO [46, 49], NO_2 [46, 49], PM_1 [47], $PM_{2.5}$ [48, 49], O_3 [46, 49] and SO_2 [46, 49]. Several of the meta-analyses were based on a very limited number of primary studies, fewer than three in some cases [47].

Methodological appraisal

Most systematic reviews on short-term effects failed to meet the minimum critical appraisal criteria of the AMSTAR2-EH tool (supplement 1.2). Only one review [47], investigating the impact of PM_1 on pneumonia incidence, met the critical requirements; however, it was based on just two primary studies.

Short-term systematic reviews (n=8) showed several methodological weaknesses (supplement 1.3). The most critical issue was the universal failure to meet item Q2 (eight negative ratings out of eight systematic reviews evaluated), which evaluates whether the review methods were established *a priori* and whether deviations from the protocol were justified. Furthermore, a large proportion of reviews did not perform risk of bias (RoB) assessments in individual studies (item Q8, seven out of eight) and failed to address the impact of RoB on the results of the meta-analysis or other evidence synthesis (item Q9, six out of eight). Additional weaknesses included lack of information on duplicate study selection (item Q4, six out of eight), incomplete literature search strategies (item Q3, five out of eight) and absence of duplicate data extraction (item Q5, four out of eight).

Assessing the quality of evidence

None of the systematic reviews assessed the quality of evidence for studies on short-term effects.

Long-term effects

Summary of evidence

Nine studies assessed the long-term effects of air pollution on ALRI, seven of which included meta-analysis (table 3). Six studies investigated the long-term effects of air pollution on ALRI as a whole [52, 54–57, 59], while one focused specifically on the impact of air pollution on bronchitis [58]. Compared to short-term studies, these reviews concentrated on more well-established pollutants, including NO_2 [52, 54, 57, 58], PM_{10} [58] and $PM_{2.5}$ [55, 56, 59], while only one study evaluated O_3 exposure, considering both annual averages and peak season levels [57]. Three studies focused on children [52, 58, 59], four on adults [52, 54, 56, 57] and one on the general population [55].

Methodological appraisal

The systematic reviews on the long-term effects were generally more rigorous and better conducted than those investigating short-term effects (supplement 1.2).

Among studies evaluating ALRI incidence in children, the review by Boogaard *et al.* [52] on the impact of NO_2 met all critical and noncritical AMSTAR2-EH criteria, except for one item missing from the

TABLE 2 Summary of the characteristics of short-term studies included in the review

Study	Target population	Outcome	Incidence/ mortality	Pollutant	Exposure contrasts	Source of information	ICD–9/10	Effect estimate (95% CI)	Heterogeneity	Studies (n)
Yee 2021 [46]	All	Pneumonia	Incidence	CO	1 ppm	Hospital and ED admission		1.042 (1.006–1.079)	85.00	7
Yee 2021 [46]	All	Pneumonia	Incidence	NO_2	10 ppb	Hospital and ED admission		1.032 (1.013–1.051)	60.00	9
Yee 2021 [46]	All	Pneumonia	Incidence	O_3	10 ppb	Hospital and ED admission		1.004 (1.000–1.008)	48.00	11
Hu 2022 [47]	All	Pneumonia	Incidence	PM_1	10 $\mu g \cdot m^{-3}$	Hospital admission	ICD10: J18	1.07 (1.04–1.10)	0	2
Yee 2021 [46]	All	Pneumonia	Incidence	PM10	10 $\mu g \cdot m^{-3}$	Hospital and ED admission		1.004 (1.002–1.006)	49.00	11
Luo 2023 [48]	All	Pneumonia	Incidence	$PM_{2.5}$	10 $\mu g \cdot m^{-3}$	Hospital admission	ICD10: J12–J18	1.0162 (1.0067–1.0258)	99.00	4
Yee 2021 [46]	All	Pneumonia	Incidence	$PM_{2.5}$	10 $\mu g \cdot m^{-3}$	Hospital and ED admission		1.010 (1.005–1.015)	70.00	17
Yee 2021 [46]	All	Pneumonia	Incidence	SO_2	10 ppb	Hospital and ED admission		1.024 (0.980–1.071)	75.00	8
Nhung 2017 [49]	Children	Pneumonia	Incidence	CO	1 ppm	Hospital and ED admission	ICD9: 466, 480–486; ICD10: J12–J18	1.01 (1–1.02)	68.10	7
Nhung 2017 [49]	Children	Pneumonia	Incidence	NO_2	10 ppb	Hospital and ED admission	ICD9: 466, 480–486; ICD10: J12–J18	1.01 (1.00–1.02)	71.10	12
Nhung 2017 [49]	Children	Pneumonia	Incidence	O_3	10 ppb	Hospital and ED admission	ICD9: 466, 480–486; ICD10: J12–J18	1.02 (1.01–1.03)	75.20	16
Nhung 2017 [49]	Children	Pneumonia	Incidence	PM_{10}	10 $\mu g \cdot m^{-3}$	Hospital and ED admission	ICD9: 466, 480–486; ICD10: J12–J18	1.02 (1.01–1.02)	66.10	13
Nhung 2017 [49]	Children	Pneumonia	Incidence	$PM_{2.5}$	10 $\mu g \cdot m^{-3}$	Hospital and ED admission	ICD9: 466, 480–486; ICD10: J12–J18	1.02 (1.01–1.03)	38.10	13
Nhung 2017 [49]	Children	Pneumonia	Incidence	SO_2	10 ppb	Hospital and ED admission	ICD9: 466, 480–486; ICD10: J12–J18	1.03 (1.00–1.05)	48.40	10

ICD: International Classification of Diseases; CO: carbon monoxide; ED: emergency department; NO_2: nitrogen dioxide; O_3: ozone; PM_x: particulate matter with a 50% cut-off aerodynamic diameter of x µm; SO_2: sulfur dioxide.

TABLE 3 Summary of the characteristics of long-term studies included in the review

Study	Target population	Outcome	Incidence/ mortality	Pollutant	Exposure contrasts	Source of information	ICD-9/10	Effect estimate (95% CI)	Heterogeneity	Studies (n)
Boogaard 2022 [52]	Children	ALRI	Incidence	NO_2	10 μg·m^{-3}	Parental questionnaires asking about doctor-diagnosed infections and administrative data such as hospital admissions records	ICD10: J12–J18, J20–J22	1.09 (1.03–1.16)	45.00	11
Mehta 2013 [59]	Children	ALRI	Incidence	$PM_{2.5}$	10 μg·m^{-3}	Hospital admissions or physician-diagnosed ALRI		1.12 (1.03–1.30)		4
Boogaard 2022 [52]	Adults	ALRI	Incidence	NO_2	10 μg·m^{-3}	Parental questionnaires asking about doctor-diagnosed infections and administrative data such as hospital admissions records	ICD10: J12–J18, J20–J22	1.07 (0.71–1.61)	71.00	3
Nedellec 2009 [58]	Children	Bronchitis	Incidence	NO_2	10 μg·m^{-3}			1.16 (1.013–1.328)		2
Nedellec 2009 [58]	Children	Bronchitis	Incidence	PM_{10}	10 μg·m^{-3}			1.489 (1.115–1.990)		4
Huangfu 2020 [54]	Adults	ALRI	Mortality	NO_2	10 μg·m^{-3}	National death records, insurance records and hospital records	ICD10: J12–J18, J20–J28	1.06 (1.02–1.10)	81.3	5
Kasdagli 2024 [57]	Adults	ALRI	Mortality	NO_2	10 μg·m^{-3}		ICD10: J12–J18, J20–J22; ICD9: 480–487	1.08 (1.04–1.12)	92	9
Orellano 2024 [56]	Adults	ALRI	Mortality	$PM_{2.5}$	10 μg·m^{-3}	Vital statistics, tax records, follow-up, mortality registries	ICD10: J12–J18, J20–J22	1.204 (1.095–1.325)	81.5	12
Kasdagli 2024 [57]	Adults	ALRI	Mortality	O_3 (annual)	10 μg·m^{-3}		ICD10: J12–J18, J20–J22; ICD9: 480–487	1.04 (0.97–1.11)	80	2
Kasdagli 2024 [57]	Adults	ALRI	Mortality	O_3 (peak/warm season)	10 μg·m^{-3}		ICD10: J12–J18, J20–J22; ICD9: 480–487	1.02 (0.99–1.04)	88	4
Chen 2020 [55]	All	ALRI	Mortality	$PM_{2.5}$	10 μg·m^{-3}	Death registries and death certificate retrieval	ICD10: J12–J18, J20–J22	1.16 (1.01–1.34)	83	4

ICD: International Classification of Diseases; ALRI: acute lower respiratory infection; NO_2: nitrogen dioxide; PM_x: particulate matter with a 50% cut-off aerodynamic diameter of x μm; O_3: ozone.

systematic review but available in the comprehensive HEI report [26]. The CRF attested to a relative risk of 1.09 (95% CI 1.03–1.16).

In adults, the review by Boogaard *et al.* [52] stands out as the only well-conducted systematic review investigating the impact of NO_2 on ALRI incidence, although the pooled effect estimate was not statistically significant (relative risk 1.07, 95% CI 0.71–1.61).

One review investigated the impact of PM_{10} and NO_2 on bronchitis incidence among children, but did not meet the minimum AMSTAR2-EH criteria [58].

Regarding ALRI mortality, two well-conducted reviews by Huangfu *et al.* [54] and Kasdagli *et al.* [57], for which the second was an update of the first, provided robust evidence for the impact of NO_2 in adults, reporting consistent effect estimates with relative risks of 1.06 (95% CI 1.02–1.10) and 1.08 (95% CI 1.04–1.12), respectively.

The only study investigating the effect of O_3 reported nonsignificant results, based on a limited number of primary studies [57].

Finally, two methodologically high-quality systematic reviews investigated the effect of $PM_{2.5}$ on ALRI mortality, one in the general population [55] and its update focusing on adults [56]. They reported substantial effect estimates with a relative risk of 1.16 (95% CI 1.01–1.34) and 1.204 (95% CI 1.095–1.325), respectively.

Figure 2 shows effect estimates on air pollution and ALRIs from methodologically high-quality reviews, defined as those meeting all critical criteria and failing no more than four noncritical ones. Only statistically significant confidence intervals are displayed, with the aim of identifying CRFs applicable to HRA.

Long-term systematic reviews (n=9) demonstrated overall better compliance with AMSTAR2-EH standards compared to short-term reviews (supplement 1.3). The most common shortcomings, though less frequent than in short-term reviews, included inadequate assessment of RoB in individual studies (item Q8, four negative ratings out of nine systematic reviews evaluated) and limited evaluation of its impact on meta-analytic results (item Q9, five out of nine). Discussion of heterogeneity was also often insufficient (item Q10, five out of nine). While these reviews generally showed stronger methodological quality, transparency issues persisted, particularly in protocol registration and duplication of study selection and data extraction (items Q2–Q5, four out of nine each). Notably, all reviews clearly defined PECO elements and performed well on environmental health-specific items, including consistent use of exposure metrics and appropriate separation of exposure durations.

Assessing the quality of evidence

Unlike the short-term systematic reviews, long-term reviews rigorously assessed the quality of evidence using the GRADE approach. The level of confidence in the association between NO_2 exposure and ALRI incidence was rated as very low in adults and moderate-to-high in children [26, 52]. Confidence in the association with ALRI mortality in adults was high [57]. For $PM_{2.5}$, the evidence linking exposure to ALRI mortality was rated as high among both adults [56] and the general population [55]. In contrast, the confidence in the association between O_3 and ALRI mortality in adults was rated as low [57].

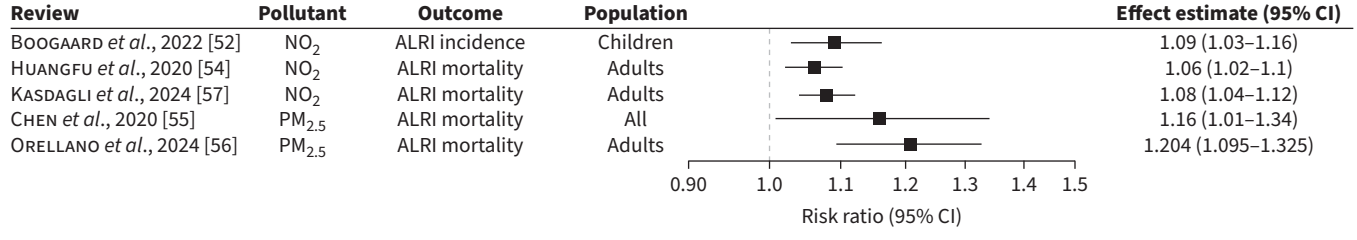

FIGURE 2 Summary of methodologically high-quality systematic reviews investigating the long-term effect of air pollution on acute lower respiratory infection (ALRI) incidence and mortality. Methodologically high-quality systematic reviews were defined as those meeting all critical AMSTAR2-EH criteria and failing no more than four noncritical criteria. Only statistically significant confidence intervals are displayed, with the aim of identifying concentration–response functions applicable to health risk assessment. NO_2: nitrogen dioxide; $PM_{2.5}$: particulate matter with a 50% cut-off aerodynamic diameter of 2.5 μm.

Discussion

This study aimed to provide a comprehensive overview and critical appraisal of existing systematic reviews and meta-analyses on the association between air pollution and ALRI. While previous reviews have primarily focused on ALRI incidence and the long-term effects of air pollution [21], to our knowledge, this study provides one of the most comprehensive overviews to date of the short-term and long-term effects of air pollution on ALRI incidence and mortality across age groups, with a focus on identifying robust CRFs. Furthermore, this is the first study to apply the newly developed AMSTAR2-EH tool outside the original context in which it was proposed [21]. By setting a minimum threshold of completeness, our approach facilitates the identification of methodologically high-quality systematic reviews suitable for HRA, while excluding those of lower methodological quality.

The systematic reviews addressing short-term effects exhibited substantial heterogeneity in terms of selection criteria, effect measures and meta-analytic methodologies, which translated into variability in effect estimates. Several reviews relied on a small number of primary studies, limiting the generalisability of their findings. Additionally, most systematic reviews did not examine specific lag structures but instead used algorithms to identify the "optimal" lag based on predefined criteria, *e.g.* primary lag (stated in abstract/*a priori*), most statistically significant lag or lag with largest effect size. While this approach offers a data-driven selection, it also introduces inconsistency, complicating the derivation of generalisable CRFs for short-term exposure in HRAs. Moreover, although the evidence on short-term effects of air pollution may appear somewhat compelling, none of the reviewed systematic reviews met the minimum critical appraisal criteria, highlighting a significant knowledge gap that needs to be addressed. Recognising the relevance of short-term HRA is essential, because it can uncover distinct mechanisms underlying health effects, mechanisms that are equally as important as those typically emphasised in long-term assessments [61, 62].

By contrast, the studies on long-term effects were methodologically accurate. Many cohort studies explored prolonged exposure to $PM_{2.5}$ or NO_2 in relation to cardiopulmonary end-points more broadly, often bundling ALRIs with other respiratory outcomes. As a result, specific risk estimates for ALRIs may be diluted and lack statistical power. Large-scale cohort studies with extended follow-up are needed to robustly evaluate the association between different particle fractions (PM_1, $PM_{2.5}$, PM_{10}) and the incidence or mortality of ALRIs over time.

In this context, the robust CRFs we identified for the impact of NO_2 on ALRI incidence in children are in line with those previously highlighted by Forastiere *et al*. [21], reinforcing the consistency of the available evidence. This finding is supported by a moderate to high level of confidence, based on the narrative evaluation and the modified Office of Health Assessment and Translation (OHAT) assessment conducted by Boogaard *et al*. [52]. Further robust CRFs concerned the association between NO_2 on ALRI mortality in adults [54, 57], and that between $PM_{2.5}$ and ALRI mortality in the general and adult population [55, 56].

Only a limited number of studies explicitly investigated the shape of the CRF, because most assumed a linear relationship. The majority of the included reviews did not test for non-linearity and reported risk estimates based on linear models [46–49, 52, 53, 59, 60]. A few studies specifically explored the shape of the NO_2–ALRI CRF and generally found linear or near-linear associations, with some evidence for respiratory mortality of supra-linear curves, *i.e.* steeper slopes at lower exposure levels [57]. For $PM_{2.5}$, non-linearity was suggested for ALRI mortality in adults in a single primary study included in the review by Orellano *et al*. [56, 63]. However, consistent with previous systematic reviews and with the 2021 WHO global air quality guidelines, the CRF for $PM_{2.5}$ is generally assumed to be linear or near-linear, with no evidence of thresholds.

Regarding O_3, most studies applied spline models (natural or penalised) and assessed linearity using model fit criteria. The vast majority reported no meaningful deviations from linearity [57] while there is limited and inconclusive evidence of a nonlinear relationship between O_3 exposure and ALRI [54].

Among the included studies, only Kasdagli *et al*. [57] provided separate estimates for peak/warm season *versus* annual O_3, showing an attenuation of the association with ALRI mortality, even if no statistically significant association was observed. The study by Bergmann *et al*. [60], although excluded during data extraction, assessed seasonal effect modification of air pollution on morbidity by comparing the relative risk associated with pollutant exposure in the warm season relative to the cold season. Using the ratio of relative risks and corresponding 95% confidence intervals, the study found higher effects of CO and O_3 on the incidence of pneumonia during the warm season. A tendency towards higher effect estimates in more

recent studies on the association between air pollution and ALRI was observed, although heterogeneity remains. Two updated long-term reviews reported higher effect estimates compared to earlier findings, and this pattern was also observed in Bergmann *et al*. [60]. Kasdagli *et al*. [57] reported a higher effect estimate for the association between NO_2 exposure and long-term ALRI mortality in adults (relative risk 1.08, 95% CI 1.04–1.12) compared to the estimate reported by Huangfu *et al*. [54] (relative risk 1.06, 95% CI 1.02–1.10). Similarly, for long-term exposure to $PM_{2.5}$ and ALRI mortality, Orellano *et al*. [56] observed a higher pooled estimate (relative risk 1.20, 95% CI 1.10–1.33) compared to Chen *et al*. [55] (relative risk 1.16, 95% CI 1.01–1.34).

A similar increase in effect estimates can be observed in short-term reviews. For example, comparing Lai *et al*. [50] (relative risk 1.0071, 95% CI 0.991–1.024) and Yee *et al*. [46] (OR 1.032, 95% CI 1.013–1.051), higher risk estimates for NO_2 exposure and short-term pneumonia morbidity were reported in the more recent study, as well as for exposures to PM_{10} and SO_2. Comparing Yee *et al*. [46] (relative risk 1.010, 95% CI 1.005–1.015) and Luo *et al*. [48] (OR 1.0162, 95% CI 1.0067–1.0258), higher effect estimates were observed for short-term $PM_{2.5}$ and pneumonia morbidity. However, it is important to note that the type of effect measure differed between the studies (risk ratios *versus* odds ratios), which complicates direct comparisons. Furthermore, Lai *et al*. [50] and Luo *et al*. [48] were conducted in a single geographic context, which may be characterised by specific environmental exposures and risk profile. These contextual differences may limit the generalisability of the findings to other settings and should be carefully considered when interpreting the results.

A key finding of this review is the necessity of methodologically rigorous reviews to derive credible CRFs. Applying the AMSTAR2-EH tool revealed significant limitations across multiple reviews, especially the lack of RoB assessment, which was considered one of the minimum critical criteria to be satisfied. Moreover, only a few studies, exclusively those assessing long-term effects, evaluated the quality of evidence using a structured tool, *i.e.* the GRADE framework [28]. It is important to distinguish between two complementary but fundamentally different assessment approaches. The AMSTAR2-EH tool includes a criterion, potentially critical, that evaluates whether systematic review authors conducted RoB assessment in individual studies, accepting tools such as ROBINS-I, Newcastle–Ottawa or the GRADE RoB item. However, AMSTAR2-EH serves as a methodological audit, focusing on whether appropriate RoB assessment occurred rather than evaluating the substance or implications of those assessments.

By contrast, GRADE operates at the evidence synthesis level, incorporating RoB judgments, along with inconsistency, indirectness, imprecision and publication bias, into a comprehensive framework that assigns specific certainty ratings (high, moderate, low, very low) to the body of evidence.

For this reason, in our methodological appraisal we chose to report the use of GRADE, where available, alongside AMSTAR2-EH, because both dimensions provide essential but distinct information for evaluating the suitability of systematic reviews for HRA: AMSTAR2-EH confirms methodological rigour in the review process, while GRADE provides the evidence certainty ratings necessary for translating findings into practice and policy recommendations.

Regarding the newly proposed questions specifically designed for environmental epidemiology, the most difficult among the critical criteria to satisfy were the registration of the review protocol before the review and evaluating the results of studies that could not be included in the meta-analysis but were pertinent. These were followed by difficulties in avoiding the inappropriate combination of results from different health outcomes or indicators. Systematic reviews that met the minimum critical criteria established by the working group consistently satisfied the critical criteria of the new questions specifically designed for environmental epidemiology (QA1, QA2 and QA4). This further emphasises the validity of the working group's selection, which allows for the completion of the additional criteria only for systematic reviews that meet the minimum completeness requirements.

Based on our findings, we propose several practical recommendations. First, future reviews and meta-analyses should adhere closely to established guidelines (*e.g.* PRISMA) and integrate environmental epidemiology-specific criteria such as AMSTAR2-EH to ensure strengthened methodological rigour. Second, systematic reviews need to adopt a comprehensive outcomes approach by examining the full spectrum of ALRIs (not limited to pneumonia) and paying special attention to vulnerable groups such as children and older adults. Third, clarifying short-term lags through more uniform definitions of exposure windows and transparent methods for lag selection can help address inconsistencies in short-term burden estimation. Fourth, larger, methodologically robust cohort studies with extended follow-up are critical for illuminating the long-term impact of different particulate matter fractions. Finally, because socioeconomic

context influences both exposure and susceptibility to ALRIs, future research should incorporate age and socioeconomic stratification to generate more nuanced findings and guide targeted public health interventions.

This overview of systematic reviews has several limitations. First, although we conducted a comprehensive literature search, we included only systematic reviews with meta-analyses, which may have excluded relevant narrative reviews or primary studies not yet synthesised. Second, we did not publish or register a formal protocol prior to conducting the review; however, a PECOS question and internal procedures were defined *a priori* and shared among the expert panel. Third, we did not perform a *de novo* certainty assessment (*e.g.* using GRADE), because our aim was to appraise existing systematic reviews rather than to reassess the body of primary evidence; however, we did extract and report whether each included systematic review applied such tools. Fourth, the methodological quality of the included systematic reviews varied considerably, particularly among those addressing short-term effects, limiting the strength of conclusions that can be drawn for certain pollutants or exposure–outcome pairs. Fifth, most systematic reviews assumed linear concentration–response relationships, with limited investigation into potential nonlinear or threshold effects, which is particularly relevant for pollutants such as O_3. Finally, heterogeneity in outcome definitions, exposure contrasts and lag structures across systematic reviews and their included studies may affect comparability and generalisability of the findings.

In conclusion, to our knowledge, this is the first comprehensive effort to critically review and systematically evaluate meta-analyses and systematic reviews dedicated to ALRIs, with a focus on the methodological robustness and credibility of the concentration–response functions used to estimate the disease burden. Our findings underscore the need for greater consistency when examining short-term and long-term effects, clearer definitions of respiratory outcomes (ALRIs *versus* specific infections such as pneumonia) and more rigorous use of evaluation tools like AMSTAR2-EH.

While the available evidence, though limited, indicates that long-term exposure to air pollution (particularly fine particulate matter and nitrogen oxides) is associated with increased ALRI risk in terms of both incidence and mortality, especially among children, further consolidation of the data is essential. Building a stronger evidence base through larger, methodologically higher quality primary studies, along with careful attention to heterogeneity and CRF validation, will be instrumental in guiding effective environmental and public health policies aimed at mitigating the substantial burden of disease linked to air pollution. Future efforts should prioritise the development of methodologically high-quality primary studies, standardised systematic review methodologies and assessments of the confidence in the evidence to inform environmental regulations more effectively.

Points for clinical practice

- Recognise $PM_{2.5}$ and NO_2 exposure as potential contributors to ALRIs, especially in children and older adults.
- Incorporate environmental exposure history into patient assessments and prevention strategies in high-risk areas.

Question for further research

- Identification of the short-term exposure durations (*e.g.* lag days) that are most predictive of ALRI onset in children *versus* adults is needed.
- Further research is needed to understand how socioeconomic status and pre-existing conditions modify the short-term and long-term impact of air pollution on ALRI risk.

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References

1 Safiri S, Mahmoodpoor A, Kolahi AA, *et al.* Global burden of lower respiratory infections during the last three decades. *Front Public Health* 2023; 10: 1028525.
2 GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; 385: 117–171.
3 Kang L, Jing W, Liu J, *et al.* Trends of global and regional aetiologies, risk factors and mortality of lower respiratory infections from 1990 to 2019: an analysis for the Global Burden of Disease Study 2019. *Respirology* 2023; 28: 166–175.
4 Welte T, Torres A, Nathwani D. Clinical and economic burden of community-acquired pneumonia among adults in Europe. *Thorax* 2012; 67: 71–79.
5 Birnbaum HG, Morley M, Greenberg PE, *et al.* Economic burden of pneumonia in an employed population. *Arch Intern Med* 2001; 161: 2725–2731.
6 Ferrari AJ, Santomauro DF, Aali A, *et al.* Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet* 2024; 403: 2133–2161.
7 Corrales-Medina VF, Alvarez KN, Weissfeld LA, *et al.* Association between hospitalization for pneumonia and subsequent risk of cardiovascular disease. *JAMA* 2015; 313: 264–274.
8 Restrepo MI, Reyes LF. Pneumonia as a cardiovascular disease. *Respirology* 2018; 23: 250–259.
9 Corrales-Medina VF, Taljaard M, Yende S, *et al.* Intermediate and long-term risk of new-onset heart failure after hospitalization for pneumonia in elderly adults. *Am Heart J* 2015; 170: 306–312.e6.
10 Akinyemi O, Fasokun M, Odusanya E, *et al.* The relationship between neighborhood economic deprivation and community-acquired pneumonia related admissions in Maryland. *Front Public Health* 2024; 12: 1412671.
11 Thörn LK, Minamisava R, Nouer SS, *et al.* Pneumonia and poverty: a prospective population-based study among children in Brazil. *BMC Infect Dis* 2011; 11: 180.

12 World Health Organization (WHO). The Top 10 Causes of Death. www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death Date last accessed: 13 March 2025. Date last updated: 7 August 2024.
13 Our World in Data. Deaths By Risk Factor. https://ourworldindata.org/grapher/number-of-deaths-by-risk-factor Date last accessed: 13 March 2025.
14 Our World in Data. Disease Burden From Lead Exposure. https://ourworldindata.org/grapher/disease-burden-lead Date last accessed: 13 March 2025.
15 Brauer M, Roth GA, Aravkin AY, *et al.* Global burden and strength of evidence for 88 risk factors in 204 countries and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet* 2024; 403: 2162–2203.
16 US Environmental Protection Agency (EPA). Air Quality - National Summary. 2016. www.epa.gov/air-trends/air-quality-national-summary Date last accessed: 13 March 2025.
17 Targa J, Colina M, Banyuls L, *et al.* Status Report of Air Quality in Europe For Year 2023, Using Validated and Up-To-Date Data. Copenhagen, European Environment Agency, 2024. Available from: www.eionet.europa.eu/etcs/all-etc-reports
18 World Health Organization (WHO). Ambient Air Pollution Data. www.who.int/data/gho/data/themes/air-pollution/ambient-air-pollution Date last accessed: 13 March 2025.
19 World Health Organization (WHO). Ambient air pollution attributable deaths. www.who.int/data/gho/data/indicators/indicator-details/GHO/ambient-air-pollution-attributable-deaths Date last accessed: 13 March 2025.
20 Monoson A, Schott E, Ard K, *et al*. Air pollution and respiratory infections: the past, present, and future. *Toxicol Sci* 2023; 192: 3–14.
21 Forastiere F, Spadaro JV, Ancona C, *et al.* Choices of morbidity outcomes and concentration-response functions for health risk assessment of long-term exposure to air pollution. *Environ Epidemiol* 2024; 8: e314.
22 Shea BJ, Reeves BC, Wells G, *et al.* AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017; 358: j4008.
23 Cohen AJ, Brauer M, Burnett R, *et al.* Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet* 2017; 389: 1907–1918.
24 Horne BD, Joy EA, Hofmann MG, *et al.* Short-term elevation of fine particulate matter air pollution and acute lower respiratory infection. *Am J Respir Crit Care Med* 2018; 198: 759–766.
25 Zhang W, Ling J, Zhang R, *et al.* Short-term effects of air pollution on hospitalization for acute lower respiratory infections in children: a time-series analysis study from Lanzhou, China. *BMC Public Health* 2023; 23: 1629.
26 Health Effects Institute (HEI). Systematic Review and Meta-analysis of Selected Health Effects of Long-Term Exposure to Traffic-Related Air Pollution. 2022. www.healtheffects.org/publication/systematic-review-and-meta-analysis-selected-health-effects-long-term-exposure-traffic Date last accessed: 2 April 2025.
27 Kohl C, McIntosh EJ, Unger S, *et al.* Online tools supporting the conduct and reporting of systematic reviews and systematic maps: a case study on CADIMA and review of existing tools. *Environ Evid* 2018; 7: 8.
28 Morgan RL, Thayer KA, Bero L, *et al.* GRADE: assessing the quality of evidence in environmental and occupational health. *Environ Int* 2016; 92–93: 611–616.
29 Buteau S, Geng X, Labelle R, *et al.* Review of the effect of air pollution exposure from industrial point sources on asthma-related effects in childhood. *Environ Epidemiol* 2019; 3: e077.
30 Yang BY, Liu Y, Hu LW, *et al.* Urgency to assess the health impact of ambient air pollution in China. *Adv Exp Med Biol* 2017; 1017: 1–6.
31 King C, Kirkham J, Hawcutt D, *et al.* The effect of outdoor air pollution on the risk of hospitalisation for bronchiolitis in infants: a systematic review. *PeerJ* 2018; 6: e5352.
32 Chen S, Liu D, Huang L, *et al.* Global associations between long-term exposure to $PM_{2.5}$ constituents and health: a systematic review and meta-analysis of cohort studies. *J Hazard Mater* 2024; 474: 134715.
33 Zhang Y, Tingting Y, Huang W, *et al.* Health impacts of wildfire smoke on children and adolescents: a systematic review and meta-analysis. *Curr Environ Health Rep* 2024; 11: 46–60.
34 Jackson S, Mathews KH, Pulanic D, *et al.* Risk factors for severe acute lower respiratory infections in children: a systematic review and meta-analysis. *Croat Med J* 2013; 54: 110–121.
35 Karanasiou A, Alastuey A, Amato F, *et al.* Short-term health effects from outdoor exposure to biomass burning emissions: a review. *Sci Total Environ* 2021; 781: 146739.
36 Liu Q, Xu C, Ji G, *et al.* Effect of exposure to ambient $PM_{2.5}$ pollution on the risk of respiratory tract diseases: a meta-analysis of cohort studies. *J Biomed Res* 2017; 31: 130–142.
37 Chang WW, Boonhat H, Lin RT. Incidence of respiratory symptoms for residents living near a petrochemical industrial complex: a meta-analysis. *Int J Environ Res Public Health* 2020; 17: 2474.
38 Troeger C, Blacker B, Khalil IA, *et al.* Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Infect Dis* 2018; 18: 1191–1210.

39 Troeger C, Forouzanfar M, Rao PC, *et al.* Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory tract infections in 195 countries: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Infect Dis* 2017; 17: 1133–1161.

40 Nicolaou L, Sylvies F, Veloso I, *et al.* Brick kiln pollution and its impact on health: a systematic review and meta-analysis. *Environ Res* 2024; 257: 119220.

41 Froes Asmus CIR, Camara VM, Landrigan PJ, *et al.* A systematic review of children's environmental health in Brazil. *Ann Glob Health* 2016; 82: 132–148.

42 Kyu HH, Vongpradith A, Sirota SB, *et al.* Age–sex differences in the global burden of lower respiratory infections and risk factors, 1990–2019: results from the Global Burden of Disease Study 2019. *Lancet Infect Dis* 2022; 22: 1626–1647.

43 Maio S, Sarno G, Tagliaferro S, *et al.* Outdoor air pollution and respiratory health. *Int J Tuberc Lung Dis* 2023; 27: 7–12.

44 Baldacci S, Viegi G. Respiratory effects of environmental pollution: epidemiological data. *Monaldi Arch Chest Dis* 2002; 57: 156–160.

45 Peden DB. Respiratory health effects of air pollutants. *Immunol Allergy Clin North Am* 2024; 44: 15–33.

46 Yee J, Cho YA, Yoo HJ, *et al.* Short-term exposure to air pollution and hospital admission for pneumonia: a systematic review and meta-analysis. *Environ Health* 2021; 20: 6.

47 Hu Y, Wu M, Li Y, *et al.* Influence of PM_1 exposure on total and cause-specific respiratory diseases: a systematic review and meta-analysis. *Environ Sci Pollut Res Int* 2022; 29: 15117–15126.

48 Luo H, Zhang Q, Niu Y, *et al.* Fine particulate matter and cardiorespiratory health in China: a systematic review and meta-analysis of epidemiological studies. *J Environ Sci (China)* 2023; 123: 306–316.

49 Nhung NTT, Amini H, Schindler C, *et al.* Short-term association between ambient air pollution and pneumonia in children: a systematic review and meta-analysis of time-series and case-crossover studies. *Environ Pollut* 2017; 230: 1000–1008.

50 Lai HK, Tsang H, Wong CM. Meta-analysis of adverse health effects due to air pollution in Chinese populations. *BMC Public Health.* 2013; 13: 360.

51 Ru M, Shindell D, Spadaro JV, *et al.* New concentration–response functions for seven morbidity endpoints associated with short-term $PM_{2.5}$ exposure and their implications for health impact assessment. *Environ Int* 2023; 179: 108122.

52 Boogaard H, Patton AP, Atkinson RW, *et al.* Long-term exposure to traffic-related air pollution and selected health outcomes: a systematic review and meta-analysis. *Environ Int* 2022; 164: 107262.

53 Kan HD, Chen BH, Chen CH, *et al.* Establishment of exposure-response functions of air particulate matter and adverse health outcomes in China and worldwide. *Biomed Environ Sci* 2005; 18: 159–163.

54 Huangfu P, Atkinson R. Long-term exposure to NO_2 and O_3 and all-cause and respiratory mortality: a systematic review and meta-analysis. *Environ Int* 2020; 144: 105998.

55 Chen J, Hoek G. Long-term exposure to PM and all-cause and cause-specific mortality: a systematic review and meta-analysis. *Environ Int* 2020; 143: 105974.

56 Orellano P, Kasdagli MI, Pérez Velasco R, *et al.* Long-term exposure to particulate matter and mortality: an update of the WHO global air quality guidelines systematic review and meta-analysis. *Int J Public Health* 2024; 69: 1607683.

57 Kasdagli MI, Orellano P, Pérez Velasco R, *et al.* Long-term exposure to nitrogen dioxide and ozone and mortality: update of the WHO air quality guidelines systematic review and meta-analysis. *Int J Public Health* 2024; 69: 1607676.

58 Nedellec V, Mosqueron L, Desqueyroux H. Effets des normes Euro IV et v sur la réduction des impacts sanitaires du trafic routier urbain en France I. Méta-analyse en vue d'établir des fonctions exposition-risques pour les enfants [Decrease in the health impact of road traffic in French urban areas attributable to European emissions standards Euro IV and V. I. Meta-analysis of epidemiological studies to derive the exposure-response function in children]. *Environnement Risques Santé* 2009; 8: 22–34.

59 Mehta S, Shin H, Burnett R, *et al.* Ambient particulate air pollution and acute lower respiratory infections: a systematic review and implications for estimating the global burden of disease. *Air Qual Atmos Health* 2013; 6: 69–83.

60 Bergmann S, Li B, Pilot E, *et al.* Effect modification of the short-term effects of air pollution on morbidity by season: a systematic review and meta-analysis. *Sci Total Environ* 2020; 716: 136985.

61 Baccini M, Biggeri A, Gruppo collaborativo EpiAir2. Impatto a breve termine dell'inquinamento dell'aria nelle città coperte dalla sorveglianza epidemiologica EpiAir2 [Short-term impact of air pollution among Italian cities covered by the EpiAir2 project]. *Epidemiol Prev* 2013; 37: 252–262.

62 Yu W, Xu R, Ye T, *et al.* Estimates of global mortality burden associated with short-term exposure to fine particulate matter ($PM_{2.5}$). *Lancet Planet Health* 2024; 8: e146–e155.

63 Guo C, Yu T, Bo Y, *et al.* Long-term exposure to fine particulate matter and mortality: a longitudinal cohort study of 400,459 adults. *Epidemiology* 2022; 33: 309–317.