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REVIEW ARTICLE

Ambient air pollutants increase the risk of immunoglobulin E–mediated allergic diseases: a systematic review and meta-analysis

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Abstract

Immunoglobulin E (IgE)–mediated allergic diseases, including eczema, atopic dermatitis (AD), and allergic rhinitis (AR), have increased prevalence in recent decades. Recent studies have proved that environmental pollution might have correlations with IgE-mediated allergic diseases, but existing research findings were controversial. Thus, we performed a comprehensive meta-analysis from published observational studies to evaluate the risk of long-term and short-term exposure to air pollutants on eczema, AD, and AR in the population (per 10-μg/m^3 increase in $PM_{2.5}$ and PM_{10}; per 1-ppb increase in SO_2, NO_2, CO, and O_3). PubMed, Embase, and Web of Science were searched to identify qualified literatures. The Cochran Q test was used to assess heterogeneity and quantified with the I^2 statistic. Pooled effects and the 95% confidence intervals (CIs) were used to evaluate outcome effects. A total of 55 articles were included in the study. The results showed that long-term and short-term exposure to PM_{10} increased the risk of eczema (PM_{10}, RR_{long} = 1.583, 95% CI: 1.328, 1.888; RR_{short} = 1.006, 95% CI: 1.003–1.008) and short-term exposure to NO_2 (RR_{short} = 1.009, 95% CI: 1.008–1.011) was associated with eczema. Short-term exposure to SO_2 (RR_{short}: 1.008, 95% CI: 1.001–1.015) was associated with the risk of AD. For AR, $PM_{2.5}$ (RR_{long} = 1.058, 95% CI: 1.014–1.222) was harmful in the long term, and short-term exposure to PM_{10} (RR_{short}: 1.028, 95% CI: 1.008–1.049) and NO_2 (RR_{short}: 1.018, 95% CI: 1.007–1.029) were risk factors. The findings indicated that exposure to air pollutants might increase the risk of IgE-mediated allergic diseases. Further studies are warranted to illustrate the potential mechanism for air pollutants and allergic diseases.

Keywords Air pollutants · Systemic review · Eczema · Atopic dermatitis · Allergic rhinitis

Introduction

Allergic diseases are inflammatory disorders that involve various types of cells and factors, including allergens, immunoglobulin (Ig)E, mast cells, basophils, cytokines, and soluble mediators. The etiological mechanisms of allergic diseases are complex (Murrison et al. 2019). The incidence of allergic diseases has increased sharply with increasing industrialization and the accompanying changes to the environment and people's lifestyles. According to one study conducted by the World Allergy Organization which involved 30 nations/region, approximately 250 million (22%) of the 1.2 billion people in those regions suffered from allergic diseases (Hu et al. 2018). Because of their high prevalence, these diseases pose a serious financial threat to affected households and consume substantial resources in socialized healthcare systems.

Allergic diseases can be divided into two categories, which are IgE mediated and non-IgE mediated. IgE-mediated allergy reactions are typically of rapid onset, and symptoms range from mild to severe. IgE, an antibody class found only in mammals, has unique properties, and plays a central role in the development of acute allergic reactions and IgE-mediated allergic diseases. IgE-mediated allergic diseases involve eczema, atopic dermatitis (AD), and allergic rhinitis (AR). The major risk factors for IgE-mediated allergic diseases studied widely were genetics and immune functions (Renz et al.

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2011; Hüls et al. 2019). However, these traditional risk factors were not changed dramatically in recent decades. Therefore, traditional risk factors alone may not be sufficient to explain the massive rise in IgE-mediated allergic disease prevalence.

Are long-term or short-term air pollution associated with the development and prevalence of IgE-mediated allergic conditions? Numerous studies have attempted to answer this question, but no consensus has reached. For instance, Schnass et al. conducted a cohort study and concluded that traffic-related air pollution would increase the prevalence of eczema for elders (Schnass et al. 2018). However, Lopez et al. found that long-term air pollution has no adverse effect on adult eczema (Lopez et al. 2021). The same dispute can also be found in AR's research. Huang et al. reported that the prevalence of AR in children would increase when exposed to $PM_{2.5}$ (Huang et al. 2019). But a cohort study established in Canada reported that $PM_{2.5}$ did not increase the risk of AR for children (To et al. 2020). There are also meta-analyses that tried to illustrate this question, and several important but inconsistent results have been received. In 2014, a meta-analysis on allergy and sensitization found an association between air pollution exposure and childhood eczema, whereas another meta-analysis found no association between air pollution and eczema (Fuertes et al. 2020).

These contrary results might reveal the impact of different inclusion criteria, regions, and other factors on the generalization of the results. Usually, clinicians tend to interchangeably use the terms eczema and AD. However, the term eczema is considered an ambiguous term and its meaning should not be considered synonymous with AD. In International Classification of Diseases (ICD), AD was only classified into the ICD-10 code L20 and ICD-9 code 691 catalogue, whereas eczema could be classified into ICD-10 code L30. A diagnosis of AD is thought to confer a worse prognosis in terms of disease severity and the potential risk for developing other comorbid diseases of an atopic nature compared with receiving a diagnosis of eczema alone. Most of the existing meta-analyses did not consider the inclusion criteria of AD and eczema and mixed these two diseases to conduct meta-analyses. Therefore, there is a need to divide these two diseases separately to conduct a meta-analysis to better understand the relationship between air pollution and IgE-mediated allergic diseases.

Based on the above evidence, IgE-mediated allergic diseases pose a great threat to human health. Previous meta-analyses only discussed a kind of IgE-mediated allergic disease, and could not draw the relationship between the diseases and air pollutants. Furthermore, it is hard to obtain a clear conclusion from contrary meta-analysis results of a single disease. And the sample size in a previous meta-analysis is small, which may have an impact on the results. Therefore, the purpose of this study is to explore the relationship between air pollutants and the IgE-mediated allergic diseases, and further identification of possible factors leads to differences in results. In addition, studying and exploring the relation can not only clarify the role of air pollutants in IgE-mediated allergic diseases, but also be of great practical significance to preventing and reducing medical expenses.

Material and methods

Search strategy

This review was conducted according to the PRISMA framework (Moher et al. 2009) (Table S1). We firstly posed the research question: "Does exposure to air pollutants increase the risks of IgE-mediated allergic diseases?" The included criteria were based on the population, exposure, comparator, and outcomes (PECO) framework. A framework was used to explore the association of air pollutant exposure with health outcomes. P refers to people who have IgE-mediated allergic diseases. E refers to air pollutants. C refers to incremental effect per unit increase in concentration of air pollutants for disease risk. O refers to the outcome of eczema, AR, and AD (Morgan et al. 2018; Marx et al. 2021) (Fig. S1).

Embase, PubMed, and Web of Science were searched to find relevant research concerning the association between air pollutants and diseases up to May 2021. Search terms included ("allergic rhinitis" OR allergic rhinitis [MeSH Terms] OR "allergic respiratory diseases" OR allergic respiratory diseases [MeSH Terms] OR "eczema" OR eczema [MeSH Terms] OR "eczematous dermatitides" OR eczematous dermatitides [MeSH Terms] OR "atopic dermatitis" OR atopic dermatitis [MeSH Terms] OR "dermatitis atopic" OR dermatitis atopic [MeSH Terms]) AND ("carbon monoxide" OR "sulfur dioxide" OR "particulate matter" OR "nitrogen dioxide" OR "ozone" OR "$PM_{2.5}$" OR "PM_{10}"). The detailed search process is shown in supplementary Table S2.

Inclusion and exclusion criteria

The inclusive criteria were as follows: (1) Articles should be epidemiologic studies focusing on the associations between the IgE-mediated allergic diseases with air pollutants exposure. (2) Eczema diagnosis was made according to ICD-10 code L30. ICD-10 code L20 and ICD-9 code 691 were used to classify AD. ICD-10 code J30 and ICD-9 code 477 were principles to detect AR. The classification of these three diseases could also be based on questionnaires of eczema or AD or AR. (3) Studies reported effect estimates (RR, OR, HR, PC) or data that could calculate the effect size. (4) Language was restricted to English. The studies would be excluded were as follows: (1) Animal studies, mechanism studies, reviews and meta-analyses, case reports, treatment effect evaluations, and studies without original data were

excluded. (2) Studies focusing on the association between indoor air pollution and prenatal and allergic diseases were also excluded.

Data extraction

Endnote software (X9 version) was used to screen eligible literature. All articles were evaluated by two investigators. First, duplicated studies were removed. Then, two investigators (Wang H and Li XB) independently screened remaining studies to select eligible studies. When controversy existed, a third investigator was asked to discuss and resolve the disagreement.

For each included study, basic characters were extracted, including disease, first author, publication year, region, study design, sample size, number of cases, age, ICD, data sources of pollutants, term of exposure (short-term or long-term) (Ibrahim et al. 2021), mean concentration of pollutants, and impact effect estimates. Investigators extracted information based on the following principle. A single-pollutant model was used to find the effect of a pollutant, and a multi-pollutant model was utilized to explore the interactions of multiple pollutants on disease risk. If the study contained single-pollutant and multi-pollutant models, the former would be chosen (Yang et al. 2018).

Data synthesis

Due to inconsistent units of pollutant concentration in some literature, we standardized all effect sizes for every 10-μg/m^3 increase in $PM_{2.5}$ and PM_{10} and 1-ppb increase in NO_2, SO_2, CO, and O_3 (Fan et al. 2020). The specific formulas were as follows: (1) ppm = 1000 ppb, 1 ppb = M/22.4 (μg/m^3). M refers to the molecular weight of each air pollutant. Adjusted relative risk (RR), odds ratio (OR), risk ratio (HR), and percentage change (PC) were used to assess the risk of eczema, AR, and AD (Ning et al. 2021). During data consolidation, PC was transformed into RR. The effect estimates (RR/OR/HR) were standardized. OR and HR were roughly regarded as RR, when outcome events were popular and the effect size was small (Chen et al. 2017). All the effect sizes were pooled by the standardized increment of environmental pollutant concentration. The standardized formulae of effect sizes were as follows:

$$RR_{(standardized)} = RR_{(original)}^{Increment(10)/Increment(original)}$$

$$OR_{(standardized)} = OR_{(original)}^{Increment(10)/Increment(original)}$$

$$HR_{(standardized)} = HR_{(original)}^{Increment(10)/Increment(original)}$$

Quality and risk bias assessment

The Newcastle–Ottawa Scale (NOS) and the Office of Health Assessment and Translation (OHAT) tool were used to evaluate the quality of included literature. Among them, NOS was used to assess the reported quality of cohort, case–control, and cross-sectional studies (Lin et al. 2021a). NOS has eight items, and its score ranged from 0 to 9. A study with a score higher than 7 was regarded as a high-quality study. A study with a score of 3 to 6 was intermediate quality. Otherwise, it was low-quality. To the best of our knowledge, there is no effective scale to assess the quality of time-series literature. Therefore, we adopted the quality scale used by Mustafic et al. This scale mainly evaluates three aspects: the validity of the outcome event, the assessment of air pollutant exposure, and the adjustment of confounding factors. When the evaluated document score was 3–5 points, it could be considered high-quality (Mustafic et al. 2012). In a meta-analysis, the OHAT tool was used to assess the risk of bias in each study (Zhang et al. 2021a).

Statistical analysis

Cochran's Q-test and I^2 statistic were used to evaluate the heterogeneity between studies. If I^2 is greater than 50%, the heterogeneity is high. Otherwise, the heterogeneity is low. If the p-value of the Q test is less than 0.05, a high heterogeneity is between the studies. Then the random effect model was chosen. The pooled RRs with 95% CIs were estimated using the fixed-effect mode, if the heterogeneity was low. Subgroup analyses were performed by age, region, and study design for each pollutant.

Funnel plots were used to represent the publication bias in studies (Bai et al. 2020). In addition, the pooled effect values were tested by determining the age (< 18 years old; ≥ 18 years old; all ages), region, and study design for each pollutant and sensitivity analyses by ICD (Chevalier et al. 2015). Limited by the number of available studies, sensitivity analyses were performed for studies that could be combined in each pollutant. All data analyses were realized by R packages "metafor" and "forestplot" in version 4.0.3.

Results

Characteristics of included studies

A total of 2478 articles were searched. After screening the titles and abstracts, 150 articles were identified. Finally,

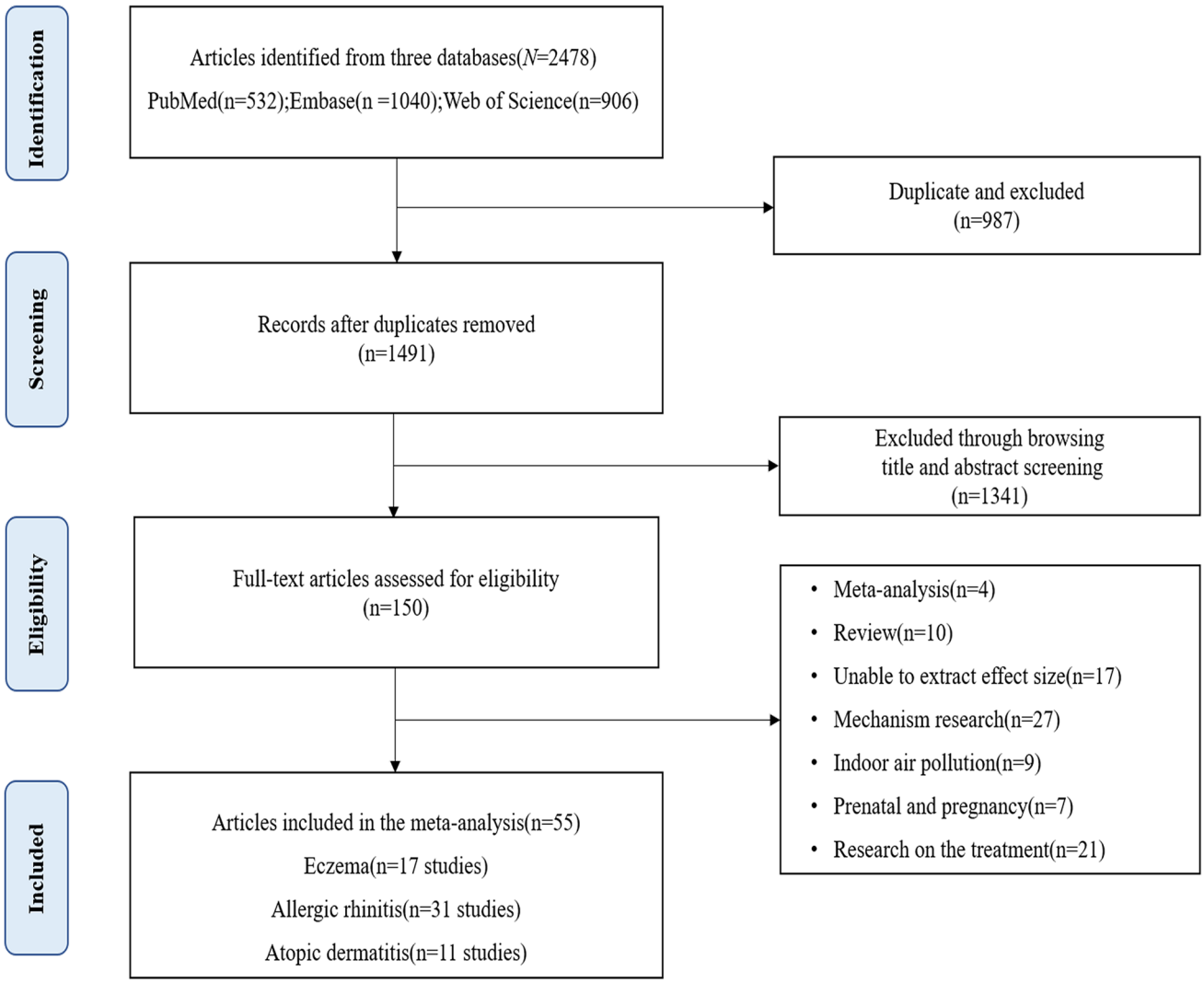

Fig. 1 Flowchart to show assessment of eligibility of identified studies

fifty-five articles were included thoroughly reading full texts. The process of literature screening is shown in Fig. 1. In four articles, two diseases were simultaneously discussed (Kim et al. 2016; Wang et al. 2016; Min et al. 2020; To et al. 2020). Therefore, seventeen studies were on eczema (six time-series, six cohorts, and five cross-sectional studies), thirty-one studies were on AR (nine time-series, nine cohorts, one case–control, and twelve cross-sectional studies), and eleven studies were on AD (four time-series, five cohorts, and two cross-sectional studies). The information extracted from the literature is shown in Table 1. According to the NOS scale and the OHAT tool, all included studies had high qualities. Scores of articles and details of risk bias assessment were listed as shown in supplementary Table S3 (eczema), Table S4 (AD), and Table S5 (AR).

Relationship between air pollution and eczema

Effect of long-term air pollution exposure on eczema

As shown in Table 2 and Fig. S2, the pooled risk for eczema was 1.583 (95% CI: 1.328–1.888) with an increment of 10 μg/m^3 in PM_{10}. However, exposures to $PM_{2.5}$, NO_2, and SO_2 were not associated with the risk of eczema. The between-study heterogeneity was low than exposure to PM_{10}, NO_2, and SO_2 ($I^2 < 50\%$). The results of publication bias are shown in Fig. S3a-S3b. In subgroup analyses according to age, study design, and region, long-term exposure to $PM_{2.5}$ and NO_2 had no impact on eczema. Other details are shown in Fig. 2a. In addition, due to the limited number of studies on CO and O_3, the analysis was not performed.

Table 1 Characteristics of included studies

Disease	First author/publication year	Region	Study design	Sample size/cases	Age (years)	Outcome assessment	Data sources of pollutants	Duration	Mean concentration	Effect size 95% CI (RR/HR/OR)
Eczema	Brauer et al. (2007)	Netherlands	Cohort	2571/—	4	Questionnaire	Monitoring campaign	Long-term	$PM_{2.5}$: 16.9 μg/m^3 NO_2: 25.2 μg/m^3	$PM_{2.5}$: 1.00 (0.83,1.21) NO_2: 1.00 (0.85,1.17)
	Krämer et al. (2009)	Germany	Cohort	2753/1741	0–6	Questionnaire	Monitoring stations	Long-term	NO_2: 23.7 μg/m^3	NO_2:1.55 (0.95,2.52)
	Gehring et al. (2010)	Netherlands	Cohort	3184/—	8	Questionnaire	Land-use regression model	Long-term	$PM_{2.5}$: 16.9 (μg/m^3)	$PM_{2.5}$: 1.11 (0.91–1.35)
	Aguilera et al. (2013)	Spain	Cohort	2199/460	1–1.5	Questionnaire	Monitoring stations	Long-term	—	NO_2: 1.02 (0.92, 1.12)
	Schnass et al. (2018)	Germany	Cohort	760/60	73.5	Questionnaire	Monitoring campaign	Long-term	$PM_{2.5}$, 32.11 μg/m^3; PM10, 48.37 μg/m^3; NO2: 37.36 μg/m^3	$PM_{2.5}$: 1.45 (1.06,1.98) PM_{10}: 1.36 (1.00,1.83) NO_2: 1.49 (1.04,2.15)
	Lopez et al. (2021)	Australia	Cohort	3152/115	53	Questionnaire	Monitoring sites	Long-term	$PM_{2.5}$: 6.4 μg/m^3; NO_2: 2.72 ppb	$PM_{2.5}$: 0.97 (0.84,1.13) NO_2: 1.01 (0.88,1.15)
	Anderson et al. (2010)	International	Cross-sectional	—/3086/per center	13–14	Questionnaire	Monitoring stations	Short-term	PM_{10}: 34 μg/m^3	PM_{10}: 0.93 (0.87,1.01)
	Liu et al. (2016)	China	Cross-sectional	3358/—	4–6	Questionnaire	Shanghai Environmental Monitoring Center	Long-term	PM_{10}: 79.4 μg/m^3; NO_2: 53.6 μg/m^3; SO_2: 43.2 μg/m^3	PM_{10}: 1.64 (1.33,2.04) NO_2: 1.63 (1.33,2.00) SO_2: 1.16 (0.96,1.40)
	Kathuria and Silverberg 2016)	USA	Cross-sectional	91,642/11895	0–17	Questionnaire	Environ mental Protection Agency	Short-term	$PM_{2.5}$: 6.187 μg/m^3; PM_{10}: 24.996 μg/m^3; NO_2, 12.851 ppm; SO_2: 2.953 ppm; CO: 1.161 ppm; O_3: 29.457 ppb	$PM_{2.5}$: 0.993 (0.989,0.998) PM_{10}: 0.847 (0.739,0.971) NO_2: 1.003 (1.001,1.004) SO_2: 1.009 (1.003,1.015) CO: 0.992 (0.949,1.038) O_3: 0.727 (0.396,1.334)
	Deng et al. (2019)	China	Cross-sectional	3167/848	3–6	Questionnaire	Monitoring stations	Short-term	$PM_{2.5}$: 72.11 μg/m^3; PM_{10}: 115.58 μg/m^3; NO_2: 38.39 μg/m^3	$PM_{2.5}$:1.273 (0.989,1.640) PM_{10}:1.305 (1.019,1.673) NO_2:1.371 (1.086,1.729)
	Min et al. (2020)	Korea	Cross-sectional	14,614/2323	1–12	Questionnaire	Monitoring stations	Short-term	$PM_{2.5}$: 25.13 μg/m^3; PM_{10}: 49.36 μg/m^3, NO_2: 35.6 μg/m^3	$PM_{2.5}$: 1.01 (0.96,1.07) PM_{10}: 1.06 (1.01,1.12) NO_2: 1.07 (1.02,1.13)

Table 1 (continued)

Disease	First author/publication year	Region	Study design	Sample size/cases	Age (years)	Outcome assessment	Data sources of pollutants	Duration	Mean concentration	Effect size 95% CI (RR/HR/OR)
	Li et al. (2016)	China	Time series	—/510,158 (outpatient visits)	—	ICD-10: L30.9	Monitoring stations	Short-term	PM_{10}: 83 μg/m^3; NO_2: 60 μg/m^3; SO_2: 42 μg/m^3	PM_{10}: 1.0081 (1.0039,1.0122) NO_2: 1.0231 (1.0117,1.0345) SO_2: 1.0222 (1.0127,1.0316)
	Li et al. (2018)	China	Time series	—/2305 (outpatient visits)	—	ICD-10: L30.9	Monitoring stations	Short-term	PM_{10}, 119.6 μg/m^3; NO_2: 55.2 μg/m^3; SO_2: 25.57 μg/m^3;	PM_{10}: 1.0041 (1.0004,1.0078) NO_2: 1.0344 (1.0012,1.0686) SO_2: 1.0530 (1.0617,1.1530)
	Wang et al. (2019)	China	Time series	—/2585 (outpatient visits)	≥ 18	ICD-10: L30.9	Monitoring stations	Short-term	$PM_{2.5}$: 101.2 μg/m^3	$PM_{2.5}$: 1.003 (1.0028,1.0033)
	Guo et al. (2019)	China	Time series	—/157,595 (outpatient visits)	—	ICD-10: L20-L30	Beijing Municipal Environmental Monitoring Center	Short-term	$PM_{2.5}$: 87.4 μg/m^3; PM_{10}: 116.6 μg/m^3; NO_2: 53.1 μg/m^3; SO_2: 27.1 μg/m^3	$PM_{2.5}$: 1.0381 (1.0292,1.047) PM_{10}: 1.0318 (1.0239,1.0397) NO_2: 1.0543 (1.0443,1.0643) SO_2: 1.0557 (1.0455,1.0658)
	Karagün et al. (2021)	Turkish	Time series	—/27,549 (outpatient visits)	—	ICD-10:L-20, L-25, and L-30	Monitoring stations	Short-term	PM_{10}: 82.8 μg/m^3; SO_2, 7.6 μg/m^3	PM_{10}: 1.0087 (1.0059,1.0115) SO_2: 1.0765 (1.0483,1.1054)
	Zhang et al. (2021b)	China	Time series	—/293,340 (outpatient visits)	—	ICD-10: L30.902	Monitoring stations	Short-term	—	NO_2: 1.0410 (1.0380,1.0440)
AD	Wang et al. (2015)	China	Cohort	2661/383	5.5	Questionnaire	Monitoring stations	Long-term	$PM_{2.5}$, 29.07 μg/m^3; PM_{10}: 48.32 μg/m^3; NO_2: 23.03 ppb; SO_2: 6.46 ppb; CO: 0.63 ppm; O_3: 27.62 ppb;	$PM_{2.5}$: 1.25 (0.85,1.82) PM_{10}: 1.00 (0.70,1.44) NO_2: 1.33 (0.98,1.79) SO_2: 1.24 (0.90,1.70) CO: 1.33 (0.98,1.80) O_3: 1.03 (0.77,1.38)
	Hüls et al. (2018)	Canada	Cohort	5132/440	7–8	Questionnaire	Land-use regression models	Long-term	NO_2	NO_2: 0.95 (0.82,1.11)

Table 1 (continued)

Disease	First author/publication year	Region	Study design	Sample size/cases	Age (years)	Outcome assessment	Data sources of pollutants	Duration	Mean concentration	Effect size 95% CI (RR/HR/OR)
	Belugina et al (2018)	Minsk	Cohort	—/12–335 cases per 100,000 person-years	0–2	ICD-10:L20.80	National Academy of Science of Belarus	Long-term	PM_{10}: 27.94%; NO_2: 36.17 μg/m^3; CO: 584.4 μg/m^3; O_3: 31.19 ppb	Boy: PM_{10}: 1.081 (1.057,1.107) NO_2: 1.091 (1.039,1.146) CO: 1.009 (1.007,1.011) O_3: 1.266 (1.191,1.345) Girl: PM_{10}: 1.070 (1.039,1.101) NO_2: 1.121 (1.056,1.192); CO: 1.007 (1.007,1.011); O_3: 1.319 (1.224,1.422)
	To et al. (2020)	Canada	Cohort	1286/958	3	ICD-9: 691.8 ICD-10: L20	Monitors	Long-term	$PM_{2.5}$: 10.88 μg/m^3; NO_2: 26.14 μg/m^3; O_3: 43.72 μg/m^3	$PM_{2.5}$: 1.01 (0.93,1.09) NO_2: 1.05 (0.99,1.11) O_3: 0.99 (0.92,1.06)
	Park et al. (2021)	Korea	Cohort	209,168/3203	—	ICD-10:L20	Korean Department of Environmental Protection	Long-term	—	$PM_{2.5}$: 1.420 (1.392,1.448), PM_{10}: 1.333 (1.325,1.341) SO_2: 1.200 (1.187,1.212) NO_2: 1.626 (1.559,1.695) CO: 1.005 (1.004,1.005)
	Kim et al. (2016)	Korea	Cross-sectional	1828/669	6–7	Questionnaire	Monitoring sites	Long-term	PM_{10}: 58.8 μg/m^3; NO_2: 29.7 ppb; SO_2: 5.2 ppb; CO: 6.5 (100 ppb); O_3: 30.7 ppb	PM_{10}: 1.06 (0.96,1.18) NO_2: 1.00 (0.99,1.01) SO_2: 1.01 (0.93,1.09) CO: 1.02 (0.95,1.10) O_3: 1.00 (0.98,1.02)
	Tang et al. (2017)	China	Cross-sectional	6115/1023	≥ 20	ICD-9: 691	Environmental Protection Agency monitoring stations	Long-term	$PM_{2.5}$: 33.6 μg/m^3; PM_{10}: 56.3 μg/m^3; NO_2: 18.6 ppb; SO_2: 4 ppb; CO: 0.5 ppb; O_3: 27.9 ppb	$PM_{2.5}$: 1.05 (1.02,1.08) PM_{10}: 0.98 (0.97,1.00) NO_2: 0.98 (0.93,1.02) SO_2: 1.07 (1.00,1.16) CO: 0.78 (0.22,2.73) O_3: 1.01 (0.97,1.05)
	Lee et al. (2010)	Korea	Time series	—/183 ± 29 (daily admissions)	< 15	ICD-10:L20	monitoring stations	Short-term	Seoul: O_3, 26.09 ppb Ulsan: O_3, 32.05 ppb	Seoul O_3: 1.28 (1.04,1.58) Ulsan: O_3:1.38 (0.80,2.36)

Table 1 (continued)

Disease	First author/publication year	Region	Study design	Sample size/cases	Age (years)	Outcome assessment	Data sources of pollutants	Duration	Mean concentration	Effect size 95% CI (RR/HR/OR)
	Kim et al. (2017)	Korea	Time series	—/117	2.0 ± 1.6	Questionnaire	National Institute of Environmental Research	Short-term	PM_{10}: 45.2 μg/m^3 NO_2: 32.4 ppb; O_3: 38.1 ppb	PM_{10}: 1.032 (1.015,1.049) NO_2: 1.005 (1.014,1.088) O_3: 1.061 (1.032,1.090)
	Guo et al. (2019)	China	Time series	64,987 (outpatient visits)	—	ICD-10: L20	Monitoring stations	Short-term	PM_{10}: 110.5 μg/m^3; $PM_{2.5}$: 79.7 μg/m^3; NO_2: 50.8 μg/m^3; SO_2: 16.9 μg/m^3	$PM_{2.5}$: 1.0042 (1.0016,1.0067) PM_{10}: 1.0034 (1.0015,1.0054) NO_2: 1.0111 (1.0038,1.0184) SO_2: 1.0106 (1.0021,1.0193)
	Baek et al. (2021)	Korea	Time series	—/513,870 (medical care visits)	—	ICD-10: L20.8, L20.9	Monitoring stations	Short-term	—	PM_{10}: 1.009 (1.007,1.012) NO_2: 0.996 (0.992,1.000) SO_2:1.033 (1.030,1.037) CO: 1.000 (0.997,1.004) O_3: 1.028 (1.023,1.033)
AR	Kim et al. (2011)	Korea	Cohort	1340/—	6.84	Questionnaire	Monitoring stations	Long-term	O_3: 37.93 μg/m^3	O_3: 1.042 (0.792,1.372)
	Fuertes et al. (2013a)	Canada	Cohort	10,027/4736	7 or 8	Questionnaire	Land-use regression modeling	Long-term	$PM_{2.5}$, NO_2, O_3	$PM_{2.5}$: 1.16 (0.96,1.41) NO_2: 1.10 (0.95,1.26) O_3:0.91 (0.77,1.08)
	Fuertes et al. (2013b)	Germany	Cohort	4623/460	10	Questionnaire	Land-use regression models	Long-term	$PM_{2.5}$: 15.3 μg/m^3; NO_2: 22.4 μg/m^3; O_3: 42.5 μg/m^3	$PM_{2.5}$: 0.87 (0.60,1.26) NO_2: 0.96 (0.85,1.09) O_3: 1.02 (0.90,1.16)
	Wang et al. (2015)	China	Cohort	2661/798	5.5	Questionnaire	Monitoring stations	Long-term	$PM_{2.5}$, 29.07 μg/m^3; PM_{10}: 48.32 μg/m^3; NO_2: 23.03 ppb; SO_2: 6.46 ppb; CO: 0.63 ppm O_3: 27.62 ppb;	$PM_{2.5}$: 1.54 (1.03,2.32) PM_{10}: 1.15 (0.79,1.66) NO_2: 0.95 (0.74,1.20) SO_2: 1.00 (0.78,1.29) CO: 1.02 (0.80,1.29) O_3: 1.01 (0.76,1.34)
	Chung et al. (2016)	China	Cohort	9960/1088	0–6	ICD-9-CM: 477.0, 477.1, 477.2, 477.8, 477.9	Environmental monitoring sites	Long-term	PM_{10}, 56.8 μg/m^3; SO_2, 4.81 ppb; CO, 561 ppb; O_3, 27.9 ppb	PM_{10}: 1.12 (0.79,1.45) SO_2: 1.05 (0.67,1.33) CO: 1.14 (1.02,1.86) O_3: 1.27 (0.76,1.70)
	Burte et al. (2018)	Europe	Cohort	1533/394	42.7	Questionnaire	Monitoring stations	Long-term	—	$PM_{2.5}$: 0.88 (0.73,1.04) PM_{10}: 0.88 (0.72,1.08) NO_2: 1.00 (0.91,1.09)

Table 1 (continued)

Disease	First author/publication year	Region	Study design	Sample size/cases	Age (years)	Outcome assessment	Data sources of pollutants	Duration	Mean concentration	Effect size 95% CI (RR/HR/OR)
	To et al. (2020)	Canada	Cohort	1286/511	3	ICD-9: 477; ICD-10: J301-J304	Monitors	Long-term	$PM_{2.5}$: 10.88 mg/m^3 NO_2: 26.14 ppb; O_3: 43.72 ppb	$PM_{2.5}$: 0.94 (0.85,1.04) NO_2: 0.94 (0.87,1.02) O_3: 1.08 (0.99,1.19)
	Lin et al. (2021b)	China	Cohort	140,911/47,276	1	ICD-9: 477.0, 477.1, 477.2, 477.8, 477.9	Novel satellite-based hybrid model	Long-term	$PM_{2.5}$: 33.84 μg/m^3	$PM_{2.5}$: 1.30 (1.23,1.36)
	Kim et al. (2021)	Korea	Cohort	3592/995	9.08	Questionnaire	National monitoring sites	Long-term	PM_{10}: 40.3 μg/m^3; NO_2: 22.9 ppb; SO_2: 5.4 ppb; CO: 533.1 ppb; O_3: 42.5 ppb	PM_{10}: 0.979 (0.962,0.997) NO_2: 1.002 (0.987,1.017) SO_2: 1.056 (1.006,1.109) CO:1.000(0.999,1.001) O_3: 1.006 (0.990,1.023)
	de Marco et al. (2002)	Italy	Cross-sectional	18,873/3529	33.1	Questionnaire	Monitoring sites	Long-term	NO_2: 31.46 μg/m^3	NO_2: 1.38 (1.12,1.69)
	Hwang et al. (2006)	China	Cross-sectional	32,143/8202	6–15	Questionnaire	Environmental Protection Agency air-monitoring station	Long-term	PM_{10}: 55.58 μg/m^3; SO_2: 3.53 ppb; CO: 664 ppb; O_3: 23.14 ppb	PM_{10}: 1.00 (0.99,1.02) SO_2: 1.43 (1.25,1.64) CO: 1.05 (1.04,1.07) O_3: 1.05 (0.98,1.12)
	Arnedo-Pena et al. (2009)	Spain	Cross-sectional	20,455/—	6–7	Questionnaire	Pollutant detection systems of centers	Long-term	NO_2: 40.4 μg/m^3; SO_2: 12.4 μg/m^3; CO: 0.8 μg/m^3;	NO_2: 1.84 (1.15,2.96) SO_2: 1.56 (1.39,1.75); CO: 1.65 (1.34,2.04)
	Lu et al. (2013)	China	Cross-sectional	2159/182	3–6	Questionnaire	Environmental Protection Agency	Long-term	PM_{10}; SO_2; NO_2	PM_{10}: 1.021 (1.003,1.039) NO_2: 1.037 (1.006,1.069) SO_2: 1.026 (1.005,1.048)
	Wood et al. (2015)	London	Cross-sectional	1808/242	8–9	Questionnaire	Dispersion models	Short-term	$PM_{2.5}$: 13.7 μg/m^3; PM_{10}: 23.4 μg/m^3; NO_2: 43.5 μg/m^3;	$PM_{2.5}$: 1.38 (1.08,1.78) PM_{10}: 1.16 (1.04,1.28) NO_2: 1.03 (1.00,1.06)
	Kim et al. (2016)	Korea	Cross-sectional	1828/673	6–7	Questionnaire	Monitoring sites	Long-term	PM_{10}: 58.8 μg/m^3; NO_2: 29.7 ppb; SO_2: 5.2 ppb; CO: 6.5 (100 ppb); O_3: 30.7 ppb	PM_{10}: 0.99 (0.89,1.10) NO_2: 1.00 (0.99,1.01) SO_2: 1.05 (0.97,1.14) CO: 1.10 (1.03,1.19) O_3: 0.99 (0.97,1.01)
	Chen et al. (2016b)	China	Time series	—/19,370	2–15	Experienced physicians diagnosed	Shanghai Environmental Bureau	Short-term	SO_2: 39.63 μg/m^3; O_3: 43.22 μg/m^3	SO_2: 1.012 (1.007,1.017) O_3: 1.02 (1.015–1.025)

Table 1 (continued)

Disease	First author/publication year	Region	Study design	Sample size/cases	Age (years)	Outcome assessment	Data sources of pollutants	Duration	Mean concentration	Effect size 95% CI (RR/HR/OR)
	Jo et al. (2017)	Korea	Cross-sectional	—/4.4 (daily admissions)	—	ICD-10: J30	Monitoring stations	Short-term	$PM_{2.5}$: 24.2 μg/m^3	$PM_{2.5}$: 0.969 (0.914,1.051) (child) $PM_{2.5}$: 1.253 (1.153,1.362) (elderly)
	Chen et al. (2018)	China	Cross-sectional	30,756/204	4.6	Questionnaire	Global Burden of Disease	Long-term	$PM_{2.5}$: 64 μg/m^3	$PM_{2.5}$: 1.15 (1.06,1.23)
	Liu et al. (2020)	China	Cross-sectional	56,137/5395	10	Questionnaire	Monitoring stations	Short-term	$PM_{2.5}$: 55.08 μg/m^3; PM_{10}: 98.75 μg/m^3; NO_2: 35.43 μg/m^3	$PM_{2.5}$: 1.28 (1.09,1.51) PM_{10}: 1.23 (1.06,1.43) NO_2: 1.22 (1.05,1.42)
	Min et al. (2020)	Korea	Cross-sectional	14,614/5286	1–12	Questionnaire	Monitoring stations	Dispersion models	$PM_{2.5}$: 25.13 μg/m^3; PM_{10}: 49.36 μg/m^3 NO_2: 35.6 μg/m^3	$PM_{2.5}$: 1.03 (0.94,1.01) PM_{10}: 1.00 (0.95,1.04) NO_2: 0.97 (0.94,1.01)
	Wang et al. (2021)	China	Cross-sectional	40,279/2658	—	Questionnaire	National Bureau of Statistics	Short-term	PM_{10}, NO_2	PM_{10}: 1.06 (0.96,1.17) NO_2: 1.17 (1.06,1.31)
	Hao et al. (2021)	China	Case–Control	3047/194	2–4	Questionnaire	Monitoring stations	Long-term	PM_{10}: 88 μg/m^3; NO_2: 31 μg/m^3; SO_2: 26 μg/m^3; CO: 970 μg/m^3; O_3: 92 μg/m^3	PM_{10}: 1.31 (1.08,1.90) NO_2: 1.15 (1.02,2.23) SO_2: 1.26 (0.73,1.97) CO: 1.13 (0.77,2.02) O_3: 0.52 (0.23,1.02)
	Zhou et al. (2021)	China	Cross-sectional	59,754/3186	10	Questionnaire	Satellite-based random forest approach	Long-term	O_3: 89.39 μg/m^3	O_3: 1.13 (1.07,1.18)
	Tecer et al. (2008)	Zonguldak	Time series	—/424 admissions	0–14	ICD-9: 470–478	Anderson automatic dichotomous sampler	Short-term	$PM_{2.5}$: 29.1 μg/m^3; PM_{10}: 53.3 μg/m^3	$PM_{2.5}$: 1.18 (1.00,1.24) PM_{10}: 1.09 (1.03,1.16)
	Zhang et al. (2011)	China	Time series	—/1506 (outpatients)	≥ 20	Questionnaire	Beijing Municipal Environmental Protection Monitoring Center	Short-term	PM_{10}: 116.092 μg/m^3; NO_2: 52.742 μg/m^3 SO_2: 44.052 μg/m^3;	PM_{10}: 1.0073 (1.0066,1.0080) NO_2: 1.0512 (1.0483,1.0542) SO_2: 1.0010 (1.0005,1.0014)
	Chen et al. (2016a)	China	Time series	—/124,773 (clinic visits)	—	ICD-9: 477	Monitoring stations	Short-term	PM_{10}: 45.79 μg/m^3; NO_2: 23.65 ppb; SO_2: 3.51 ppb; CO: 0.62 ppm; O_3: 23.77 ppb	PM_{10}: 1.09 (1.07,1.10) NO_2: 1.16 (1.14,1.17) SO_2: 1.05 (1.04,1.07) CO: 1.20 (1.18,1.22) O_3: 1.06 (1.05,1.08)

Table 1 (continued)

Disease	First author/publication year	Region	Study design	Sample size/cases	Age (years)	Outcome assessment	Data sources of pollutants	Duration	Mean concentration	Effect size 95% CI (RR/HR/OR)
	Teng et al. (2017)	China	Time series	—/23,344 (out patients)	—	ICD-9:477	Changchun Municipal Environmental Protection Monitoring Center	Short-term	$PM_{2.5}$: 66.5 μg/m^3; PM_{10}: 114.4 μg/m^3; NO_2: 43.6 μg/m^3; SO_2: 37 μg/m^3; CO: 0.93 μg/m^3; O_3: 71.1 μg/m^3	$PM_{2.5}$: 1.102 (1.055,1.151) PM_{10}: 1.049 (1.008,1.092) NO_2: 1.111 (1.058,1.165) SO_2: 1.085 (0.982,1.198) CO: 0.977 (0.907,1.053) O_3: 0.993 (0.941,1.048)
	Hu et al. (2020)	China	Time series	2,410,392/646,975	< 18	ICD-10:J30	Shanghai Environmental Protection Agency	Short-term	NO_2: 49.1 μg/m^3; O_3: 68.5 μg/m^3	NO_2: 1.0243 (1.0202,1.0284) O_3: 1.0325 (1.0284,1.0367)
	Chu et al. (2019)	China	Time series	—/33,063	—	Medical history, clinical symptoms, and the relevant test	Environmental Monitoring Centre	Short-term	$PM_{2.5}$: 57.3 μg/m^3; PM_{10}: 98.9 μg/m^3;	$PM_{2.5}$: 1.0539 (1.0273,1.0812) PM_{10}: 1.0586 (1.0300,1.0881)
	Wang et al. (2020)	China	Time series	—/14,965 (outpatients)	—	ICD10:J30	China's National Urban Air Quality Real-time Publishing Platform	Short-term	$PM_{2.5}$: 75.7 μg/m^3; PM_{10}: 132.1 μg/m^3; SO_2: 33.2 μg/m^3; NO_2: 48.4 μg/m^3; O_3: 59.4 μg/m^3; CO: 1377 μg/m^3	$PM_{2.5}$: 1.0070 (1.0000,1.0141) PM_{10}: 1.0079 (1.0035,1.0123) NO_2: 1.0445 (1.0301,1.0608) SO_2: 1.0343 (1.0147,1.0539) CO: 1.0007 (1.0002,1.0012) O_3: 1.0097 (0.9989,1.0205)
	Wang et al. (2020)	China	Time series	—/229,685 (outpatient visits)	—	ICD-10:J30.4 01	Monitoring stations	Short-term	$PM_{2.5}$: 99.5 μg/m^3	$PM_{2.5}$: 1.0047 (1.0039,1.0055)

Table 2 Pooled estimates of the effect on the risk of diseases

Prevalence/incidence disease	Duration	Pollutants	Number of studies	RR [95%CI]	I^2	*P* value for heterogeneity	Publication bias (*p*)
Eczema	Long-term	$PM_{2.5}$	4	1.171 [0.944,1.453]	77.97%	0.0044	> 0.05
		PM_{10}	2	1.583 [1.328,1.888]*	0.00%	0.9654	—
		NO_2	6	1.033 [0.970,1.101]	0.00%	0.9050	> 0.05
		SO_2	1	1.101 [0.897,1.351]	0.00%	1.0000	—
	Short-term	$PM_{2.5}$	5	1.001 [0.994,1.007]	72.91%	0.0033	> 0.05
		PM_{10}	8	1.006 [1.003,1.008]*	63.25%	< 0.0001	> 0.05
		NO_2	7	1.009 [1.008,1.011]*	10.84%	0.2555	> 0.05
		SO_2	5	1.004 [0.999,1.009]	12.41%	0.4648	> 0.05
		CO	1	1.000 [0.956,1.046]	0.00%	1.0000	—
		O_3	1	0.628 [0.342,1.152]	0.00%	1.0000	—
AD	Long-term	$PM_{2.5}$	4	1.153 [0.962,1.381]	98.65%	< 0.0001	> 0.05
		PM_{10}	5	1.101 [0.947,1.280]	99.29%	< 0.0001	> 0.05
		NO_2	7	1.048 [0.984,1.116]	97.80%	< 0.0001	> 0.05
		SO_2	4	1.223 [0.954,1.568]	97.34%	< 0.0001	> 0.05
		CO	5	1.006 [0.998,1.013]	73.30%	0.0033	> 0.05
		O_3	5	1.003 [0.986,1.020]	0.44%	0.1920	> 0.05
	Short-term	$PM_{2.5}$	1	1.004 [1.002,1.007]*	0.00%	1.0000	—
		PM_{10}	3	1.011 [0.995,1.028]	98.35%	0.0036	> 0.05
		NO_2	3	1.000 [0.997,1.004]	0.00%	0.8268	> 0.05
		SO_2	2	1.008 [1.001,1.015]*	62.27%	0.1035	—
		CO	1	1.004 [0.999,1.009]	0.00%	1.0000	—
		O_3	3	1.033 [0.990,1.078]	82.22%	0.0035	> 0.05
AR	Long-term	$PM_{2.5}$	7	1.058 [1.014,1.222]*	90.81%	< 0.0001	< 0.05
		PM_{10}	8	1.004 [0.988,1.020]	27.66%	0.1230	> 0.05
		NO_2	11	1.003 [0.995,1.011]	0.78%	0.6720	< 0.05
		SO_2	8	1.014 [0.996,1.033]	0.00%	0.9395	> 0.05
		CO	7	1.127 [0.893,1.422]	99.68%	< 0.0001	> 0.05
		O_3	11	1.004 [0.992,1.016]	0.00%	0.7592	> 0.05
	Short-term	$PM_{2.5}$	9	1.049 [0.995,1.107]	99.27%	< 0.0001	> 0.05
		PM_{10}	11	1.028 [1.008,1.049]*	98.69%	< 0.0001	< 0.05
		NO_2	9	1.018 [1.007,1.029]*	87.91%	< 0.0001	> 0.05
		SO_2	5	1.009 [1.000,1.018]	83.78%	< 0.0001	> 0.05
		CO	3	1.000 [1.000,1.001]	0.00%	0.6335	> 0.05
		O_3	4	1.010 [0.998,1.022]	68.28%	0.0138	> 0.05

RRs were shown per 10 μg/m^3 increase in $PM_{2.5}$ or PM_{10} and 1 ppb increase in SO_2, NO_2, CO, and O_3

*Indicates that air pollutants increase the risk of IgE-mediated allergic disease

Effect of short-term air pollution exposure on eczema

In this meta-analysis, we found that an increment of 10 μg/m^3 in PM_{10} and 1 ppb in NO_2 was associated with the risk of eczema (PM_{10}, RR = 1.006, 95% CI: 1.003–1.008; NO_2: RR = 1.009, 95% CI: 1.008–1.011), and $PM_{2.5}$ and SO_2 were irrelevant with the risk of eczema (Table 2; Fig. S2). The between-study heterogeneity and publication bias are illustrated in Table 2 and Fig. S3c-S3f. Sensitivity analyses by ICD did not change the overall effect in PM_{10} and NO_2 (Fig. S4). In all age groups, PM_{10} and NO_2 increased the risk of eczema. The study design (cross-sectional) group showed no correlation on eczema in $PM_{2.5}$, PM_{10}, and NO_2, and the study design (time-series) group suggested that each increment unit in $PM_{2.5}$, PM_{10}, and NO_2 increased the risk of eczema. Exposures to $PM_{2.5}$, PM_{10}, and NO_2 were related to the risk of eczema in region (Asia) group (Fig. 2a) Studies on pollutants CO and O_3 were not enough for combining analyses at present.

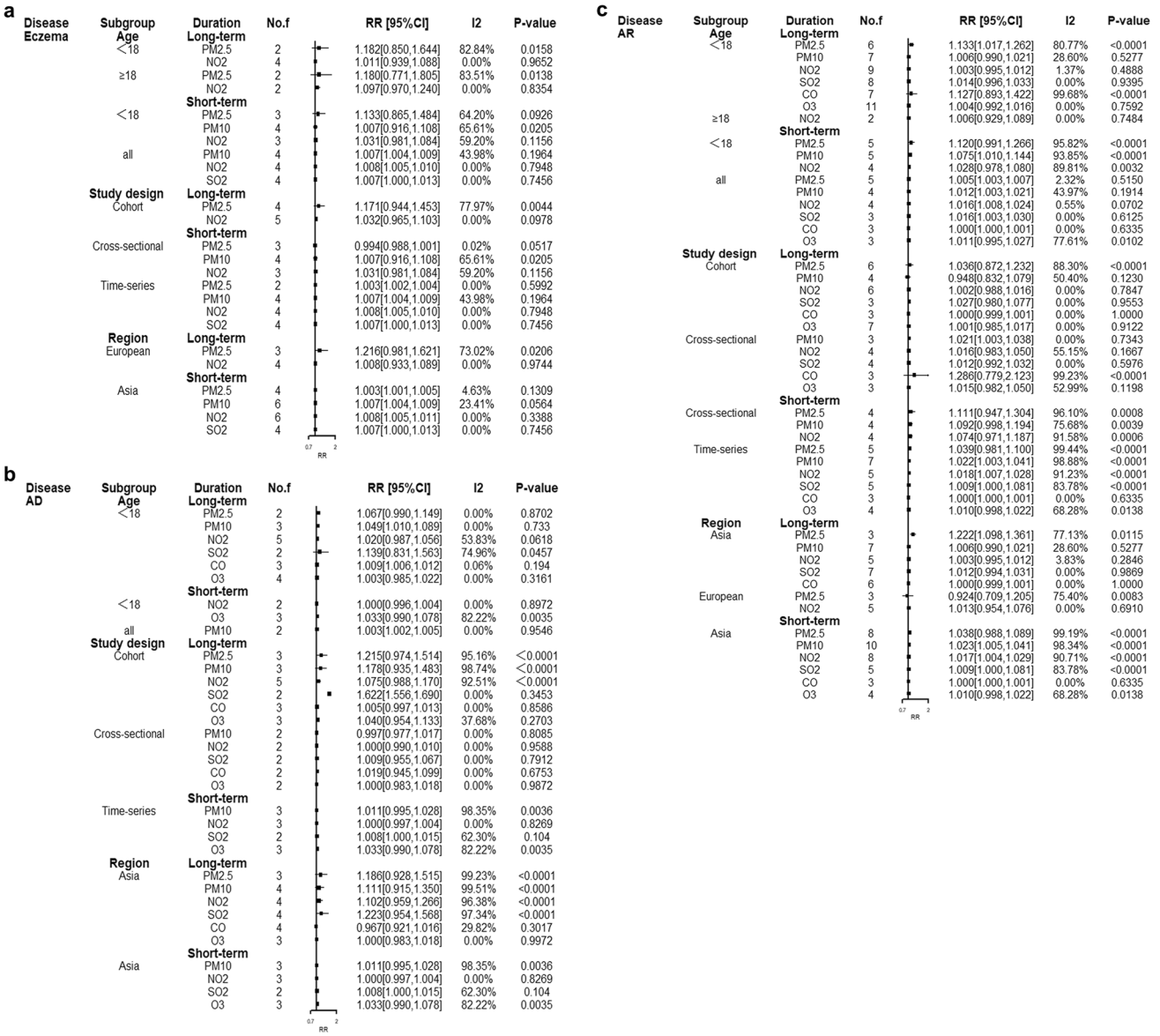

Fig. 2 Forest plot of subgroup analysis for diseases. **a** Forest plot of subgroup analysis for eczema. **b** Forest plot of subgroup analysis for AD. **c** Forest plot of subgroup analysis for AR. No.f: number of; ICD: International Classification of Diseases

Relationship between air pollution and AD

Effect of long-term air pollution exposure on AD

A total of eleven studies on AD were included in this meta-analysis. However, significant associations were not found between AD and exposure to six air pollutants (Table 2; Fig. S5). The results of heterogeneities and funnel plots are displayed in Table 2 and Fig. S6a-S6f. From Fig. 2b, ICD sensitivity analyses did not change the overall estimates (Fig. S4). The age under 18 group indicated that each increment unit in PM_{10} and CO was harmful to the occurrence of AD with low between-study heterogeneity ($I^2 < 50\%$), while $PM_{2.5}$, NO_2, SO_2, and O_3 were irrelevant. The study design (cohort) group was observed to have a significant association between AD and SO_2 (Fig. 2b). The evidence of the detailed subgroup analyses is showed in Fig. 2b.

Effect of short-term air pollution exposure on AD

As we can see from Table 2 and Fig. S5, SO_2 increased the risk of AD by 1.008 with an increment of 1 ppb (95% CI: 1.001–1.015). PM_{10}, NO_2, and O_3 had no impact on AD. The sensitivity analyses of ICD suggested that PM_{10}, SO_2, and O_3 were correlated with AD in short time (Fig. S4). PM_{10} increased the risk of AD in all age groups. The details in subgroup analyses are shown in Fig. 2b.

Relationship between air pollution and AR

Effect of long-term air pollution exposure on AR

The results showed that only $PM_{2.5}$ (an increment of 10 μg/m^3) had a harmful effect to the occurrence of AR (RR = 1.058, 95% CI: 1.014–1.222), and the heterogeneity between articles was high ($I^2 > 50\%$) (Table 2; Fig. S7). PM_{10}, NO_2, SO_2, CO, and O_3 had no effect on the risk of AR, and the specific analyses are shown in Fig. S7. The evidence of publication bias is displayed in supplementary material Fig. S8a-S8f. Sensitivity analyses in the ICD group showed no association between AR and $PM_{2.5}$ and O_3 (Fig. S4). According to subgroup analyses in Fig. 2c, in the age under 18 group, the effect estimate was increased by 1.133 for an increment of 10 μg/m^3 of $PM_{2.5}$. The study design (cross-sectional) group found a correlation between PM_{10} and AR. In the region (Asia) group, $PM_{2.5}$ strengthened the risk of AR, and all results were as shown in Fig. 2c.

Effect of short-term air pollution exposure on AR

As shown in Table 2 and Fig. S7, an increment unit in PM_{10} and NO_2 was associated with the risk of AR (PM_{10}: RR = 1.028, 95% CI: 1.008–1.049; NO_2: RR = 1.018, 95% CI: 1.007–1.029). $PM_{2.5}$, SO_2, CO, and O_3 were not associated with the risk of AR. High heterogeneity was observed in $PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3 ($I^2 > 50\%$). Funnel plots for publication bias are displayed in Fig. S8g-S8l. Sensitivity analyses by ICD, PM_{10}, NO_2, and SO_2 were harmful factors for the risk of AR. In a subgroup analysis of age, PM_{10} was harmful to the population aged < 18. For all age groups, $PM_{2.5}$, PM_{10}, NO_2, and SO_2 increased the risk of AR. The study design (time-series) group indicated that PM_{10} and NO_2 were potential risk factors for AR. In the region (Asia) group, PM_{10} and NO_2 were associated with AR risk, and more details are shown in Fig. 2c.

Discussion

In the current systematic review and meta-analysis of 55 epidemiological studies, we performed a comprehensive evaluation of available data on ambient air pollution and IgE-mediated allergic diseases. Most included studies reported a positive association between certain air pollutants' level and greater risk of IgE-mediated allergic diseases (Table 1). The meta-analysis results showed significant associations of long-term exposure to $PM_{2.5}$ with AR and AD. Besides, long-term exposure to PM_{10} was found to be related to the increased risk of eczema. Although point estimates indicate higher risk of exposure to NO_2, SO_2, CO, and O_3, the difference was not statistically significant in terms of confidence intervals. Short-term exposures to PM_{10} and NO_2 were related with eczema and AR, and short-term exposures to SO_2 and PM2.5 were associated with AD.

Actually, it is difficult to assess the health effects of individual ambient pollutants, because these substances are rarely produced in isolation. For example, a study of 317,926 children found a significant positive association between traffic-related pollution and AD in both sexes. However, analysis of individual traffic-related pollutants only revealed associations of AD with NO_x and CO in females (Lee et al. 2008). Therefore, synergistic effects of multiple pollutants can be missed when studying the effects of a single pollutant. Besides, between-study heterogeneity for these meta-analyses was high. These might be partly explained by varied study designs, regions, ages outcome definition, and exposure assessment of the included studies. Results of studies highlighted that early childhood exposure to air pollutants from birth to 5 years of age was associated with new onset of IgE-mediated allergic diseases throughout childhood and there was evidence to suggest that air pollutants may have an ongoing effect with a lag time of about 3 years (Bowatte et al. 2015). Therefore, the longer the observational duration from birth, the higher the likelihood of finding the relationship between air pollutants and IgE-mediated allergic diseases. When we conducted subgroup analyses based on age, we found that people age under 18 had a higher risk of IgE-mediated allergic diseases compared with adults aged above 18. Nevertheless, many of these subgroups are $I^2 > 50$, so age might not be the only source of heterogeneity.

Rapid urbanization, economic growth, increase in the number of vehicles, clean energy use, and proportion of primary and secondary industries reveal the different kinds and levels of pollutants in different regions (Song et al. 2017; Tan et al. 2021). Therefore, when included studies mainly came from developed countries or mainly from only limited numbers of countries, the differences of meta-analysis tend to show no statistical significance in terms of confidence intervals. When we conducted subgroup analyses based on regions, we found the impact of air pollution more severe on Asian countries. Asian regions have the most number. Many Asian countries now experienced industrialization, thus deteriorating the environment. Nevertheless, many of these subgroups are $I^2 > 50$, so the region factor might not be the only source of heterogeneity. Moreover, sample sizes vary among studies. When the differences are not statistically significant in studies with larger sample sizes, the meta-analysis always failed to find statistical significance due to the high weights of large sample size studies. In the subgroup analyses of diagnosis methods, short-term exposures to PM_{10} and NO_2 were still positively related to the risk eczema and AR, when ICD was used as classification tools in a sensitivity analysis. These evidences increase the likelihood of PM_{10} and NO_2 as risk factors of IgE-mediated allergic diseases.

To our knowledge, studies focusing on the relationship between air pollutants and risks of IgE-mediated allergic

diseases have been systematically reviewed by at least four meta-analyses. Among these, three related to AR and one related to eczema. All published meta-analyses reported a positive relationship for air pollutants to risks of IgE-mediated allergic diseases. However, the characteristics of included studies among these meta-analyses are different. Therefore, the methodology and the results they got were inconsistent. For AR, a systematic review by Zou et al. only included 13 studies investigating air pollutants and children AR prevalence. The literatures they retrieved were from January 1, 2000, to January 1, 2018. Only children aged under 18 were included. Their emphasis was put on the different impacts of air pollutants in Europe and Asia. NO_2 and $PM_{2.5}$ might be the main pollutants related to the increasing prevalence of AR on both continents (Zou et al. 2018). Lin et al. performed another meta-analysis to study the effect of particulate matter exposure on the prevalence of AR in children. More literatures were included, but only the relationship between $PM_{2.5}$/PM_{10} and AR was studied (Lin et al. 2021a). The above studies shared a shortcoming that they neglected the risk of air pollutant on adults. The prevalence of AR on adults was increased in recent years. There is an urgent need to systematically analyze the influence of air pollutants and AR in adults. More recently, Li et al. performed a meta-analysis on the same topic. This time, thirty-five studies across 12 countries were included, and the relationship between air pollutants and AR in adults was reported (Li et al. 2022). However, they did not discuss the impact of duration of exposure on the risk of having AR. For eczema, a meta-analysis extracted data from European birth cohorts (Fuertes et al. 2020). Other meta-analyses related to skin or allergic diseases might mentioned eczema (Bowatte et al. 2015; Ngoc et al. 2017). But eczema was not analyzed in detail. Our studies considered impact factors more comprehensively. In all, the results from these published meta-analyses were not exactly the same as those from our current study. We updated the literature and did subgroup analyses based on age, region, and study design. Thus, we believe our estimates on AR would be more comprehensive and targeted.

The mechanism of air pollutants' exposure on the development of allergic diseases and immunomodulating effects has not yet been fully understood. Three mechanisms have been suggested: (1) skin barrier dysfunction, (2) oxidative damage, and (3) inflammatory dysfunction. Results from our meta-analysis showed that both long-term and short-term exposures to $PM_{2.5}$ increase the risk of AD, and both long-term and short-term exposures to PM_{10} increase the risk of eczema. These results indicate the severe impact of particulate matter (PM) on IgE-mediated allergic diseases. Exposure to PM disturbed the balance of oxidant and antioxidant by reducing the transcription of antioxidant enzymes (Cachon et al. 2014; Lawal. 2017). The exposure increased reactive oxygen species, then further induced oxidative stress and activated inflammatory response, leading to epithelial barrier dysfunction (Yang et al. 2017). After exposure to NO_2, mixed Th2/Th17 adaptive immune response and neutrophils would appear. Eosinophils and neutrophils were recruited to the airway, causing inflammation and AR (Martin et al. 2013) (Fig. 3).

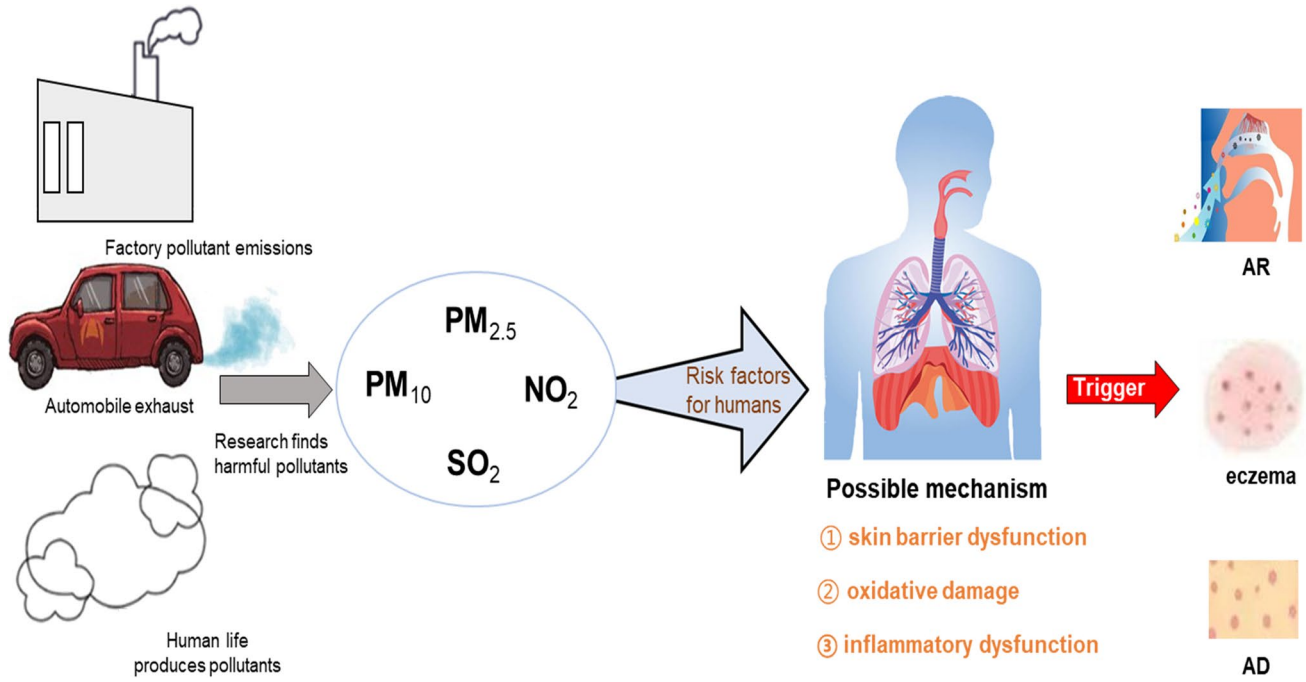

Fig. 3 Schematic diagram of mechanism

The advantages of this analysis included update studies of short-term and long-term exposure to air pollutants. There were six pollutants and a larger sample size to analyze the pooled effects, and the results were more comprehensive. Then, based on the widely accepted NOS and OHAT inclusion of the study tools, the quality and risk of deviations were carefully assessed. All included studies had high qualities. Moreover, included studies have adjusted for potential confounding factors, which can provide more accurate results and increase the statistical efficiency. However, the study limitations should be considered. A significant association was also found in subgroup analyses, but the included studies varied in study design, outcome definition, and exposure assessment, and the number of studies for some pollutants was limited. In addition, the conducted studies have limitations in correlation with other unmeasured air pollutants, uncontrolled confounding (e.g., physical activity, smoking), other environmental exposures (e.g., indoor, occupational, smoking, greenspace), and comorbidities.

In conclusion, this comprehensive meta-analysis found that air pollutants may be potentially harmful to IgE-mediated immune diseases. The adverse effect on vulnerable population age under 18 and living in developing counties should be paid more attention in future studies. Cohort studies included in this meta-analysis are limited, and few reliable evidences are provided. Therefore, more cohort studies with larger sample sizes are needed to further verify effects of air pollutants on IgE-mediated immune diseases. Previous studies usually focus on a single impact of every air pollutant, while ignoring the mixed effect of air pollutants. In fact, this effect should not to be neglected and be paid more attention. Moreover, various confounding factors should be controlled in future studies to make results more reliable. Based on the results of this meta-analysis, reducing air pollution exposure may be an effective protective measure for the occurrence of IgE-mediated immune diseases, alleviating people from diseases and saving medical resources.

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Data availability Not applicable.

Declarations

Ethics approval Not applicable.

Consent to participate Not applicable (this study does not contain any individual person's data in any form).

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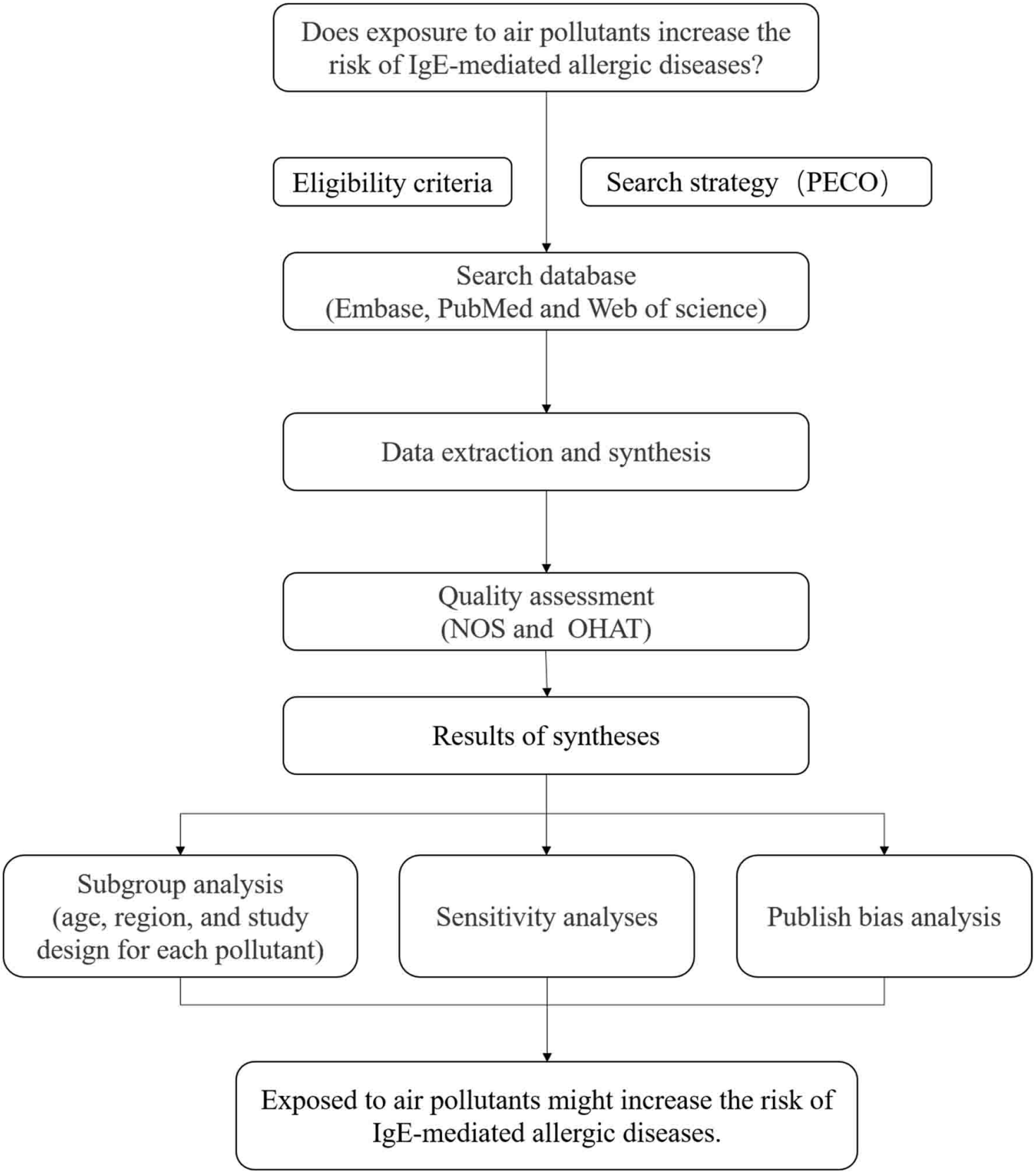
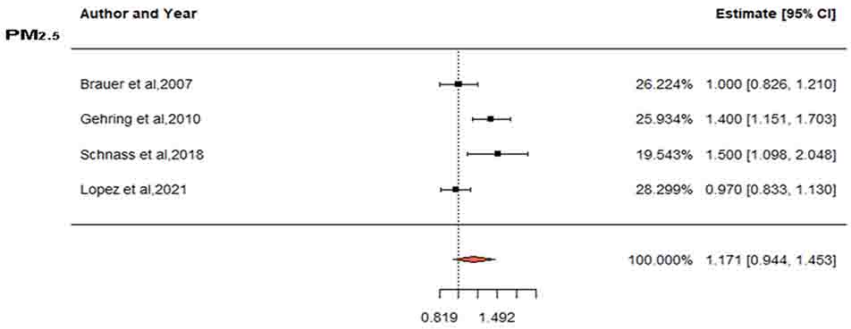
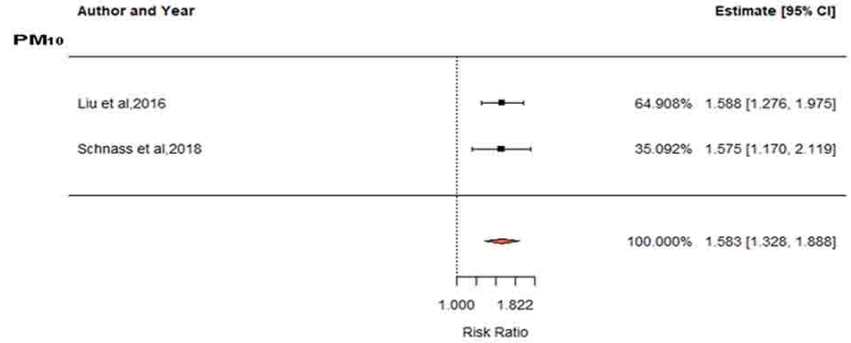
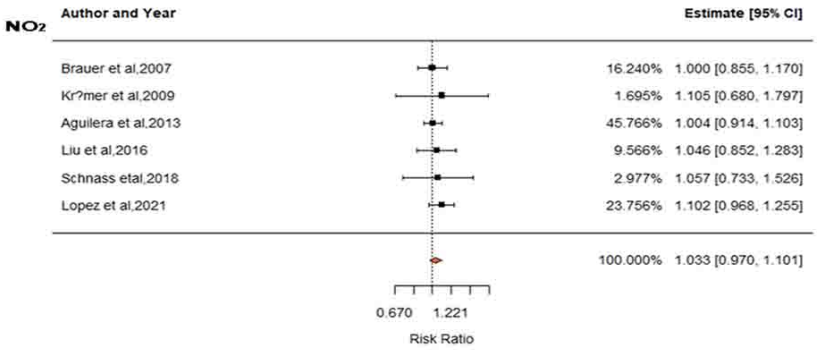

Does exposure to air pollutants increase the risk of IgE-mediated allergic diseases?
Eligibility criteria
Search strategy（PECO）
Search database (Embase, PubMed and Web of science)
Data extraction and synthesis
Quality assessment (NOS and OHAT)
Results of syntheses
Subgroup analysis (age, region, and study design for each pollutant)
Sensitivity analyses
Publish bias analysis
Exposed to air pollutants might increase the risk of IgE-mediated allergic diseases.

Long-term







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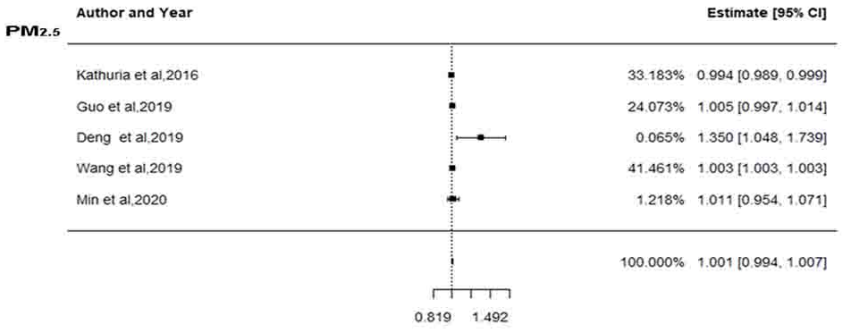

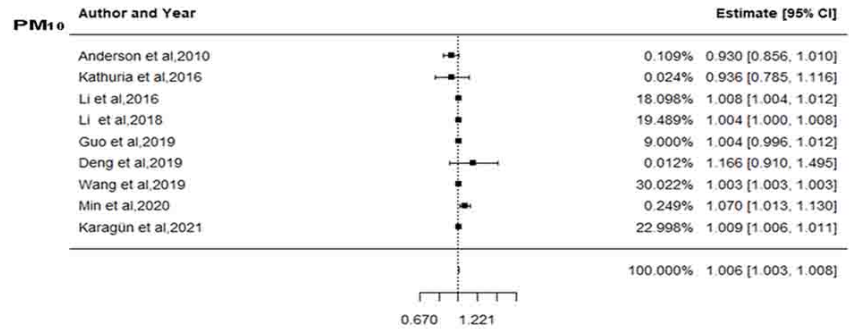

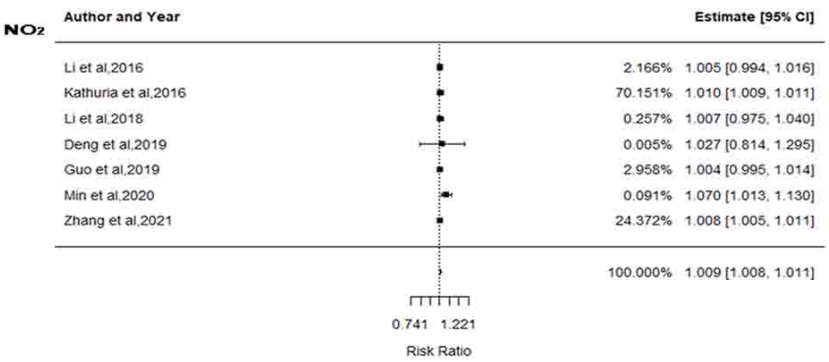

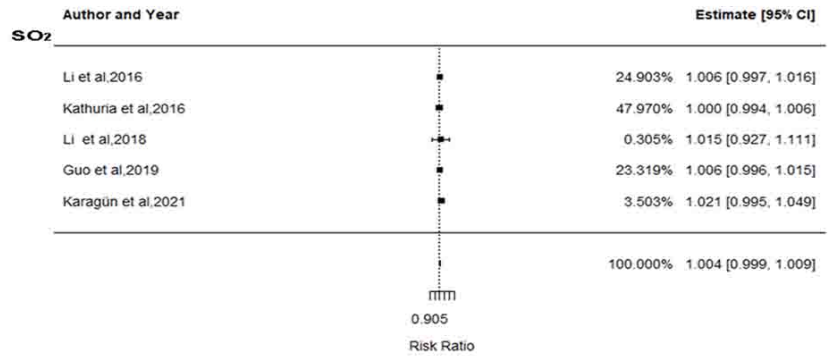

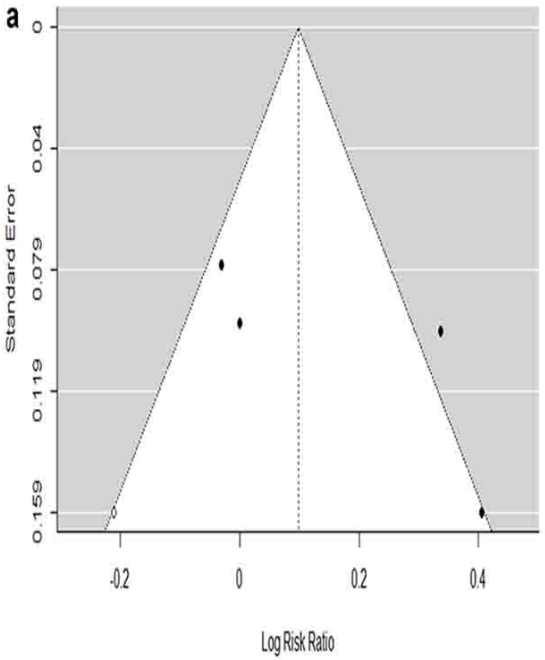

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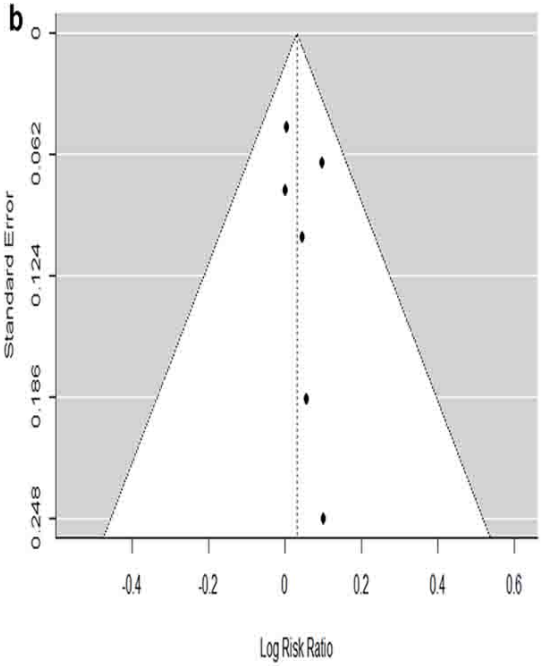

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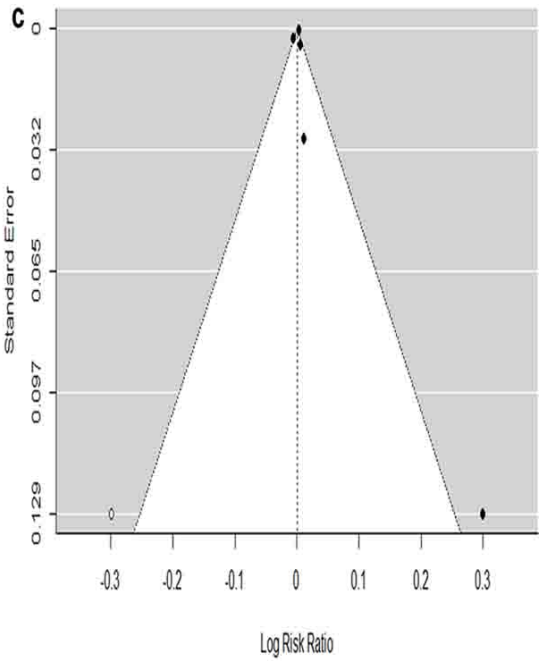

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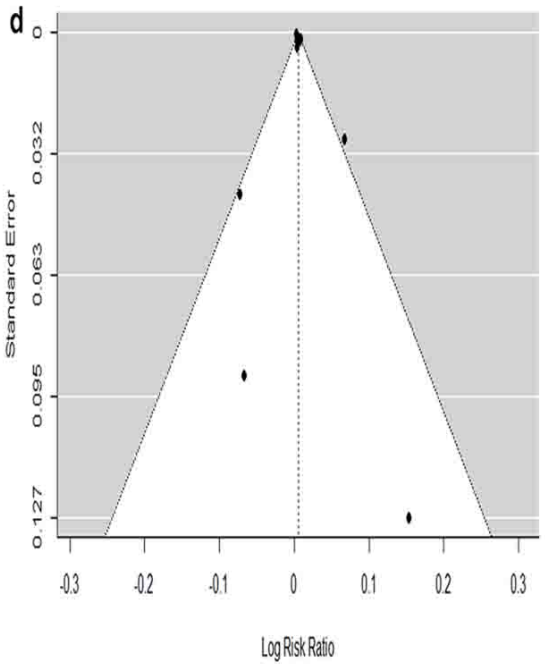
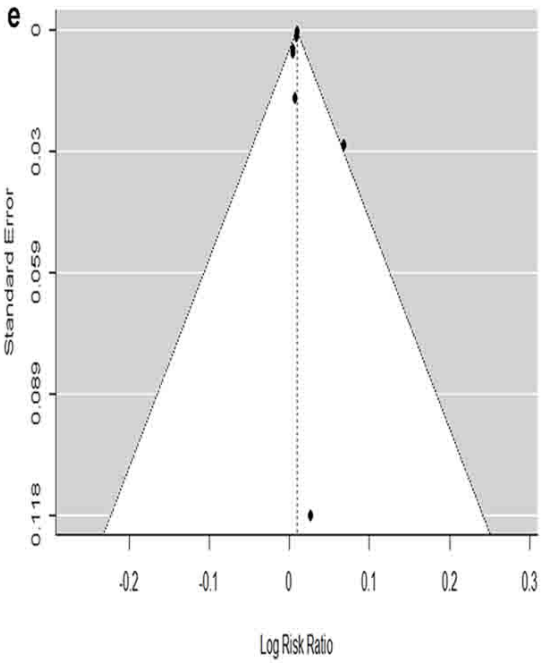


PM_{10}



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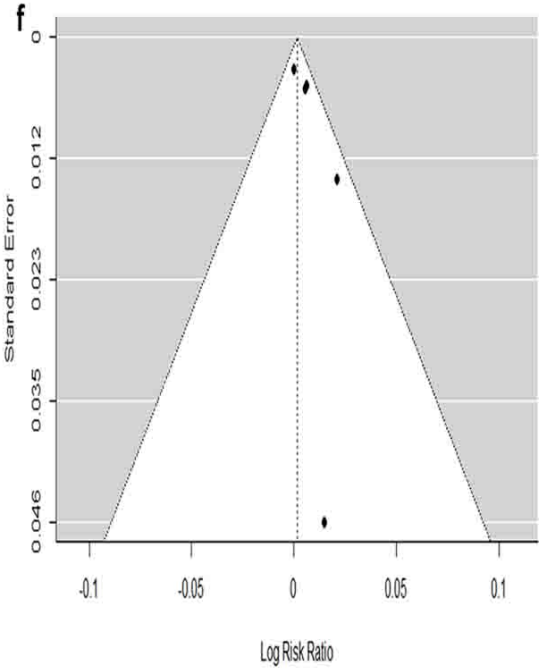
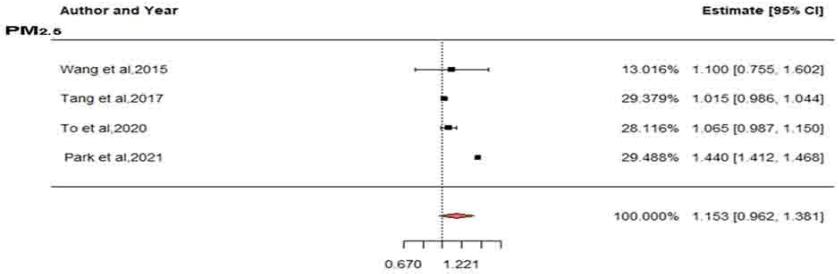
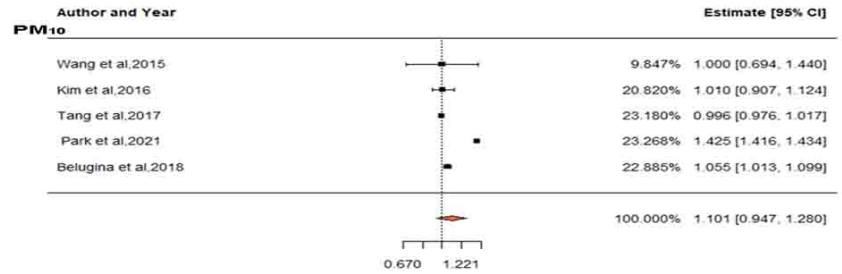


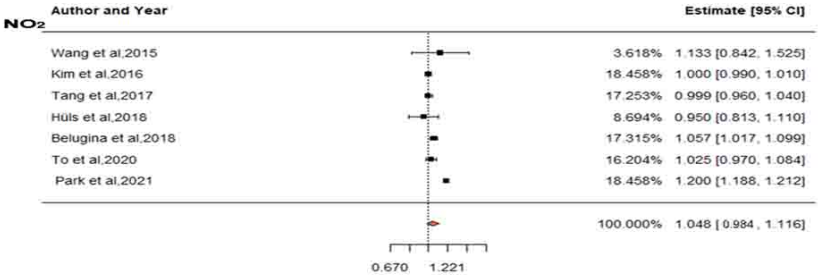
SO_2

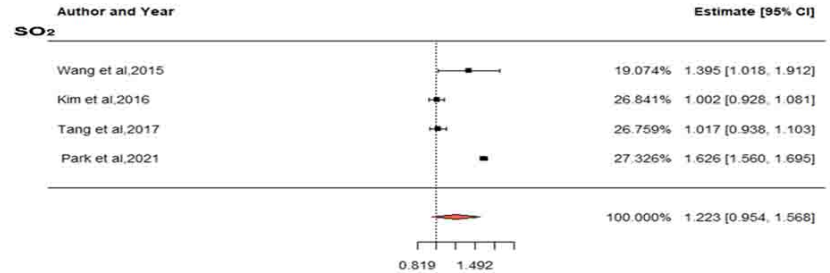
Disease	Group	Duration	No.f	RR [95%CI]	I2	P-value
Eczema	**ICD**	**Short-term**				
		PM2.5	3	0.999[0.988,1.010]	80.02%	0.0253
		PM10	6	1.005[1.003,1.008]	63.72%	0.0002
		NO2	5	1.009[1.007,1.011]	18.20%	0.4915
AD	**ICD**	**Long-term**				
		PM2.5	3	1.160[0.934,1.441]	99.27%	<0.0001
		PM10	3	1.101[0.947,1.280]	99.29%	<0.0001
		NO2	7	1.048[0.984,1.116]	97.80%	<0.0001
		SO2	2	1.288[0.813,2.039]	99.02%	<0.0001
		CO	3	1.005[0.997,1.013]	84.94%	0.0020
		O3	3	1.003[0.985,1.022]	0.00%	0.3161
		Short-term				
		PM10	2	1.003[1.002,1.005]	0.00%	0.9546
		NO2	2	1.000[0.997,1.004]	0.00%	0.5446
		SO2	2	1.008[1.001,1.015]	62.27%	0.1035
		O3	2	1.012[1.007,1.017]	0.00%	0.9795
AR	**ICD**	**Long-term**				
		PM2.5	2	1.145[0.885,1.480]	95.37%	<0.0001
		O3	2	1.040[0.949,1.140]	0.00%	0.8273
		Short-term				
		PM2.5	5	1.032[0.968,1.100]	99.53%	<0.0001
		PM10	6	1.030[1.004,1.056]	97.79%	<0.0001
		NO2	5	1.022[1.009,1.035]	75.66%	0.0003
		SO2	3	1.016[1.003,1.030]	0.00%	0.6125
		CO	3	1.000[1.000,1.001]	0.00%	0.6335
		O3	3	1.003[0.994,1.012]	0.00%	0.9664

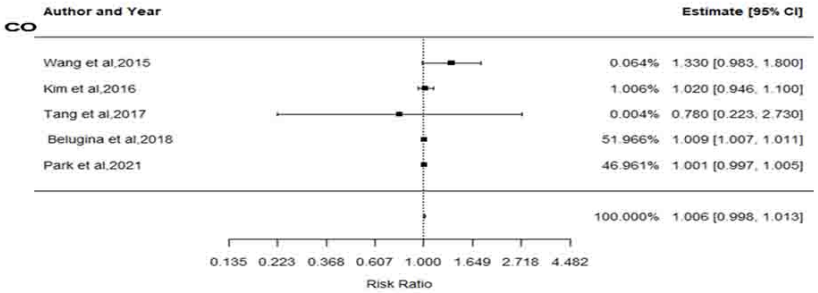
Long-term

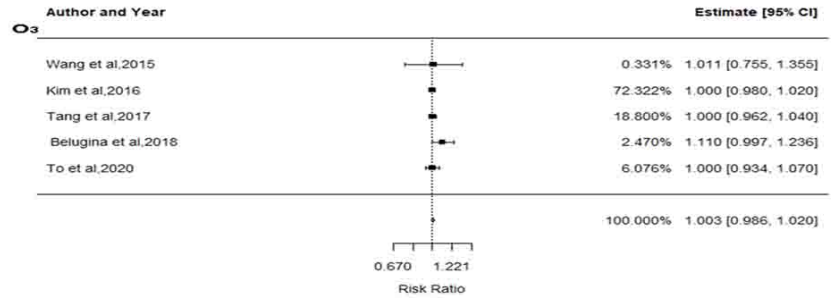




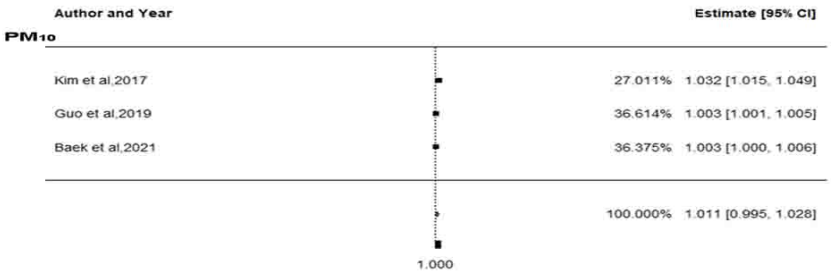


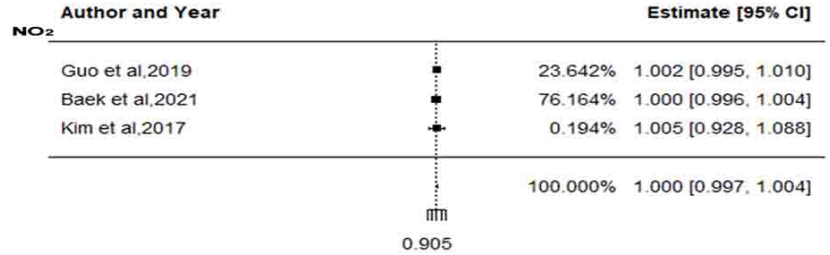


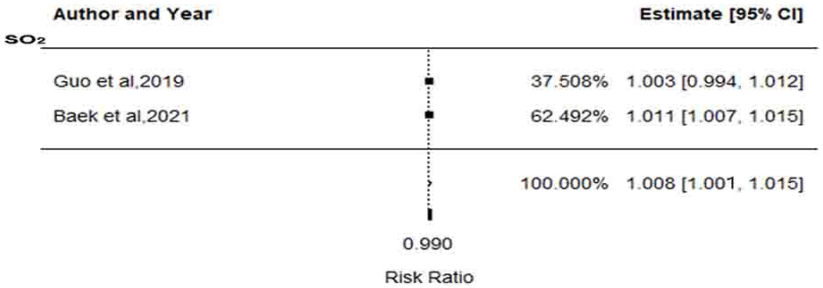


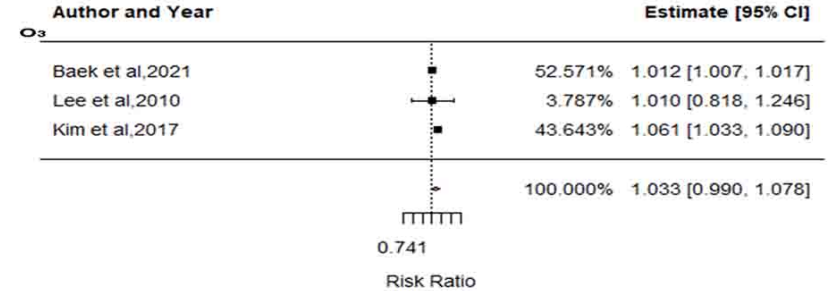


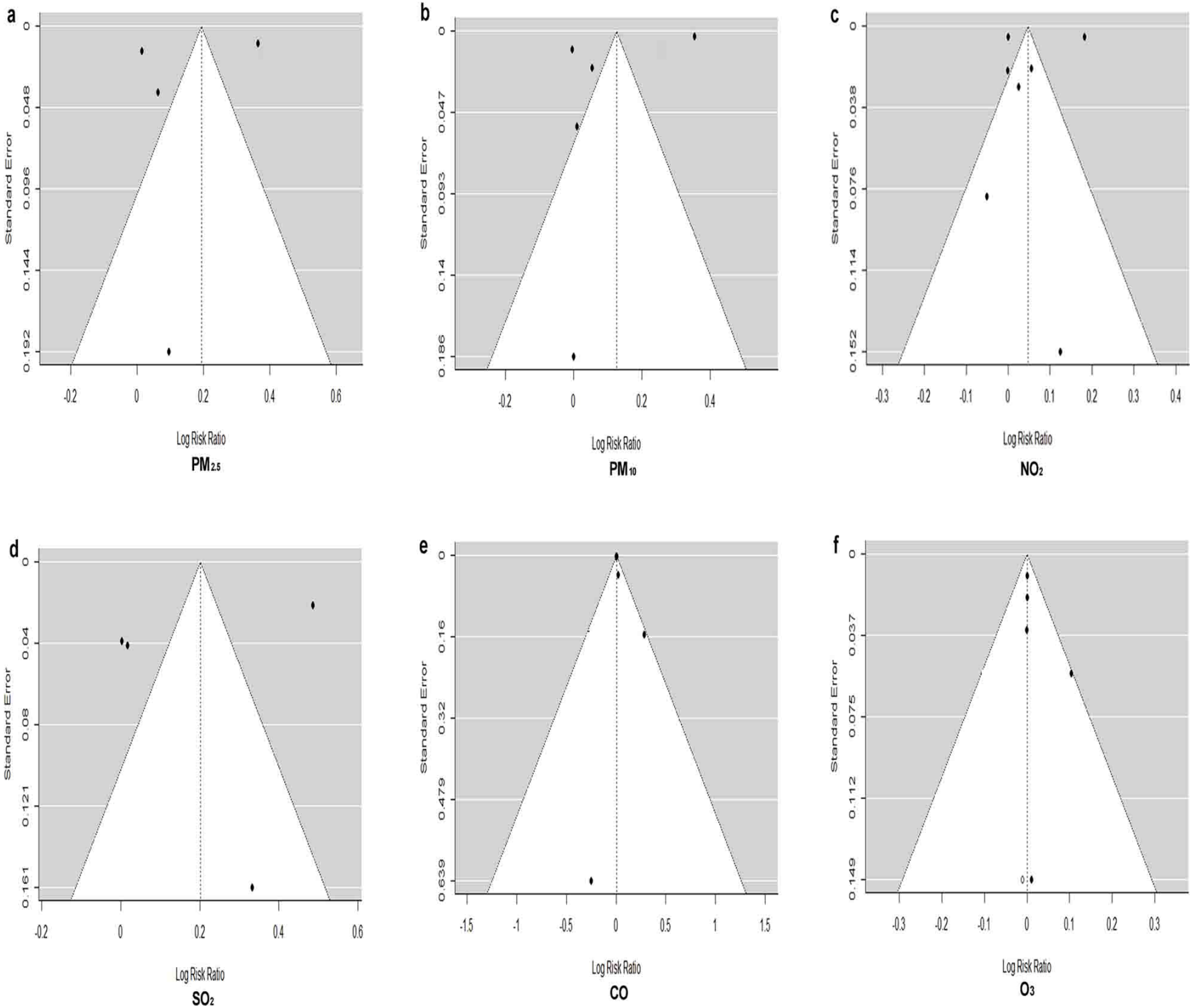
Short-term







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Log Risk Ratio
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0.4
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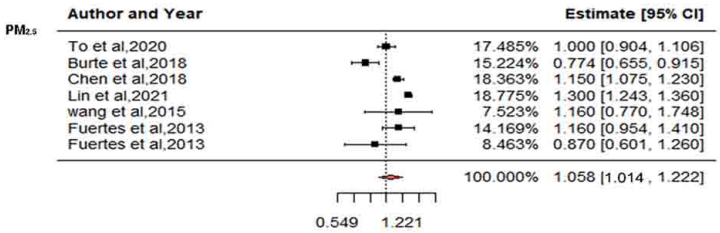
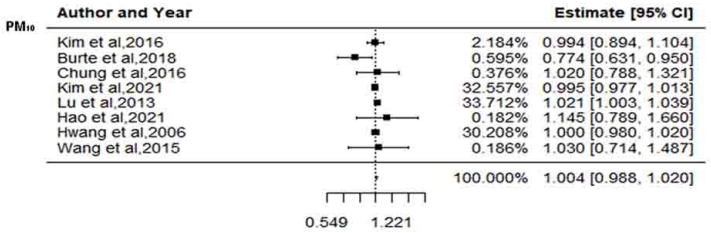
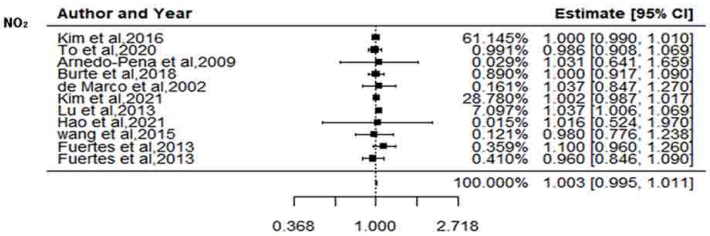
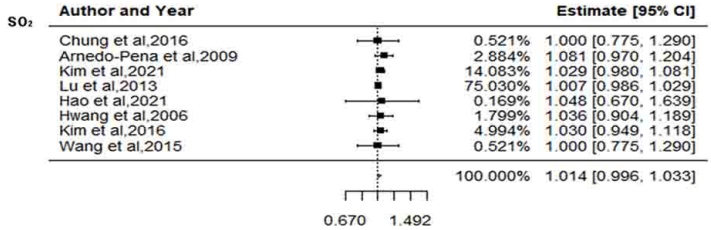
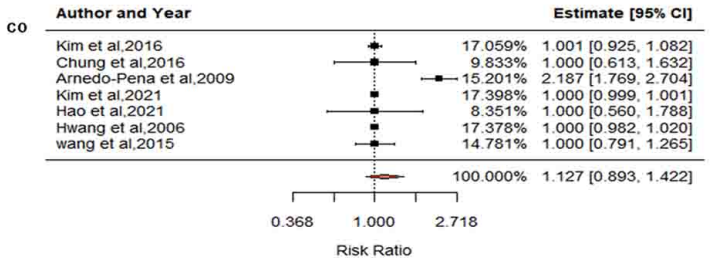
Long-term

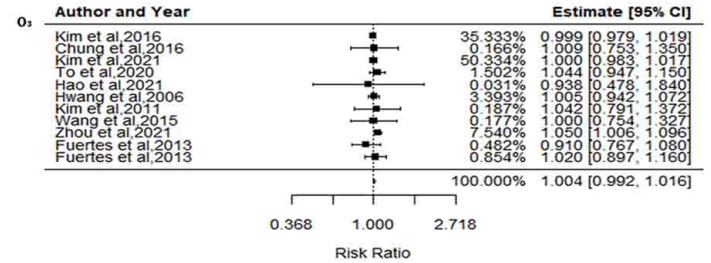




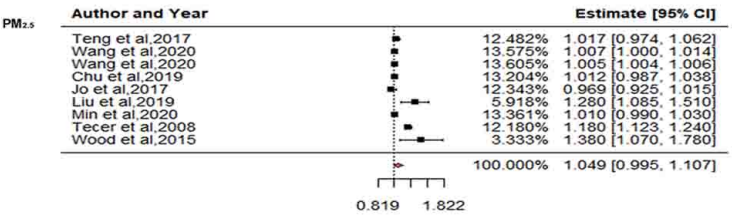


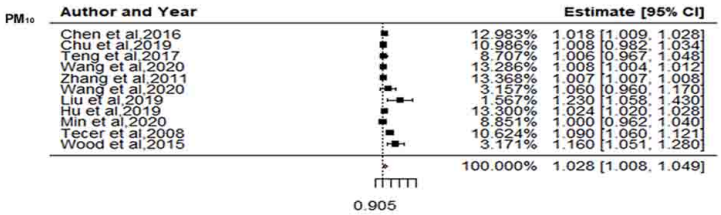


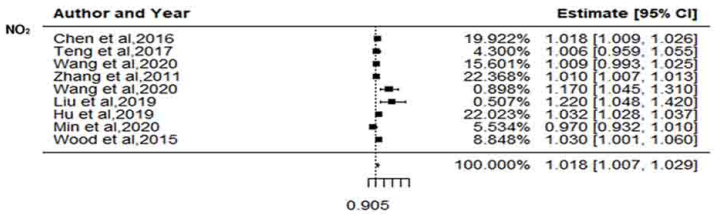


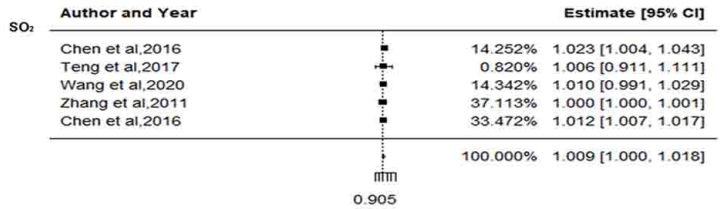


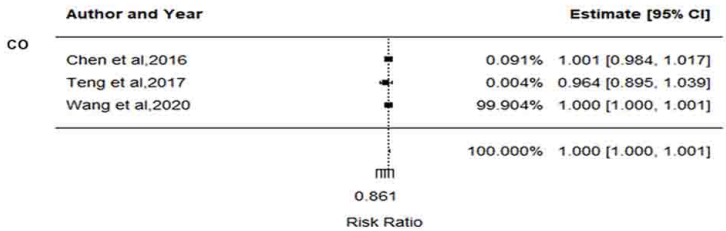
Short-term

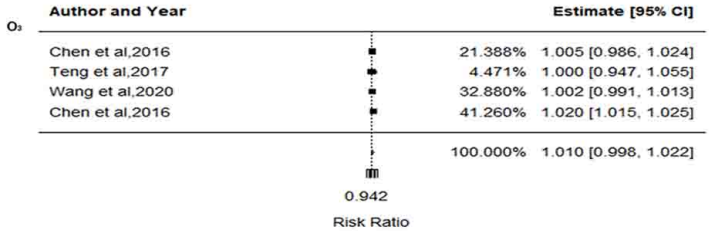


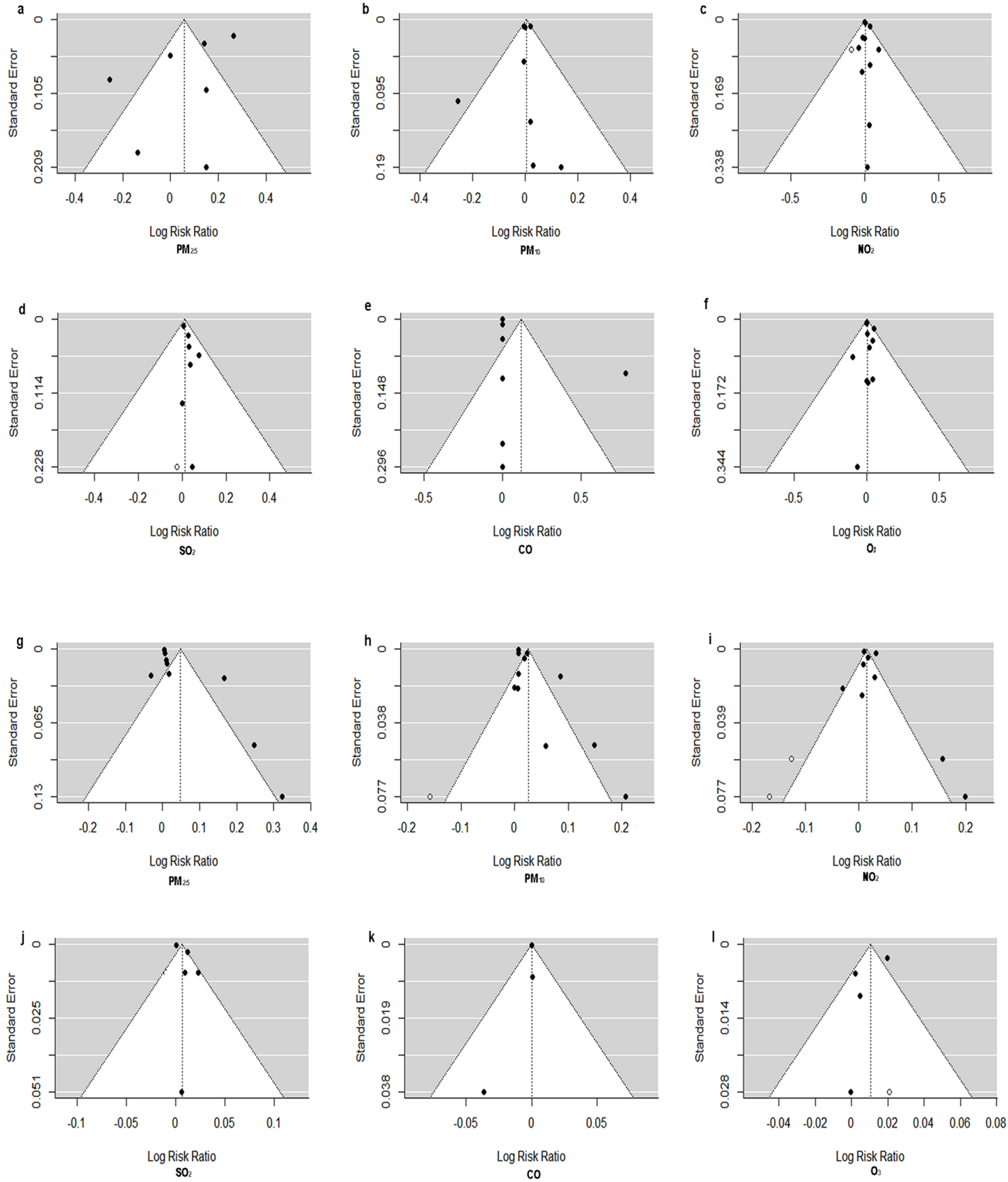











Long term
Short term
a
b
c
d
e
f
g
h
i
j
k
l
Standard Error
Log Risk Ratio
PM2.5
PM10
NO2
SO2
CO
O3