

The relationship between outdoor air pollutants and atopic dermatitis of adults: A systematic review and meta-analysis

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Abstract

Background: Atopic dermatitis (AD) poses a significant disease burden in adults. Environmental factors are essential in its pathogenesis.

Objective: Given the possible role of air pollutants in allergic diseases, it is worthwhile to summarize the effects of outdoor air pollution on adult AD.

Methods: We undertook a systematic review based on PubMed and EMBASE as of August 16, 2021, and found 20 relevant studies. A random-effects meta-analysis was carried out.

Results: Regarding long-term effects (within months to years), traffic-related air pollution and particulate matter < 2.5 µm in diameter (PM_{2.5}, per 10 µg/m³ increment) are associated with the prevalence of adult AD (OR 1.40, 95%CI [1.24, 1.58] and 1.67, 95%CI [1.26, 2.21]). Exposures to PM_{2.5} and nitrogen dioxide are associated with incident AD, with ORs of 2.30 (95%CI: 1.25, 4.25) and 1.30 (95%CI: 1.04, 1.61) per 10 µg/m³ increment. In terms of short term effects (within days), exposure to particulate matter < 10 µm in diameter (PM₁₀) and sulfur dioxide (SO₂) are associated with exacerbations of AD at lag day 0 based on those time-series studies, with an excessive risk of 2.9%, in particular, per 10 µg/m³ increment in SO₂ exposure. In addition, both short-term and long-term exposures to these air pollutants are associated with AD symptoms (eczema, pruritus, and sleep disturbance).

Conclusions: Outdoor air pollutants exert both short-term and long-term adverse effects on adult AD, contributing to its development, severity and exacerbation of symptoms. The influence of air pollution should be considered in the management of adult AD.

Key words: Air Pollution, Atopic Dermatitis, Nitrogen Dioxide, Particulate Matter, Sulfur Dioxide

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Introduction

Atopic dermatitis (AD) is a chronic, relapsing, eczematous disease characterized by severe pruritus and skin dryness. It poses a heavy burden on patients' quality of life and healthcare resources.¹ The human skin is in direct contact with a variety of environmental factors, such as humidity,

allergens, chemical substances, etc., which play an essential role in the pathogenesis of AD.² The prevalence of AD is increasing globally, especially in the developing countries.³ One predisposing factor is likely pollutants in the ambient air. Growing evidence supports the contribution of air pollution to allergic diseases like asthma and AD in children with some controversy.⁴⁻⁶ Recent epidemiological studies reported a high prevalence of AD in adults, reaching 10-17% in the general population.⁷⁻⁹ However, few studies have been published on the influence of air pollution on adult AD.¹⁰⁻¹²

In recent decades, a number of studies have been conducted to investigate this issue. We hypothesized that outdoor air pollutants adversely affects AD in adults and therefore undertook a comprehensive systematic review to summarize current knowledge on the influence of these air pollutants on adult AD.

Methods

Literature search

Our review focused on studies investigating the relationship between AD in adults (≥ 18 years) and outdoor chemical air pollutants, including traffic-related air pollution, particulate matter, nitrogen dioxide (NO₂), sulfur dioxide (SO₂), ozone (O₃), and carbon monoxide (CO). The algorithm followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist. We searched both the EMBASE and MEDLINE databases, and reviewed English literature till August 16, 2021. A review is exempted from the Institutional Review Board of Taichung Veterans General Hospital. This systematic review was registered in PROSPERO (CRD42022310716).

Selection of studies

Three authors (YY Hsiao, YH Chen, and KT Tang) independently assessed the titles and abstracts identified by the searches described above. The relevant full-text articles were then retrieved. Two authors (YY Hsiao and KT Tang) independently evaluated the full-text articles for eligibility. We selected articles, including conference abstracts, relevant to the relationship between outdoor air pollution and adult AD. These studies included cohorts, cross-sectional, case-control, and time-series studies. The references for the selected articles were also reviewed for relevance. Studies excluded were those enrolling children and/or adolescents only (< 18 years of age). We also excluded those studies concerning exclusively occupational exposure, indoor air pollutants, and/or tobacco smoking. Studies published in languages other than English were excluded. In case of controversy, it was resolved through group discussion. Finally, a total of 20 studies were finally identified (Figure 1).¹⁰⁻²⁹ We categorized selected studies into studies regarding long-term effects (within months to years) and short-term effects (within days) of air pollutants on AD, with the cut-off duration of 30 days.

Data extraction

Information regarding the influence of outdoor chemical air pollutants on the incidence, prevalence and/or severity of AD in adults was independently retrieved from each study by two authors (YY Hsiao and KT Tang), and recorded in a standardized Excel file. The outcome measures included odds ratios (ORs) and risk ratios per 10 $\mu\text{g}/\text{m}^3$ increment in exposure levels to air pollutants. For a time-series study, risk ratios derived from either the single or cumulative lag model were recorded. We did not contact authors for unreported data.

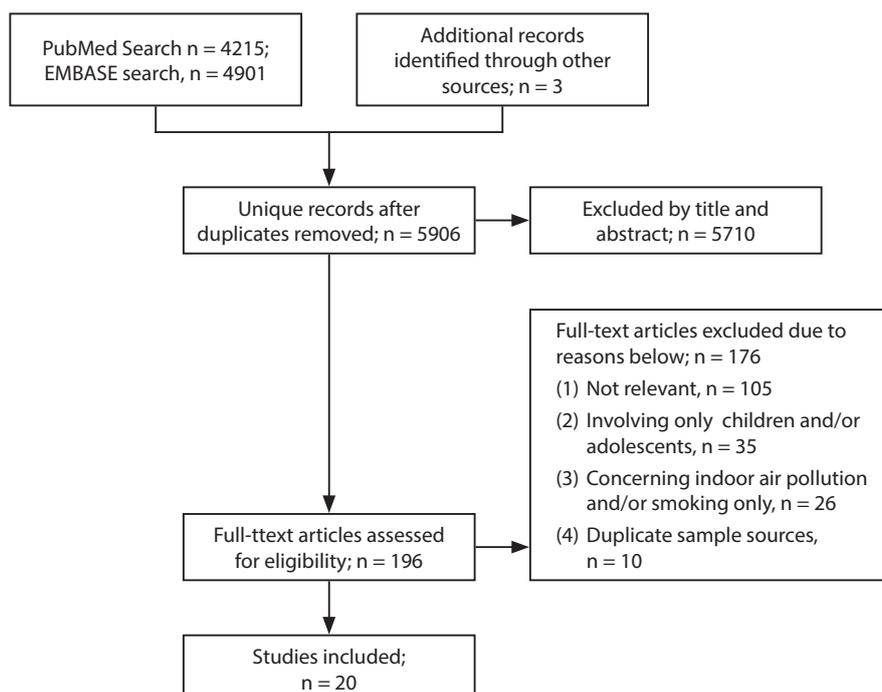


Figure 1. The algorithm of study selection.

Risk of bias

Risk of bias was evaluated using the tool: Risk of Bias in Non-Randomised Studies of Interventions (ROBINS-I).³⁰ This tool incorporates 7 domains, including confounding, selection of participants, classification of intervention, deviation from interventions, missing outcome data, measurement of outcomes, and selection of reported result. The overall risk of bias was rated as follows: 0, no information; 1, low risk; 2, moderate risk; 3, serious risk; and 4, critical risk. Two authors (YY Hsiao and KT Tang) independently assessed these risks of bias. In case of disagreement, it was resolved through group discussion.

Statistical analyses

Statistical analyses were performed using Stata version 14.0 (StataCorp, College Station, TX, USA). The summary estimates of odds ratio and risk ratio were derived using the command “metan” according to a random effects model following the procedure of DerSimonian & Laird provided data were obtained from two or more studies of similar design (e.g. cohorts or cross-sectional studies).³¹ Risk ratios from the time-series studies were presented as excessive risks. The heterogeneity across studies was quantified based on Tau^2 , Chi^2 , and I^2 measures derived from the Mantel-Haenszel model. Begg’s and Egger’s tests were used to assess publication bias, while funnel plots were presented to visualize asymmetry. A p value < 0.05 was considered statistically significant. The Bonferroni correction was undertaken in the meta-analyses regarding different lag times in the time-series studies.

Stratification and sensitivity analyses

Analyses after stratification according to gender and season were performed whenever data were available. In addition, sensitivity analyses were performed after excluding studies conducted in a single center or studies with an overall high risk of bias (serious or critical).

Results

Characteristics of selected studies

Characteristics of the selected studies are listed in **Table 1**. In the 9 studies on long-term effects of air pollutants, there were 4 cohorts and 5 cross-sectional studies. In these studies, female constituted around 50% of the subjects. The only exception was the Study on the influence of Air pollution on Lung Function Inflammation and Ageing (SALIA) cohort, in which only women were recruited as subjects.¹⁴ Their mean age was also older (74 years) when compared with those in other studies.

In the 11 studies on short-term effect of air pollutants, most were time-series studies. Only one was a time-stratified cross-over study.²⁹ Since a time-stratified cross-over air pollution study is considered equivalent to a time-series study,³² we synthesized their data altogether. While adult cases constituted the majority of subjects, all ages were

accounted for in these studies. The proportion of female subjects was 50-60% in most of the studies except for an Iranian study, in which 84% of participants were female.²¹

Most outcome measures in these time-series studies were based on hospital records of outpatient and/or emergency department visits due to AD. Only one study was based on questions on AD symptoms.²¹ These studies were all conducted in Asian countries and 7 of them were single-center studies.

Long-term effects of air pollutants on adult AD

As shown in **Figure 2a**, exposures to traffic-related air pollution and PM_{2.5} were associated with prevalent adult AD (OR 1.40, 95% CI [1.24, 1.58] and 1.67, 95%CI [1.26, 2.21]). Exposures to particulate matter < 2.5 μ m in diameter (PM_{2.5}) and NO₂ were associated with incident AD, with ORs of 2.30 (95% CI: 1.25, 4.25) and 1.30 (95% CI: 1.04, 1.61) per 10 μ g/m³ increase respectively. Regarding effect of particulate matter < 10 μ m in diameter (PM₁₀) on prevalent AD, the inter-study heterogeneity was moderate across studies. The study of Patella et al. recruited 58 pediatric and adult AD patients and recorded their monthly disease activity based on the index of SCORing Atopic Dermatitis (SCORAD).¹⁵ An increase of 10 μ g/m³ in PM₁₀, NO₂, and O₃ concentrations were associated with an increase of AD symptoms by 3.0% (95% CI: 0.3, 4.2), 2.7% (95% CI: 0.7, 4.7), and 3.0% (95% CI: 1.2, 4.7) respectively. Furthermore, exposures to these pollutants were more predictive of disease severity than weather factors.

Short-term effects of air pollutants on adult AD

Results of meta-analyses on short-term effects of air pollutants on AD exacerbations (outpatient and/or emergency department visits) based on time series studies are summarized in **Figure 2b and 2c**. Data with respect to CO are not shown due to wide 95% confidence intervals. In the single lag model, PM_{2.5}, PM₁₀ and SO₂ were associated with AD exacerbations at lag day 0, although the association between PM_{2.5} and AD exacerbations was not statistically significant after correction of multiple comparisons. In particular, exposures to SO₂ was associated with excessive risks of 2.9% (95%CI: 1.3, 4.7) per 10 μ g/m³ increase at lag day 0. We also observed a trend in which the effects of pollutants PM_{2.5}, PM₁₀, SO₂, and NO₂ were attenuated with the increasing lag time. In contrast, O₃ was significantly associated with AD exacerbations at lag day 4 and 7. On the other hand, in the cumulative model, some of the associations regarding PM₁₀, SO₂, and O₃ were statistically significant, despite no obvious trend. In particular, SO₂ exposure was significantly associated with an excessive risk of 2.3-3.7% for AD exacerbations per 10 μ g/m³ increment. In addition, Nakhjirgan et al. reported that both PM_{2.5} and PM₁₀ are associated with skin itching and sleep disturbance at lag day 0, 1, and 2 in AD patients.²¹

Table 1. Study characteristics.

Study ^r	Country	Study design (duration)	Sample size (proportion of female)	Mean/median age (years)	Outcome ascertainment methods	Statistical methods	Confounders adjusted for in the analysis	Measurement of exposure to air pollutants
Long-term effects (within months or years)								
Montnemery et al. (2009) [10]	Sweden	Cross-sectional	8469	20–59 [‡]	Questionnaire	Logistic regression	Age, sex, and occupation	Questionnaire
Pesce et al. (2015) [11]	Italy	Cross-sectional	10464	20–44 [‡]	Questionnaire	Logistic regression	Age, sex, education level, occupation, smoking, proximity to industrial plants, residential area, geo-climatic area, season, center-specific rank of response, and type of survey	Questionnaire
Seo et al. (2016) [12]	Korea	Cross-sectional	N.A.	N.A.	Health insurance claims data	Linear regression	Socioeconomic and weather factors	Monitoring stations
Tang et al. (2017) [13]	Taiwan	Cross-sectional	5115 (57%)	44	Health insurance claims data	Logistic regression	Age, sex, levels of urbanization, family income, and exposures to other air pollutants	Monitoring stations
Huls et al. (2018) [14]	Germany	Cohort (19 years) and cross-sectional	834 (100%)	74	Questionnaire	Logistic regression	Age, body mass index, educational status, indoor combustion of fossil fuels, smoking, and exposure to second-hand smoke	Land-use regression
Patella et al. (2020) [§] [15]	Italy	Cohort (1.5 years)	60 (47%)	24	Hanifin and Rajka criteria	Generalized linear mixed model	Age, sex, baseline disease severity, weather factors, and use of topical corticosteroids	Monitoring stations
Tang et al. (2020) [§] [16]	Taiwan	Cross-sectional	34 (50%)	33	Hanifin and Rajka criteria	Mann-Whitney U test	Nil	Urine metabolites
Park et al. (2021) [17]	Korea	Retrospective cohort (4.9 years)	2091.68 (54%)	N.A.	Health insurance claims data	Cox proportional hazards regression	Age, sex, income, comorbidity, and meteorological variables	Monitoring stations
Lopez et al. (2021) [18]	Australia	Cohort (10 years)	3153 (50%)	53	ISAAC definition	Logistic regression	Age, sex, household cooking by indoor combustion of solid and gas fuels, occupation, education level, smoking, and second-hand smoking	Satellite-based land-use regression

Table 1. (Continued)

Study [†]	Country	Study design (duration)	Sample size (proportion of female)	Mean/median age (years)	Outcome ascertainment methods	Statistical methods	Confounders adjusted for in the analysis	Measurement of exposure to air pollutants
Short-term effects								
Li et al. (2016) [§] [19]	China	Time-series study (5 years)	510158	N.A.	Hospital records	GAM	Calendar day, day of the week, and holidays	A monitoring station
Li et al. (2018) [§] [20]	China	Time-series study (5 years)	72305 (51%)	N.A.	Hospital records	Distributed lag nonlinear model	Day of the week and holidays	Monitoring stations
Nakhjirgan et al. (2019) [§] [21]	Iran	Time-series study (62 days)	31 (84%)	24	Questionnaire	Generalized estimating equations	Humidity and outdoor stay	Monitoring stations
Wang et al. (2019) [22]	China	Time-series study (2 years)	1966991 (60%)	58	Health insurance claims data	GAM	Day of the week, calendar time, national holidays, temperature, and humidity	A monitoring station
Guo et al. (2019) [§] [23]	China	Time-series study (5 years)	64987 (60%)	N.A.	Hospital records	GAM	Seasonal and long-term trends, day of the week, and holidays	Monitoring stations
Baek et al. (2021) [24]	Korea	Time-series study (4 years)	513870 (52%)	N.A.	Health insurance claims data	GAM	Temperature, humidity, season, day of the week, and public holidays	Monitoring stations
Karagün et al. (2021) [25]	Turkey	Time-series study (6.5 years)	27549 (58%)	N.A.	Hospital records	Distributed lag nonlinear model	Day of the week and temperature	Monitoring stations
Wang et al. (2021) [§] [26]	China	Time-series study (5 years)	29972 (51%)	N.A.	Hospital records	GAM	Temperature and humidity	Monitoring stations
Wang et al. (2021) [§] [27]	China	Time-series study (6 years)	16891 (62%)	N.A.	Hospital records	GAM	Temperature, humidity, day of the week, calendar day, and holidays	Monitoring stations
Zhang et al. (2021) [§] [28]	China	Time-series study (6 years)	300751 (50%)	N.A.	Hospital records	GAM	Temperature, humidity, calendar day, and day of the week	Monitoring stations
Park et al. (2021) [29]	Korea	Time-stratified cross-over study (one year)	18316	N.A.	Health insurance claims data	Conditional logistic regression	Meteorological factors and national holidays	N.A.

GAM, generalized additive model; ISSAC, the International Study of Asthma and Allergies in Childhood; N.A., not available.

[†]Reference number of the study was specified in brackets.

[§]Only range reported.

[§]single-center studies.

a

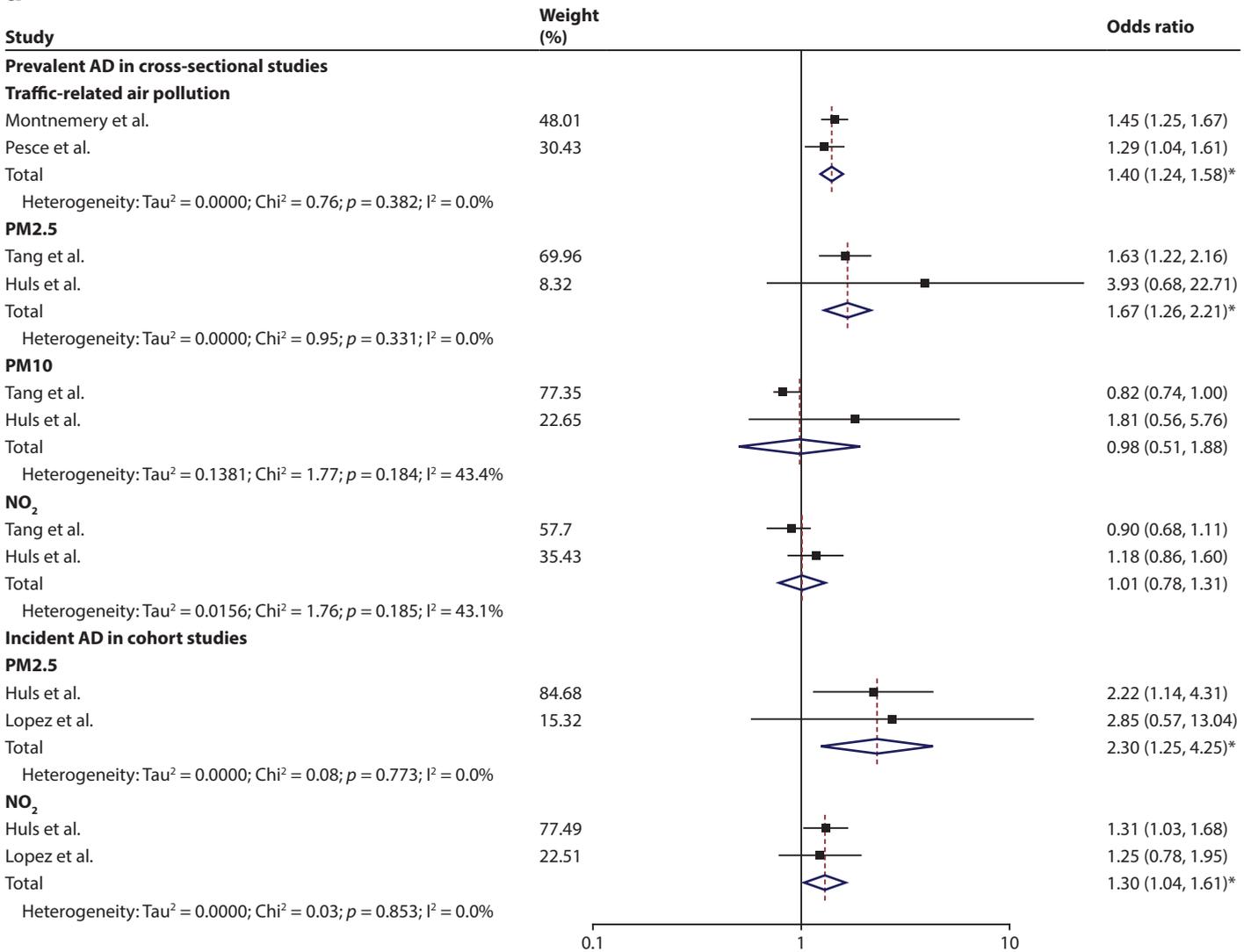
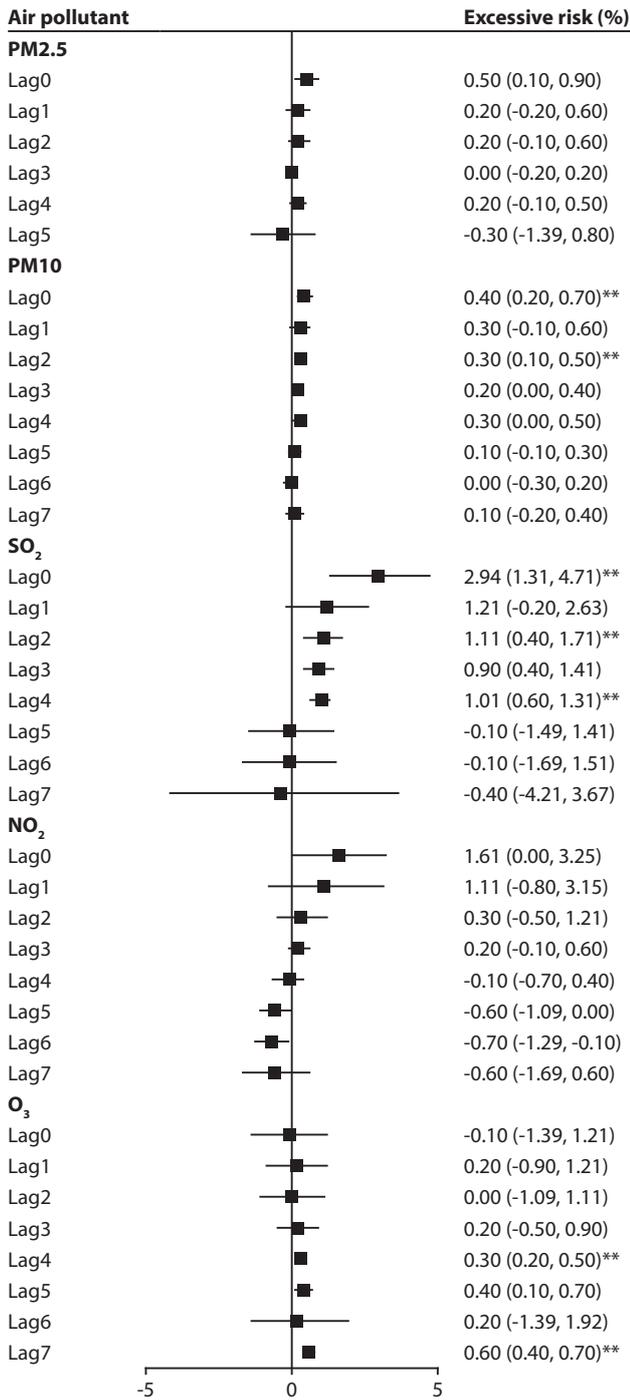


Figure 2. The meta-analyses of the (a) long-term effects and short-term effects (exacerbations), in either (b) the single lag, or (c) the cumulative lag model, of outdoor air pollutants (per 10 µg/m³ increment) on adult AD in adults. The black squares represent the effect estimates of the individual studies and the diamonds represent the summary effect estimates.

AD, atopic dermatitis; PM2.5, particulate matter < 2.5 µm in diameter; PM10, particulate matter < 10 µm in diameter.

*p < 0.05; **p < 0.006; ***p < 0.007, based on the Bonferroni correction.

b



c

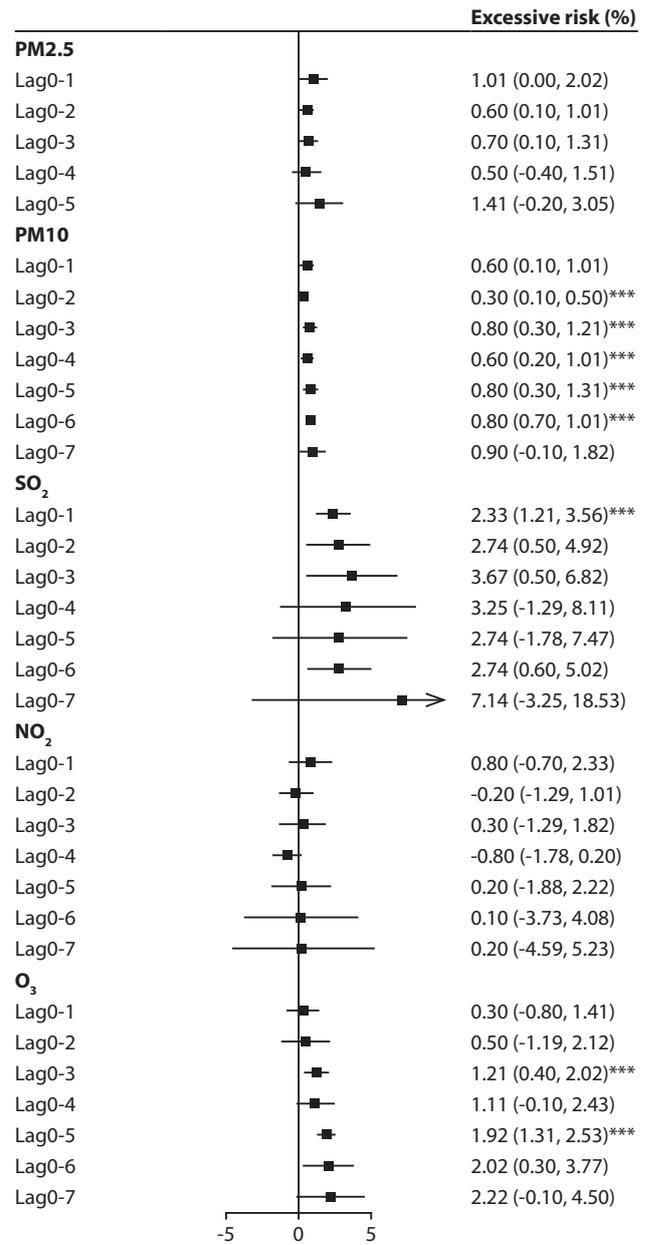


Figure 2. (Continued)

Potential effect modifiers

Potential effect modifiers regarding the influence of outdoor air pollutants on adult AD are summarized in **Table 2**. In addition, we noted in several studies that children and adolescents were more vulnerable to the short-term effects of air pollutants on AD exacerbations.^{24,26,28,29}

Table 2. Potential effect modifiers with regards to the influence of air pollutants on adult AD.

Factors	Characteristics of the vulnerable subpopulations	Reference number
Age	Older age	12, 21, 27, 28
Sex	Men	12, 17
Socioeconomic status	Higher socioeconomic status	23
Geographic area	Certain areas	11
Genetics	Low genetic predisposition to AD	13
Temperature	Higher temperature	22
Seasons	Warm and cold seasons	18, 23, 25, 28

AD, atopic dermatitis.

Stratification analyses

In terms of seasons, we observed no modifying effect regarding short-term effects of air pollutants (**Figure 3**). Owing to limited data, we did not undertake meta-analyses after stratification according to seasons regarding long-term effects of air pollutants, nor after stratification according to sex regarding long-term and short-term effects of air pollutants.

Risk of bias

In the 9 studies on long-term effects of air pollutants, 3 of them were recognized as having a serious risk. In the 11 studies on short-term effects of air pollutants, 3 of them were recognized as having a serious risk.

Sensitivity analyses

After we had excluded single-center studies, in the single lag model, the associations between AD exacerbations and PM10 at lag day 0 and 2 became non-significant whereas the association between AD exacerbations and SO₂ at lag day 0 was enhanced. NO₂ exposure became negatively associated with AD exacerbations at lag day 2 and 6. In the cumulative lag model, the associations between SO₂ exposure and AD exacerbations were enhanced whereas NO₂ exposure

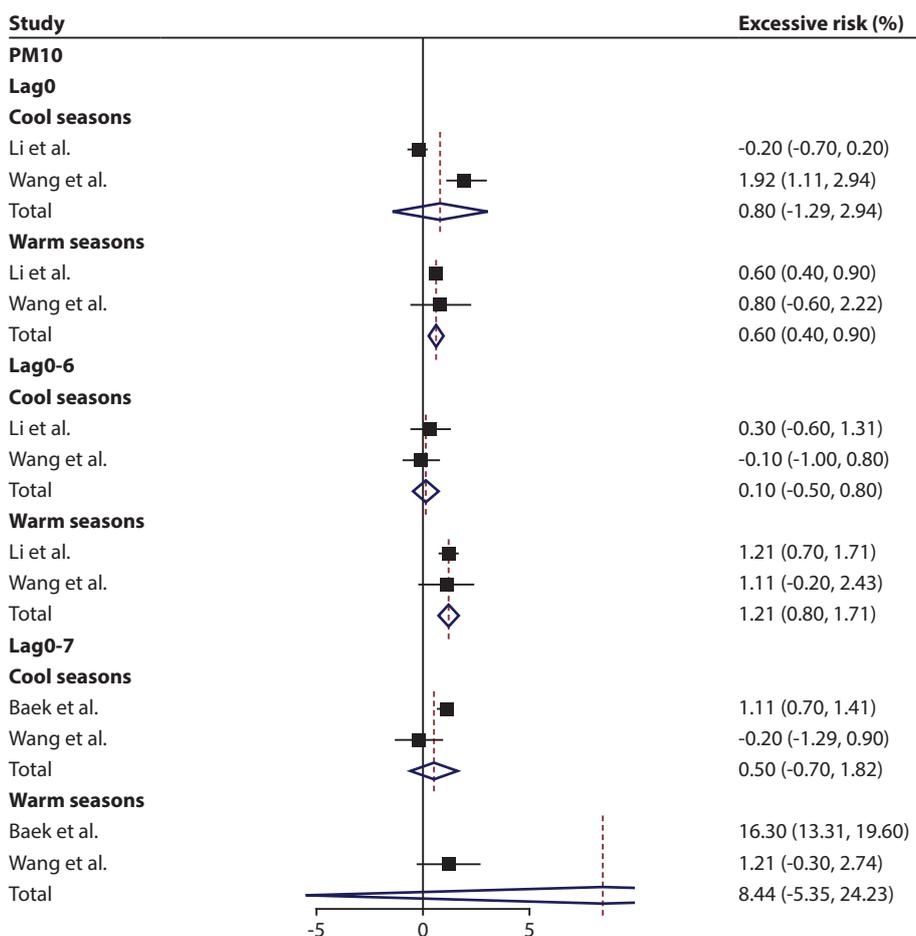


Figure 3. The meta-analyses of the short-term effects of outdoor air pollutants (per 10 µg/m³ increment) on exacerbations of adult atopic dermatitis after stratification according to seasons. The black squares represent the effect estimates of the individual studies and the diamonds represent the summary effect estimates.

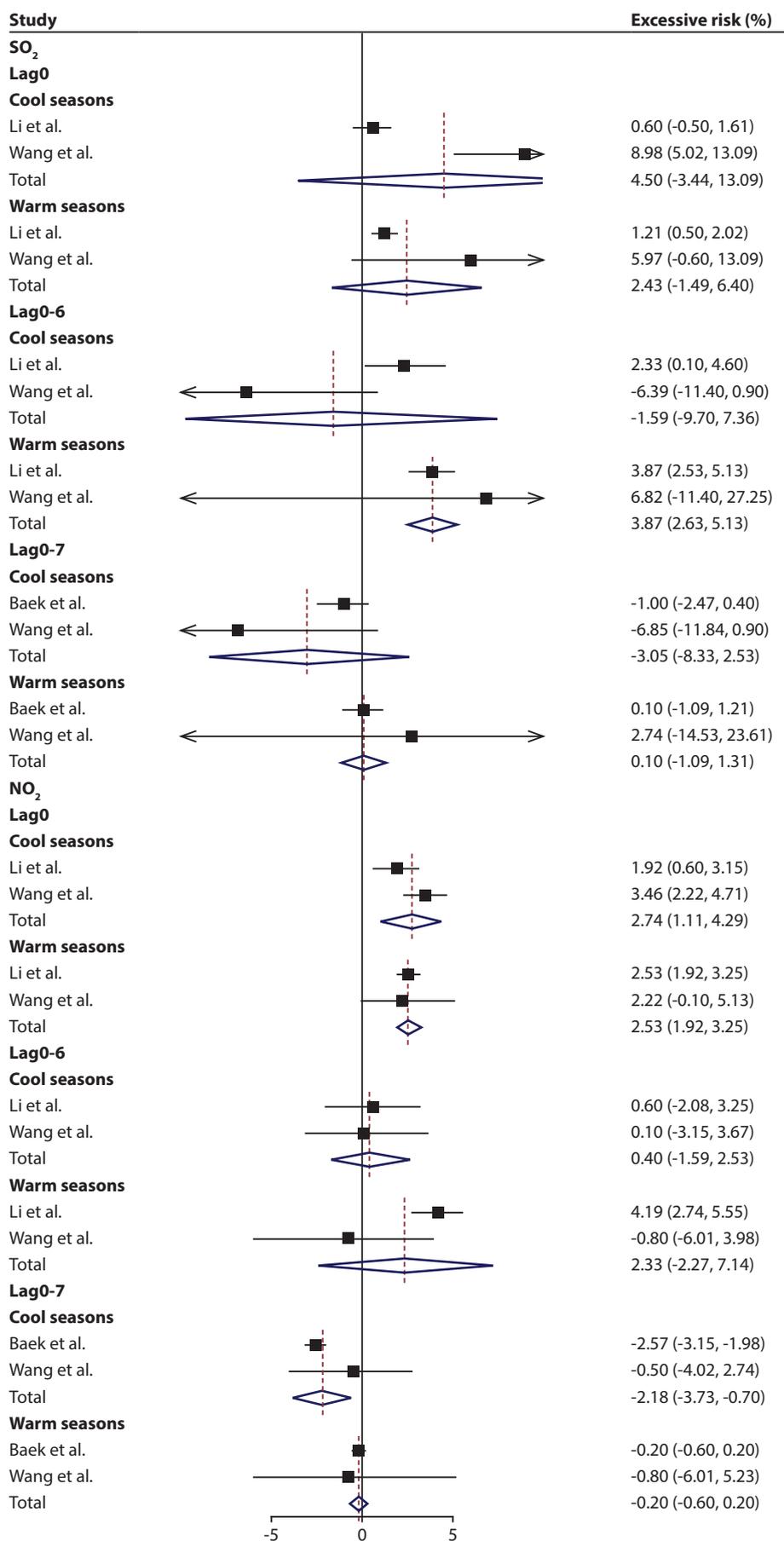


Figure 3. (Continued)

became negatively associated with AD exacerbation. After excluding those studies with an overall high risk of bias, the results remained similar except for SO₂ exposure whose associations with AD exacerbations became significant at lag day 0-2, 0-3, 0-4, and 0-5 in the cumulative model.

Publication bias

Asymmetry in the funnel plot was found in most studies on short-term effects of air pollutants. The Begg’s and Egger’s test results were statistically significant in only a few of them.

Discussion

This systematic review and meta-analysis have comprehensively summarized the effects of various outdoor air pollutants on AD in adults. We found that the exposure to these air pollutants had both short-term and long-term adverse effects, and it was associated with the incidence, prevalence, symptom severity, and exacerbation of AD. Furthermore, short-term effects emerge as early as the same day of exposure.

The pathogenesis of AD is complex. Impaired skin barrier function allows skin penetration of allergens and microbes such as *Staphylococcus aureus* (“outside-in”). Owing to inherent dysregulation of the immune system (“inside-out”), these stimuli overzealously activate immune

cells, predominantly Th2 cells and mast cells.³³ Meanwhile, IgE produced by B cells and infiltrating neutrophils enter the skin tissue. Keratinocytes and fibroblasts are also activated to promote inflammation and epidermal proliferation. Outdoor air pollutants could disrupt the skin barrier,³⁴⁻³⁶ increase reactive oxygen species (ROS) production,^{35,37} alter the balance between T helper cells,³⁸ facilitate skin infiltration by neutrophils,³⁹ increase IgE production,³⁹ activate keratinocytes, fibroblasts, and mast cells,^{35,39} and promote the secretion of pro-inflammatory cytokines, chemokines, and matrix metalloproteinases (MMPs) (Figure 4).³⁵ The end result is to promote the generation and propagation of allergy in the skin.^{35,40,41}

Outdoor air pollution is known to be associated with allergic diseases such as allergic rhinitis and asthma in children from several earlier meta-analyses.^{5,42} The associations with childhood AD were also reported in some studies, despite weaker evidence and inconsistent findings.⁴ A recent meta-analysis of 5 European birth cohorts revealed no association between outdoor air pollutants and childhood prevalent AD.⁶ The evidence on the associations between these air pollutants and adult AD has not been systematically reviewed. Our review comprehensively showed the short-term and long-term negative impacts of these air pollutants on adult AD in several aspects,

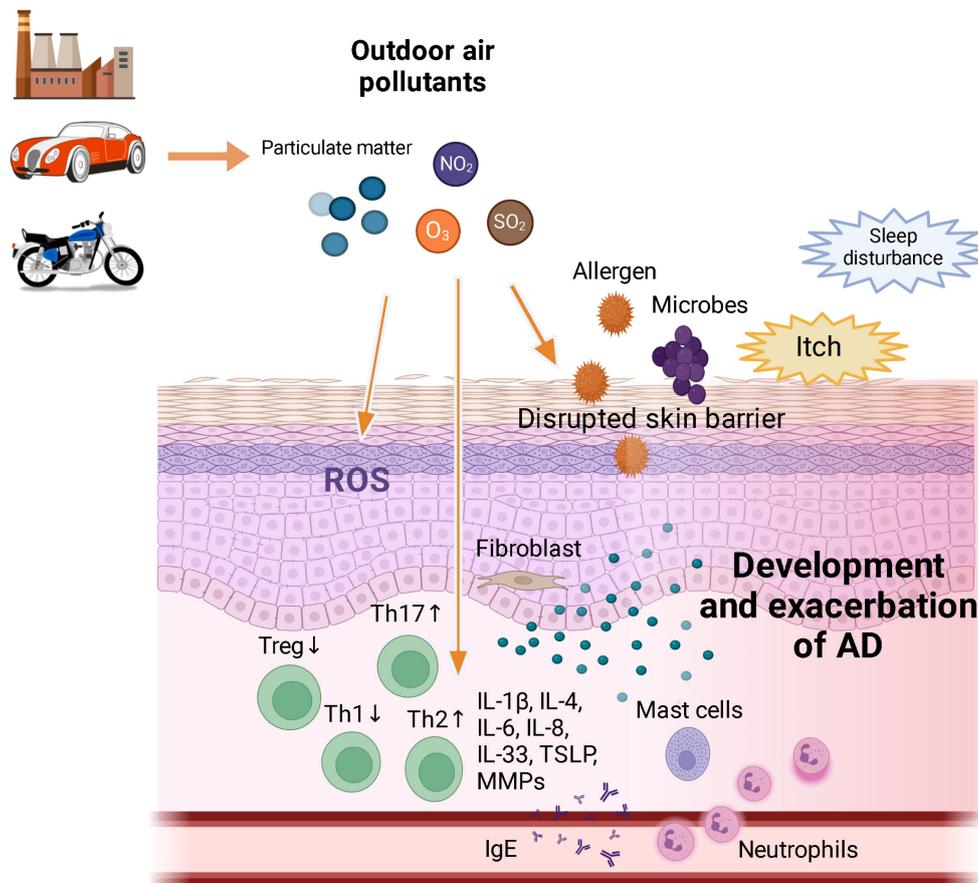


Figure 4. The adverse effects of air pollutants on adult atopic dermatitis (AD) and underlying mechanisms.

IL, interleukin; ROS, reactive oxygen species; TSLP, thymic stromal lymphopietin.

Figure created using Biorender (<https://biorender.com/>).

including its incidence, prevalence, symptoms and exacerbation. The discrepancy between our results (some based on Asian studies) and the null findings in European pediatric birth cohorts⁶ may be due to the geographic difference (e.g., disparate racial gene-environment interactions,^{14,43} background air pollutant levels, etc). Nevertheless, interventional studies are required to verify the contributory role of these air pollutants in adult AD.

In terms of long-term effects of air pollutants on AD, our meta-analysis showed that traffic-related air pollution, PM_{2.5}, and NO₂ were associated with either the prevalence or the incidence of AD in adults. Notably, PM_{2.5} was associated with a two-fold increased odds for incident AD. In addition, Seo et al. conducted a geographic information system (GIS) analysis which showed that PM₁₀ concentrations were ecologically associated with the prevalence of AD at the subdistrict level of Seoul, despite the existence of geographical variations.¹² We previously also collected urine samples from a small group of adult AD patients and found higher levels of exposure to certain polycyclic aromatic hydrocarbons based on urine metabolites, when compared with healthy controls.¹⁶ In line with these findings, Park et al. used a healthcare insurance database (consisting of 209,168 Korean subjects) to show that incident AD is associated with the exposure to PM_{2.5}, PM₁₀, SO₂, NO₂, and CO based on a Cox proportional hazard model.¹⁷ Taken together, long-term exposure to outdoor air pollutants may well contribute to the development of AD in adults. Reducing exposure to these air pollutants is a potential strategy to prevent the development of AD in the at-risk population.

In terms of short-term effects of air pollutants on AD, our meta-analysis of time-series studies demonstrated that the exposure to some air pollutants was associated with increased outpatient and/or emergency department visits for AD in the single lag model, especially at lag day 0. In addition, the effect of single air pollutants remained significant even after adjusting for the exposure to other air pollutants.^{19,20,23,28} These findings implied that the short-term effect of outdoor air pollutants on exacerbations of AD symptoms was immediate and shared by several air pollutants. This might be explained by an underlying common and immediate pathogenic mechanism, e.g. an increased oxidative stress.³⁷ In summary, outdoor air pollutants likely contribute in a collective way to the exacerbation of AD symptoms within a relatively short time period. More studies are required to confirm such a possibility and clinical benefits of minimizing exposure to these air pollutants in the management of AD exacerbations.

Effects of air pollutants may be modified by several factors. Both the elderly and children are likely more vulnerable to the effect of outdoor air pollutants, a finding which is compatible with previous reports.^{4,44} Children are more vulnerable probably due to their immature immune and respiratory systems, more outdoor activities, and a relatively small volume of distribution.⁴ On the other hand, impaired respiratory function and pre-existing chronic diseases may predispose the elderly to the adverse effects of air pollutants.⁴⁴ Sex was found to be a potential modifying

factor and the association between air pollutants and adult AD appeared more prominent in men. This finding is in contradiction with previous reports on asthma patients, in which women seemed more vulnerable to the effect of air pollution. However, such gender role may vary according to different life stages and hormonal status, making a firm conclusion difficult to draw.⁴⁵ Genetics also plays a role. Huls et al. found that the associations with air pollutants among the elderly tend to be stronger in subjects carrying fewer risk alleles for AD.¹⁴ This finding implied that genetic and environmental factors probably independently contribute to the development of adult AD.

The strength of the present study is that it is the first systematic review and meta-analysis on the impact of outdoor air pollutants on adult AD. We have comprehensively analyzed effects regarding a variety of air pollutants on several domains relevant to AD, including its incidence, prevalence, severity, and exacerbation. Furthermore, reviews on the effect of air pollutants with respect to allergy in adults are scarce. Our review is expected to fill the knowledge gap.

Our review has some limitations. First, the study population, measurement of exposure to air pollutants, and outcome ascertainment methods differed considerably across studies. Such heterogeneity limited the strength in interpreting the results. Second, underrepresentation, e.g. ethnic groups other than Asians regarding short-term effects of air pollutants, would raise concerns when trying to generalize our findings. Third, the publication bias was significant and may undermine our conclusions. Fourth, smoking and/or second-hand smoke were not adjusted for in most of these studies, despite their importance as a source of ambient indoor air pollution and their reported association with the development of AD.⁴⁶ Last, we only searched two large databases: EMBASE and MEDLINE. We might not identify all relevant studies. Some of the meta-analyses included few studies and the study heterogeneity was difficult to estimate.⁴⁷ Despite all these limitations, our review can still provide an updated and valuable overview of the relationship between outdoor air pollutants and adult AD.

Conclusion

Our systematic review showed that the exposure of outdoor air pollutants has both short-term and long-term adverse effects on adult AD with regards to its development and symptom severity. The short-term effect appeared as early as within the same day of exposure. Study heterogeneity and publication bias should be taken into account when interpreting the results. Interventional studies are needed to verify the beneficial effects of reducing exposure to these air pollutants in adult AD patients.

Acknowledgements

None.

Conflict of interests

The authors declare no conflict of interest.

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Authors' contributions

- All authors made substantive intellectual contributions to the present study and approved the final manuscript.
- Y-YH, Y-HC, and K-TT performed the literature search and retrieved relevant articles.
- Y-YH, W-TH, and K-TT appraised the selected articles.
- Y-YH, Y-HC, and K-TT drafted the manuscript.

Data availability

The data that support the findings of this study are available upon request from the corresponding author.

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