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SYSTEMATIC REVIEW

Air pollution and global healthcare use for atopic dermatitis: A systematic review

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Abstract

Increasing air pollution is common around the world, but the impacts of outdoor air pollution exposure on atopic dermatitis (AD) are unclear. We synthesized the current global epidemiologic evidence for air pollution exposure and associated medical visits for AD among adults and children. This review followed PRISMA guidelines, and searches were conducted on PubMed, MEDLINE, Web of Science and EMBASE databases. The searches yielded 390 studies, and after screening, 18 studies around the world assessing at least 5,197,643 medical visits for AD in total were included for the final analysis. We found that exposure to particulate matter ≤2.5 μm in diameter ($PM_{2.5}$) [(10/11) of studies], particulate matter ≤10 μm in diameter (PM_{10}) (11/13), nitrogen dioxide (NO_2) (12/14) and sulfur dioxide (SO_2) (10/13) was positively associated with AD visits. Results were equivocal for ozone [(4/8) of studies reported positive association] and limited for carbon monoxide [(1/4) of studies reported positive association]. When stratifying results by patient age, patient sex and season, we found that the associations with particulate matter, NO_2 and O_3 may be affected by temperature. Exposure to selected air pollutants is associated with AD visits, and increasingly poor worldwide air quality may increase global healthcare use for AD.

INTRODUCTION

Air pollution is a pervasive public health issue that has been reported to be associated with increased risk for skin-related symptoms and diseases.[1,2] Currently, 91% of the world's population resides in areas where the levels of air pollutants exceed exposure limits set by the World Health Organization, and 7 million annual deaths are attributable to ambient and household air pollution exposure.[3] Air pollution is a complex mixture of gases, suspended liquid particles and solid particulate matter. Common sources include household combustion appliances, industrial activities that use fossil fuels and wildfires.[3] Increased air pollution in certain areas around the world can be attributable to increasing frequency of wildfires,[4] expanding industrialization and continued reliance on fossil fuels; in 2017, approximately 3.9 billion people in the world lived in urban regions.[5] Air pollution exposure harms several organs of the human body, including the skin, and may increase risk for and/or exacerbate one of the most common skin conditions, atopic dermatitis (AD). The incidence of AD has been increasing in industrialized countries over the past century, and the disease now affects approximately 15% to 20% of children and up to 10% of adults worldwide.[6] Studies have examined population-level relationships between air pollution exposure and cutaneous conditions psoriasis, acne and AD, with the largest body of literature for AD.[2,7] AD is a chronic inflammatory skin disease characterized by a defective skin barrier and dysregulated immune response to environmental triggers, such as air pollution.[8]

Overall, the epidemiologic evidence on air pollution impacting AD outcomes is mixed, likely due to the great heterogeneity of methodologies. Studies vary in pollutants studied, method of pollutant measurement, geographic area and method of AD assessment. Cross-sectional and longitudinal studies have been performed with populations around the world, and while many have reported positive results,[9–16] some have found no significant associations.[17–22] These studies focused on prevalence or incidence of patient-reported

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AD symptoms in a population rather than medical visits for AD over time as the outcome.

Recently, researchers have been using time-series analyses and provider-confirmed diagnosis of AD for less heterogeneous outcome assessments. These studies also aim to quantify how air pollution exposure has system-level impacts on healthcare utilization and costs, assessing the burden of increasing air pollution on care delivery systems.[23] To our knowledge, no prior systematic review has focused on evaluating data from these newer studies on air pollution and healthcare utilization for AD, which includes clinic and Emergency Department visits and hospitalizations. Our aims were to comprehensively synthesize and interpret data from studies performed around the world that examined the associations of outdoor air pollutants and AD-related healthcare use, to increase understanding of how air pollution may increase risk for AD disease activity and affect healthcare utilization for skin disease.

MATERIALS AND METHODS

We conducted a systematic review of air pollution and healthcare use for AD in accordance with the most recent Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations.[24] The review protocol was prospectively registered with PROSPERO (ID: CRD42022295310).

Search strategy and selection criteria

We performed a search of the existing literature using 4 databases—PubMed, MEDLINE, Web of Science and EMBASE—for relevant research articles published before 15 January 2022. The search strategy included combinations of Medical Subject Headings (MeSH) terms related to AD and air pollution (Appendix S1). The initial searches yielded a total of 390 studies that were then reviewed for meeting eligibility criteria.

Studies included for analysis met the following criteria: cross-sectional, case-crossover, longitudinal or time-series study design; outcome of interest was medical visits for eczema/AD (determined by ICD codes, such as L20.8, L20.9, L30.9), and exposure to at least one outdoor air pollutant was assessed. Studies that did not include primary epidemiologic data, did not focus on healthcare use for AD as the outcome, were conference abstracts and did not assess air pollution exposure were excluded. We did not restrict the search by language, and only one article in a non-English language met criteria for analysis; this article was translated to English by a team member fluent in Chinese, and the data were subsequently extracted.

Data screening and extraction and quality assessment

After the removal of duplicates, both the titles and abstracts of 327 studies were independently screened by two team members (E.C. and A.J.) (Figure 1). Then, the full-text versions of the remaining articles were assessed based on pre-determined inclusion and exclusion criteria for final inclusion in this review. Data screening was performed using the online systematic review management platform Covidence,[25] and all discrepancies were mediated by discussion with a third team member (R.P.F.). Data extraction on each study's population demographics, exposure and outcome assessment methodologies, and measures of association for the findings were independently performed by E.C., A.J., J.Y.C. and R.P.F and reviewed by M.L.W. and K.A.; all discrepancies were resolved by team discussions. A summary of the key characteristics for the final 18 included studies is presented in Table 1. Each individual study was assessed for quality and potential biases by four team members (E.C., A.J., Y.C. and R.P.F.) based on a modified version of the Newcastle-Ottawa Scale for cross-sectional studies (Table 2).[26] The following scoring was used: 7–10 was high quality, 4–6 was moderate quality, and 0–3 was low quality.

Synthesis methods

Studies were characterized based on the types of air pollutants that were measured: particulate matter ≤2.5 μm in diameter ($PM_{2.5}$), particulate matter ≤10 μm in diameter (PM_{10}), nitrogen dioxide (NO_2), carbon monoxide (CO), sulfur dioxide (SO_2) and ozone (O_3) (Table 3). We focused on individual air pollutants because concentrations differ across the world based on emission sources, and each can have unique health risks.[27] Study findings were defined as positive (+), negative (−) or null/inconclusive associations (0), for each pollutant. Results were further stratified based on age, sex and temperature or season, if reported in the study (Table 3). Due to the wide heterogeneity of air pollution exposures (pollutant levels and characterization of exposure changes for statistical analyses) and types of measures of association reported among the studies, estimates of pooled effects were not calculated, as in other air pollution reviews.[28–30] Instead, the quantitative results presented in each study, as well as the approach for exposure characterization used and measure of association calculated, are presented in Table 4 for the air pollutants found to have overall positive associations ($PM_{2.5}$, PM_{10}, NO_2 and SO_2) and Table S2 for the air pollutants found to have overall inconclusive associations (O_3 and CO).

RESULTS

The initial searches yielded 390 studies; 327 were screened after the removal of duplicates; 117 full-text articles were assessed for eligibility (excluded studies and rationale listed in Table S1); and 18 were included in the final analysis (Figure 1).[31–48]

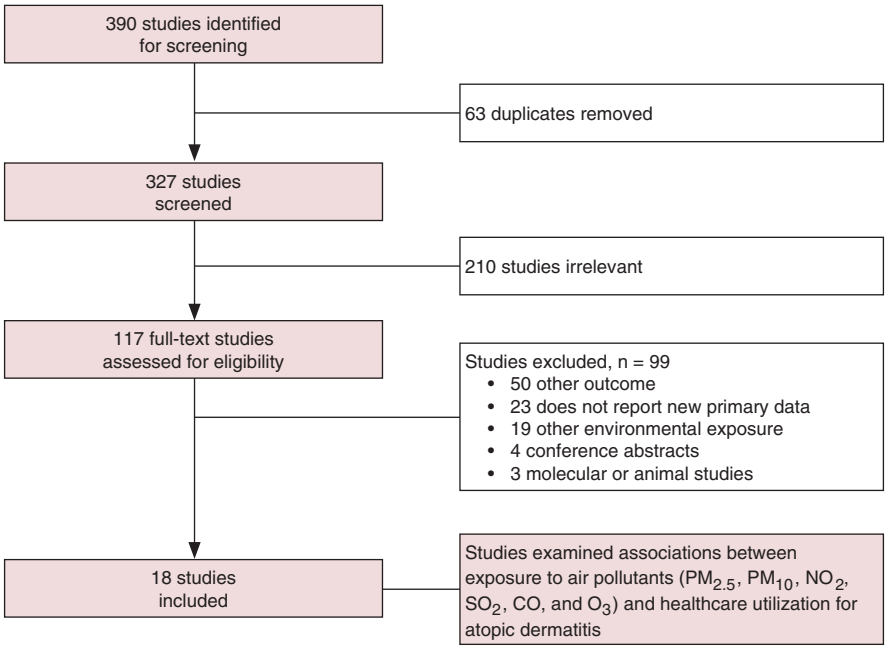

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Chart. Abbreviations: particulate matter <2.5 μm in diameter ($PM_{2.5}$), particulate matter ≤10 μm in diameter (PM_{10}), nitrogen dioxide (NO_2), carbon monoxide (CO), sulfur dioxide (SO_2) and ozone (O_3).

Overview of included studies

This systematic review included 18 studies published from 2010 to 2021; they used either cross-sectional time-series analysis (17 studies) or time-stratified case-crossover (1 study) analysis (Table 1). In total, over 5,197,643 medical visits for AD were included, and studies were located in China (12/18), South Korea (4/18), the United States (1/18) and Turkey (1/18). All studies identified visits by ICD-10 codes; most studies included both adults and children with AD, but 3 studies focused specifically on children,[37,38,41] and 1 study focused specifically on adults.[46] One study approximated the severity of AD with prescribed medications for treatment.[31] Healthcare utilization data were collected for clinic visits, Emergency Department visits and/or hospitalizations for AD. Covariates most often included in statistical analyses were environmental factors (18/18 studies), such as temperature (18/18 studies) and humidity (17/18 studies), and the day of the week (14/18 studies). Air pollutants examined across studies were $PM_{2.5}$ (11 studies), PM_{10} (13), NO_2 (14), SO_2 (13), O_3 (8) and CO (4). The studies used exposure lags of varying intervals and duration, but overall, earlier exposure lags for these air pollutants were associated with higher risks for AD visits. All studies performed exposure assessment using data from ground-level air monitoring stations and used single pollutant modelling; 11 studies also used multi-pollutant models. Air pollution source was not specified except in one study, which specifically examined wildfire smoke;[31] however, all studies were in urban settings. Almost all studies (17/18) were determined to have low risk for bias (Table 2). We used the five GRADE domains (study limitations, consistency of effect, precision, directness and publication bias)[49] to evaluate the overall body of evidence on the association between air pollution and healthcare use for AD and determined a moderate grade of certainty (Appendix S1). This was primarily due to consistent results across studies for most air pollutants, precision of the results of analyses conducted with large sample sizes, and the directness of measuring physician-diagnosed AD with health services data. The results presented in the following sections are summarized in Table 3.

Particulate matter ($PM_{2.5}$ and PM_{10})

Almost all studies on $PM_{2.5}$ (10/11) and PM_{10} (11/13) found significant, positive associations between air pollution exposure and increased medical visits for AD. For $PM_{2.5}$, the majority of studies found positive associations even when the outcome was stratified by age (both children and adults), sex (both males and females) and temperature (both warm and cold). For PM_{10}, more studies had positive results for warm (5/8) vs. cold (3/8) seasonality.

One study found that $PM_{2.5}$ exposure specifically from wildfires increased visits for both AD and itch symptoms.[31] In general, earlier $PM_{2.5}$ exposure lags had a higher risk for AD medical visits; for example, at lag 0, a 10 $\mu g/m^3$ increase in weekly $PM_{2.5}$ concentration was associated with a 5.1% increase in the rate of paediatric AD clinic visits, which decreased to a 2.5% increase at lag 2.[31] PM exposure has been shown to affect the number of medical visits for AD[45] as well as have additive effects with other air pollutants like NO_2 and SO_2.[43] It was also associated with increased visits for other inflammatory dermatoses like psoriasis, seborrheic dermatitis and rosacea.[44,45]

TABLE 1 Individual study descriptions.

	Demographics				Environmental		Outcomes			
Author (year)	Time period	Type of analysis	*N*	Location	Air pollutants included	Multi-pollutant models used?	Type of visit	ICD-10 codes used	Covariates included in analysis	Overall findings
Baek (2021)[32]	2012–2015	Cross-sectional	513,870 visits	Incheon, Republic of Korea; urban	PM_{10}, O_3, NO_2, CO, SO_2, and $PM_{2.5}$	No	Outpatient, Hospitalizations, and ED visits	L20.8, L20.9	Temperature, humidity, season, day of week, holidays	$PM_{2.5}$ (+) PM_{10} (+) CO (0) NO_2 (0) O_3 (+) SO_2 (+)
Chao (2021)[33]	2015–2018	Cross-sectional	Not reported	Xinxiang, China; urban	NO_2	No	Clinic	L50.9, L30.9	Temperature, humidity, seasonality, holidays, and day of week	NO_2 (+)
Fadadu (2021)[31]	2015–2019	Cross-sectional	4147 patients; 6439 visits	San Francisco, California, USA; urban	$PM_{2.5}$	No	Clinic	L30.9, L20.82, L20.84, L20.9, H01.139, H01.136, H01.133, and L28.0	Temperature, humidity, patient age, total patient volume in clinics, holidays	$PM_{2.5}$ (+)
Guo (2019a)[34] 'Ambient…'	2012–2014	Case-crossover	157,595 visits	Beijing, China; urban	$PM_{2.5}$, PM_{10}, NO_2, SO_2	Yes	Outpatient (Clinic and emergency)	L20-L30	Temperature, humidity, day of the week	$PM_{2.5}$ (+) PM_{10} (+) NO_2 (+) SO_2 (+)
Guo (2019b)[35] 'The interactive…'	2013–2017	Cross-sectional	64,987 visits	Beijing, China; urban	$PM_{2.5}$, PM_{10}, NO_2, SO_2	Yes	Outpatient (Clinic and emergency)	L20	Temperature, humidity, seasonal trends	$PM_{2.5}$ (+) PM_{10} (+) NO_2 (+) SO_2 (+)
He (2021)[36]	2013–2017	Cross-sectional	Not reported	Lanzhou, China; urban	$PM_{2.5}$, PM_{10}, NO_2, SO_2	Yes	Clinic	L20	Temperature, humidity, day of the week, holidays	$PM_{2.5}$ (0) PM_{10} (0) NO_2 (+) SO_2 (+)
Hu (2020)[37]	2007–2017	Cross-sectional	787,646 visits	Shanghai, China; urban	$PM_{2.5}$, PM_{10}, NO_2, SO_2 and O_3	Yes	Clinic	L23	Temperature, humidity, wind speed, air pressure, seasonality, long-term trend, day of week, public holiday	$PM_{2.5}$ (+) PM_{10} (+) NO_2 (+) O_3 (0) SO_2 (−)
Hu (2021)[38]	2009–2017	Cross-sectional	1,043,240 visits	Shanghai, China; urban	$PM_{2.5}$, PM_{10}, NO_2, O_3, SO_2	Yes	Outpatient	L20	Holidays, day of the week, seasonality, temperature, humidity	$PM_{2.5}$ (+) PM_{10} (+) NO_2 (+) O_3 (0) SO_2 (+)

TABLE 1 (Continued)

Author (year)	Demographics				Environmental		Outcomes			
	Time period	Type of analysis	*N*	Location	Air pollutants included	Multi-pollutant models used?	Type of visit	ICD-10 codes used	Covariates included in analysis	Overall findings
Karagün (2021)[39]	2013–2019	Cross-sectional	27,549 visits	Düzce province, Turkey; urban	PM_{10}, SO_2	Yes	Clinic	L20, L25, L30	Temperature, relative humidity, pressure	PM_{10} (+) SO_2 (+)
Kim (2016)[40]	2003–2011	Cross-sectional	Not reported	South Korea; urban	PM_{10}, CO, NO_2, O_3, and SO_2	No	Outpatient, Hospitalizations	L20	Seasonality	PM_{10} (0) CO (–) NO_2 (+) O_3 (–) SO_2 (0)
Lee (2010)[41]	2004–2005	Cross-sectional	Not reported	Seoul and Ulsan, South Korea; urban	O_3	No	Hospitalizations	L20	Temperature, humidity, days of the week	O_3 (+)
Li (2016)[42]	2007–2011	Cross-sectional	510,158 visits	Shanghai, China; urban	PM_{10}, NO_2, SO_2	Yes	Outpatient	L30.9	Holidays, seasonal trends, day of the week	PM_{10} (+) NO_2 (+) SO_2 (+)
Li (2018)[43]	2011–2015	Cross-sectional	72,305 visits	Chengdu, Sichuan, China; urban	PM_{10}, SO_2, NO_2	Yes	Outpatient	L30.9	Temperature, time, date of week, holiday	PM_{10} (+) NO_2 (+) SO_2 (+)
Park (2021)[44]	2015–2019	Cross-sectional	Not reported	Seoul, Busan, Incheon, Daegu, Gwangju, Daejeon, Ulsan and Jeju Island in South Korea; mostly urban	$PM_{2.5}$, PM_{10}, O_3, NO_2, SO_2, CO	No	Outpatient	L20	Temperature, wind speed, humidity, days with rain, days per month, holidays year, level of metropolitan city	$PM_{2.5}$ (+) PM_{10} (+) CO (+) NO_2 (0) O_3 (0) SO_2 (+)
Wang (2019)[46]	2010–2012	Cross-sectional	1,966,991 visits	Beijing, China; urban	$PM_{2.5}$	No	Outpatient	L30.9	Daily average temperature, relative humidity, day of week, holiday, long time-series	$PM_{2.5}$ (+)

TABLE 1 (Continued)

Author (year)	Demographics: Time period	Demographics: Type of analysis	Demographics: *N*	Demographics: Location	Environmental: Air pollutants included	Environmental: Multi-pollutant models used?	Outcomes: Type of visit	Outcomes: ICD-10 codes used	Outcomes: Covariates included in analysis	Overall findings
Wang (2021a)[45] 'Association…'	2013–2017	Cross-sectional	29,972 visits	Guangzhou, China; urban	$PM_{2.5}$, PM_{10}, SO_2, NO_2, O_3	Yes	Outpatient	L20.9	Seasonal patterns, temperature, relative humidity, day of week	$PM_{2.5}$ (+) PM_{10} (+) NO_2 (+) O_3 (+) SO_2 (+)
Wang (2021b)[47] 'Short-term…'	2014–2019	Cross-sectional	16,891 visits	Beijing, China; urban	$PM_{2.5}$, PM_{10}, CO, SO_2, NO_2, O_3	Yes	Emergency	L20–30	Day of the week, holiday, calendar time, humidity, temperature	$PM_{2.5}$ (+) PM_{10} (+) CO (0) O_3 (+) NO_2 (+) SO_2 (0)
Zhang (2021)[48]	2013–2018	Cross-sectional	Not reported	Guangzhou, China; urban	NO_2	Yes	Outpatient	L30.902	Temperature, humidity, seasonal trend, day of week	NO_2 (+)

Note: Each row represents a study included in the final analysis. All studies used individual-level patient data. + indicates positive association, − indicates negative association, and 0 indicates no or inconclusive association.

Abbreviations: AD, atopic dermatitis; $PM_{2.5}$, particulate matter <2.5 μm in diameter; PM_{10}, particulate matter <10 μm in diameter; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone; CO, carbon monoxide.

Nitrogen dioxide (NO_2)

Twelve out of 14 studies on NO_2, a major component of traffic-related air pollution, found greater healthcare use for AD with increased air pollutant exposure. The majority found positive associations for both children (8/10) and adults (6/8) with AD and female sex (5/8). Eight of the nine studies found positive results during cool temperatures and five during warm temperatures. One of these studies reported a positive exposure-response relationship and found that greater NO_2 exposure was also associated with increased visits for additional dermatologic diseases: acne vulgaris, psoriasis and vitiligo.[33]

Sulfur dioxide (SO_2)

The majority of studies on SO_2 (10/13) found positive associations with medical visits for AD. When stratified by age, most (5/8) found a positive association with AD visits, but for sex and temperature, 50% or less of the studies found a positive association.

Ozone (O_3)

Half of the studies on O_3 (4/8) reported that air pollutant exposure was positively associated with healthcare use for AD. Two of three studies found positive results for adults, none found positive results during warm temperatures, and three of five studies found positive results for cool temperatures. Half of the studies (1/2) noted a positive association with both men and women when stratified for sex. One study reported a linear exposure-response relationship between O_3 and AD visits after a threshold.[46]

Carbon monoxide (CO)

Among all air pollutants, CO exposure was examined in the fewest number of studies, and 1 out of 4 reported a positive association with medical visits for AD.[44]

DISCUSSION

To our knowledge, this is the first systematic review to focus on evaluating global studies that examined the relationship between air pollution and AD by measuring medical visits for AD, assessing this association from a healthcare utilization perspective. We found 18 studies that analysed exposure to multiple air pollutants—PM, NO_2, SO_2, O_3 and CO—with over 5 million visits for AD. Overall, most studies found positive, significant associations between increased concentrations of $PM_{2.5}$, PM_{10}, NO_2 and SO_2 and greater healthcare use for AD; the evidence for O_3 was mixed, and of the few studies examining CO exposure, 3 of 4 found no significant

TABLE 2 Quality and bias assessment of studies.

Author (year)	Selection (*****)				Comparability (**)	Outcome (***)			
	1. Representativeness of sample (*)	2. Sample size justified (*)	3. Selection of participants (*)	4. Ascertainment of air pollution exposure (**)	5. Comparability of subjects (**)	6. Assessment of outcome (**)	7. Statistical test (*)	8. Total (10)	Risk of bias
Baek (2021)[32]	*	*	*	**	**	**	*	10	Low
Chao (2021)[33]		*	*	**	*	**	*	8	Low
Fadadu (2021)[31]		*	*	**	**	**	*	9	Low
Guo (2019a)[34]		*	*	**	**	**	*	9	Low
Guo (2019b)[35]		*	*	**	*	**	*	8	Low
He (2021)[36]	*	*	*	*	**	**	*	9	Low
Hu (2020)[37]	*	*	*	**	*	**	*	9	Low
Hu (2021)[38]	*	*	*	**	*	**	*	9	Low
Karagün (2021)[39]		*	*	*	*	**	*	7	Low
Kim (2016)[40]	*	*	*	**	*	**	*	9	Low
Lee (2010)[41]			*	**		**	*	6	Moderate
Li (2016)[42]		*	*	**	**	**	*	9	Low
Li (2018)[43]		*	*	**	*	**	*	8	Low
Park (2021)[44]	*	*	*	**		*	*	7	Low
Wang (2019)[46]	*	*	*	*	**	**	*	9	Low
Wang (2021a)[45]		*	*	**	**	**	*	9	Low
Wang (2021b)[47]		*	*	**	**	**	*	9	Low
Zhang (2021)[48]		*	*	**	**	**	*	9	Low

Note: Each asterisk represents one point awarded to a study for meeting the respective criteria, for a total of 10 possible points.

1. One star awarded if several clinical sites included; zero stars awarded if one clinical site or no explanation for limiting number of sites. 2. One star awarded if the number of visits and time period analysed are reasonable enough to confer adequate statistical power to determine significant differences in effect; zero stars awarded if number of visits is low (indicating an underpowered study) or time period is shortened without reasonable explanation. 3. One star awarded if selection of patients is reasonable; zero stars awarded if patients were excluded from analysis without proper explanation. 4. Two stars awarded if city-level or more granular data used and daily or weekly measurements used; one star if either city-level or more granular data used or daily or weekly measurements used; zero stars if data collected over geographic area larger than city or monthly or annual data used. 5. Two stars awarded if study adjusted for patient sex or age and temperature or humidity; one star awarded if study adjusted for either patient sex or age or temperature or humidity; zero stars awarded if no adjustment for patient or environmental factors. 6. Two stars awarded if correct ICD codes used for diseases of interest and if type of visits (clinic, hospitalization, or ED) stated; one star awarded if either ICD codes match diseases of interest or type of visits stated; zero stars if neither ICD 10 codes match diseases of interest or type of visits stated. 7. One star awarded if statistical methods are described and measures of effect are reported with corresponding confidence interval or *p*-value, zero stars if no description of statistical methods or measures of effect reported without CI or *p*-value. 8. Assessed as follows: 7–10 = low risk, 4–6 moderate risk and 0–3 = high risk.

TABLE 3 Summary of overall findings organized by air pollutant and stratified by age, sex and temperature.

Air pollutant	Studies finding a positive association	Minimum # of AD medical visits analysed	Studies finding a positive association when stratified by:		
			Age	Sex	Temperature or season
$PM_{2.5}$	10/11	4,587,631	Children: 6/8	Male: 3/5	Warm: 4/6
			Adult: 5/7	Female: 3/5	Cool: 4/6
PM_{10}	11/13	3,224,213	Children: 4/8	Male: 2/6	Warm: 5/8
			Adult: 2/6	Female: 2/6	Cool: 3/8
NO_2	12/14	3,196,664	Children: 8/10	Male: 4/8	Warm: 5/9
			Adult: 6/8	Female: 5/8	Cool: 8/9
SO_2	10/13	3,224,213	Children: 5/8	Male: 2/6	Warm: 3/8
			Adult: 3/6	Female: 3/6	Cool: 4/8
O_3	4/8	2,391,619	Children: 3/6	Male: 1/2	Warm: 0/5
			Adult: 2/3	Female: 1/2	Cool: 3/5
CO	1/4	530,761	Children: 1/2	Male: 1/2	Warm: 1/3
			Adult: 0/2	Female: 0/2	Cool: 0/3

Abbreviations: AD, atopic dermatitis; $PM_{2.5}$, particulate matter ≤2.5 μm in diameter; PM_{10}, particulate matter <≤10 μm in diameter; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; O_3, ozone; CO, carbon monoxide.

association. The most consistent results were reported for $PM_{2.5,}$ in that a majority of studies found a positive association overall and also when results were stratified for age, sex or temperature. For PM_{10}, more studies found positive associations during warmer temperatures compared to cooler temperatures, and for NO_2 and O_3, more studies reported positive associations during cooler temperatures. For all air pollutants overall, earlier exposure lags were associated with higher risk for AD visits,[31,42,46] suggesting relatively immediate impacts of air pollution exposure on the skin. Across studies, exposure assessment, performed with data from ground-level air monitoring stations, and outcome assessment, determined by diagnostic codes from health service databases, were consistent. We determined a low risk of bias across 94% (17/18) of studies.

Some studies conducted focused exposure assessments or additional analyses that produced notable findings. One study found increased AD visits for children and adults associated with exposure to air pollution from a wildfire[31]; wildfires are increasing in frequency and severity around the world likely due to climate change[51,52] and can lead to short-term increases in air pollution in areas with baseline good air quality.[53] Across five studies that generated exposure-response curves, $PM_{2.5}$, PM_{10}, NO_2 and O_3 showed a linearly increasing trend in AD medical visits with more air pollution exposure,[33,38,41,42,46] though not all were statistically significant.[42,46] This suggests that air pollution levels, which can vary significantly between and within countries, often with marginalized populations suffering from much higher exposure,[27,54] could contribute to disparities in AD prevalence and exacerbations in different parts of the world. One analysis found that risk significantly increased after a certain concentration of exposure, such as 50 $\mu g/m^3$ for NO_2,[38] suggesting a threshold effect for some pollutants, after which air pollution can exacerbate skin health. This supports the need for stronger environmental policies that limit air pollution emissions in order to reduce the risk for harm to skin health. For certain air pollutants, both warmer and cooler seasonalities were found to affect the relationship between air quality and healthcare use for AD. These findings are consistent with studies showing that extremes in temperature and humidity can increase risk for AD flares,[9,10] perhaps rendering the skin vulnerable to the effects of specific pollutants at those extremes. It is important to note that multiple environmental factors interact with one another, such as how smog can reduce surface-level ultraviolet ray exposure, and this can impact AD prevalence and severity—a reason why these variables should be adjusted for in epidemiology studies on this topic. In addition, differences in AD risk for males compared to females exposed to certain air pollutants have been inconsistent across studies; proposed explanations include geographic differences related to lifestyle practices (e.g. use of cosmetic products and time spent outside), pollutant composition and levels, and prevalence of other skin disorders.[16,36] Regarding vulnerable patient populations with AD, two studies found children exposed to poor air quality experienced greater risk for AD exacerbations compared to adults.[31,46] This may be related to higher prevalence of AD among children.[6] Of note, other research has shown that adults who are 65 years of age or older may be at increased risk for air pollution-associated AD flares compared to younger adults.[55] Differences in the pathogenesis of AD in children and adults due to age-related differences in immune regulation, epidermal barrier function and dysbiosis[56] may explain why risk for air pollution-associated AD flares differ with age. Lastly, some studies found positive associations with poor air quality and medical visits for other dermatologic diseases, including psoriasis, acne, vitiligo and seborrheic dermatitis, suggesting that air pollution exposure can affect skin diseases beyond AD.[33,44,45]

TABLE 4 Results from included studies for $PM_{2.5}$, PM_{10}, NO_2 and SO_2.

Author (year)	Baek (2021)[32]	Chao (2021)[33]	Fadadu (2021)[31]	Guo (2019a)[34]	Guo (2019b)[35]	He (2021)[36]	Hu (2020)[37]	Hu (2021)[38]	Karagün (2021)[39]	Kim (2016)[40]	Li (2016)[42]	Li (2018)[43]	Park (2021)[44]	Wang (2019)[46]	Wang (2021a)[45]	Wang (2021b)[47]	Zhang (2021)[48]
Exposure change characterization	IQR increase	10 μg/m^3 increase	10 μg/m^3 increase	IQR increase	10 μg/m^3 increase	10 μg/m^3 increase	IQR increase	10 μg/m^3 increase	10 μg/m^3 increase	Parts per million increase	10 μg/m^3 increase	10 μg/m^3 increase	10 μg/m^3 increase ($PM_{2.5}$, PM_{10}); 1 part per billion increase (NO_2, SO_2)	10 μg/m^3 increase	10 μg/m^3 increase	10 μg/m^3 increase ($PM_{2.5}$, PM_{10}); 8 hour maximum (SO_2, NO_2)	10 μg/m^3 increase
Measure of association	Risk ratio	Mean % change	Rate ratio	Mean % change	Mean % change	Excess risk ($PM_{2.5}$; PM_{10}); Relative risk (NO_2 and SO_2)	Relative risk	Relative risk	Relative risk	Mean estimate (standard error)	Mean % change	Relative risk	Mean % change or Exp(B)	Mean % change	Excess risk	Mean % change	Relative risk and mean % change
Air pollutant ($PM_{2.5}$) and lag	$PM_{2.5}$ (lag0)	–	$PM_{2.5}$ (lag0)	$PM_{2.5}$ (lag0)	$PM_{2.5}$ (lag0)	$PM_{2.5}$ (lag0)	–	$PM_{2.5}$ (lag0)	–	–	–	–	$PM_{2.5}$	$PM_{2.5}$ (lag0)	$PM_{2.5}$ (lag0)	$PM_{2.5}$ (lag0-1)	–
Result	1.008 (1.000–1.015)	–	1.49 (1.07–2.07)	4.72 (3.88–5.56)	0.42 (0.16–0.67)	0.56 (−0.03–1.16)	–	1.03 (1.01–1.04)	–	–	–	–	2.71% (0.76%–4.71%)	0.30% (0.28%–0.33%)	2.67% (1.67–3.67%)	+, data only shown in graph	–
Air pollutant (PM_{10}) and lag	PM_{10} (lag0)	–	–	PM_{10} (lag0)	PM_{10} (lag0)	PM_{10} (lag 0)	–	PM_{10} (lag0)	PM_{10} (lag5)	PM_{10} (spring)	PM_{10} (lag0)	PM_{10} (lag0)	PM_{10}	–	PM_{10} (lag0)	PM_{10} (lag0-1)	–
Result	1.009 (1.007–1.012)	–	–	3.53 (2.78–4.28)	0.34 (0.15–0.54)	0.20 (−0.15 −0.39)	–	1.02 (1.01–1.04)	1.0069 (1.0040–1.0099)	(0.00009 +/− 0.00002)	0.40 (0.18, 0.61)	1.0024 (1.0003; 1.0046)	2.01% (0.92%–3.11%)	–	1.9% (1.2–2.7%)	+, data only shown in graph	–
Air pollutant (NO_2) and lag	NO_2 (lag0)	NO_2 (lag0)	–	NO_2 (lag0)	NO_2 (lag0)	NO_2 (lag 0)	NO_2 (lag0)	NO_2 (lag0)	–	NO_2 (spring)	NO_2	NO_2 (lag0)	NO_2	–	NO_2 (lag0)	NO_2 (lag0-1)	NO_2 (lag0)
Result	0.996 (0.992–1.000)	2.44 (0.08–4.80)	–	6.69 (5.75–7.63)	1.11 (0.38–1.84)	1.95 (1.09–2.82)	+, data shown in graph	1.05 (1.03–1.07)	–	59.34203 +/− 0.09460	2.15 (1.54, 2.76)	1.0056 (1.0014; 1.0111)	1.0004 (0.9971–1.0037)	–	3.1% (2.05–4.26%)	+, data only shown in graph	1.0410 (1.0380–1.0440); 4.10% (3.80–4.40)
Air pollutant (SO_2) and lag	SO_2 (lag0)	–	–	SO_2 (lag0)	SO_2 (lag0)	SO_2 (lag6)	–	SO_2 (lag0)	SO_2 (lag5)	SO_2 (spring)	SO_2 (lag0)	SO_2 (lag0)	SO_2	–	SO_2 (lag0)	SO_2 (lag0-1)	–
Result	1.033 (1.030–1.037)	–	–	4.5(3.5–5.49)	1.06 (0.21–1.93)	1.52 (0.48–2.54)	–	1.04 (1.01–1.06)	1.0534 (1.0246–1.0575)	−63.48328 ±0.63210	0.97 (0.40, 1.54)	1.0305 (1.0105; 1.0509)	2.26% (1.35%–3.17%)	–	6.1% (3.11–9.21%)	Null; data only shown in graph	–

Note: This table lists representative results from the included studies that examined the associations between exposure to $PM_{2.5}$, PM_{10}, NO_2 and SO_2 and healthcare use for atopic dermatitis. Results presented in parentheses are 95% confidence intervals (CI), unless otherwise stated. Some studies did not report the lag for certain results or used seasonal lagged analysis.

Abbreviations: $PM_{2.5}$, particulate matter <2.5 μm in diameter; PM_{10}, particulate matter <10 μm in diameter; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; IQR, interquartile range; CI, confidence interval.

The evidence for an association between air quality and healthcare utilization for AD primarily shows a positive association, with the data for $PM_{2.5}$ showing the most consistency. While most of the studies found in this review found positive and significant associations, other cross-sectional studies using patient-reported disease outcomes, modelled environmental exposure data and non-healthcare utilization AD outcomes have found null results.[17,21,57] However, most longitudinal studies, which employ a stronger study design, have reported positive associations for both children and adults.[11,15,58,59] Regarding molecular mechanisms, air pollutants may contribute to AD symptoms by disrupting skin barrier function, activating the aryl hydrocarbon receptor pathway, promoting oxidative stress and initiating a pro-inflammatory response.[60,61,62] Further research is needed on the synergistic effects of combined air pollutants on AD incidence and severity, at both molecular and population levels.

Some of the heterogeneity in findings across studies included in this review can be explained by differences in study design and characteristics of air pollutants. While outcome assessment using a billing database allows for the inclusion of provider-diagnosed cases of AD, different provider specialties or training may result in practice variations in the diagnosis of AD, possibly leading to overestimation or underestimation of the outcome. The number of studies finding positive, significant results decreased in many of the age, sex and season (e.g. temperature and humidity) stratifications for each air pollutant compared to the overall findings. However, these variables were also accounted for as confounders in regression analyses for the overall results, and some of the stratified results demonstrated positive but non-significant associations with wider confidence intervals likely due to the smaller sample size. In addition, studies were conducted in cities around the world with varying magnitude of air pollution.[63] The chemical composition of particulate matter may also differ around the world depending on the source, and different components can have varying health impacts.[64] The overall lack of evidence for an association between carbon monoxide and AD could be partially due to the fact that CO primarily harms organs by affecting oxygen transport in the blood and inducing hypoxemia,[65] without a clear connection to the chronic skin inflammation underlying AD pathology.

The results of our systematic review provide further evidence that air pollution can serve to exacerbate AD, which can help guide patient counselling on skin health risks during exposure to poor air quality. Regarding clinical management, the use of emollients, which improve skin barrier function in patients with AD,[66,67] could reduce pollution-related AD symptoms. However, emollients could also potentially serve as a depot for air pollutants to adhere to and have prolonged effects on the skin, so studies on the effectiveness of this intervention are needed. It is also plausible that long articles of clothing may help to limit pollution exposure to the skin, similar to protection from ultraviolet radiation.[68] Additional research on the effectiveness of these and other clinical interventions to prevent and mitigate air pollution-induced skin disease exacerbations is needed. Global reduction of air pollution generation, such as eliminating fossil fuel use,[69,70] is important to promote better skin health. In addition, improvement of indoor air pollution has been shown to reduce AD prevalence and severity of symptoms.[71]

The results of this review highlight the significant impacts of air pollution on healthcare systems that provide care for patients with dermatologic diseases. As air pollution continues to increase inequitably around the world,[1] it is important to ensure that the general practitioner and dermatologist work forces are prepared to manage an increased burden of skin diseases, such as AD. In addition, pharmacies could be prepared to be well-stocked with medications to treat AD during times of worsening air quality. Interventions that reduce air pollution will likely contribute to improving patients' dermatologic health and reduce strain on healthcare system utilization.

Limitations

Many of the studies lacked individual-level air pollution exposure data; there was the possibility of residual confounding by unmeasured variables; and there may be underreporting of cases due to patients who may have chosen not to receive treatment or received benefits from other treatments, such as systemic steroids for pollution-induced asthma exacerbation. The generalizability of results may be limited by the distribution of study locations in urban areas, since the composition of air pollution in non-urban regions, such as rural communities, may differ.

CONCLUSIONS

In this systematic review, we found evidence that exposure to several air pollutants, i.e. particulate matter, NO_2 and SO_2, was associated with increased medical visits for AD. This indicates that increased air pollution exposure to certain air pollutants can be a risk factor for AD flares and that air pollution affects the utilization of healthcare services for skin disease. These results can assist clinicians and public health practitioners to recognize the roles of environmental pollution when counselling patients and the public on the prevention and management of AD. More studies assessing the effectiveness of preventative and treatment strategies are needed. Interventions to reduce air pollution generation may decrease global AD burden and utilization of healthcare systems.

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DATA AVAILABILITY STATEMENT

This study is a systematic review; data are from published studies.

ETHICAL APPROVAL

No IRB approval was needed for this systematic review paper.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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