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The interactive effects between air pollution and meteorological factors on the hospital outpatient visits for atopic dermatitis in Beijing, China: A time-series analysis

Running head: pollution, meteorology, atopic dermatitis

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Abstract:

Background: The prevalence of atopic dermatitis dramatically increased over these years and environmental factors were considered as potential contributors toward these trends.

Objective: This study aimed to explore several major environmental exposures, including air pollution, temperature and relative humidity, in order to identify potential modifiable risk factors and their interactive effects on atopic dermatitis.

Methods: We applied a bivariate response surface model and stratification model based on time-series Poisson generalized additive models (GAMs) to examine the interactive effects of air pollution and meteorological factors on atopic dermatitis.

Results: A total of 64,987 outpatient visits for atopic dermatitis were recorded from Jan 1, 2013 to Dec 31, 2017. Interactive effects were found between air pollutants and meteorological factors. Enhanced positive associations between pollutants and outpatient visits for atopic dermatitis were found at the highest quartile temperature level. A $10\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$, PM_{10} , NO_2 and SO_2 were associated with 0.42% (95%CI: 0.16%-0.67%), 0.34% (95%CI: 0.15%-0.54%), 1.11% (95%CI: 0.38%-1.84%) and 1.06% (0.21%-1.93%) increase in outpatient visits for atopic dermatitis at the highest quartile temperature level.

Conclusion: That effects of air pollutants on atopic dermatitis can be modified by meteorological factors, with enhanced effects on hot days.

Keywords: atopic dermatitis; air pollution; temperature; relative humidity; interactive effects

Introduction

Atopic dermatitis (AD) is a common chronic or recurrent inflammatory skin disease which poses a significant burden on health-care resources [1] and patients' quality of life [2, 3]. Rising prevalence of AD over the last 30 to 40 years has been established [4, 5], especially in many developing countries [6]. Importantly, such a rapid rise in prevalence suggests a major role for environmental factors [7].

Although the exact pathogenesis of AD remains unknown, birth cohort studies have suggested that air pollutants such as PM, NO₂ or phthalate may play an important role in AD development [8-11]. Air pollutants have also been revealed to contribute to the aggravating of pre-existing AD [12, 13]. In addition, studies of biological mechanism suggested that dust particles and diesel exhaust particulates can exert toxicological effects on human skin [14].

Meteorological factors such as temperature and relative humidity have also been suggested to affect the prevalence and severity of AD and should be considered in the management of AD [15, 16]. Moreover, the meteorological factor is a major driving force of air pollution concentration [17, 18]. For example, higher temperature speeds up chemical reactions in the air; lower temperature makes the particulate matter (PM) dissipate in the air more slowly than usual; and rain washes out water-soluble pollutants and PM. Thus, environmental studies of AD must account for both the meteorological factors and pollutant levels simultaneously to address potential confounding. An increasing number of studies began to draw an insight to

the interaction between meteorological factors and air pollution on health problems, but similar studies focusing on the interactive effects of air pollution and meteorological factors on AD are still limited.

The use of Emollients, topical corticosteroids and calcineurin inhibitors are the mainstay of the treatment for AD [19], meaning that AD rarely lead to hospitalization and are more suitable for outpatient treatment. Outpatient visits were used as outcomes to estimate the effects of air pollution and meteorological factors on skin conditions in several previous studies [20-22]. Considering the above-mentioned, this study was conducted to explore the interactive effects between air pollutants (PM_{2.5}, PM₁₀, NO₂ and SO₂) and meteorological factors (temperature and relative humidity) on the number of outpatient visits for AD in a dermatological hospital in Beijing, China.

Materials and Methods

Data of outpatient visits

Hospital outpatient and emergency visits for AD from Jan 1, 2013 to Dec 31, 2017 were collected from the Department of Dermatology, the General Hospital of Air Force of People's Liberation Army (PLA) in Beijing, China. Either a new AD case or a relapse of a previous patient was included when counting the number of outpatient visits. AD was defined according to the International Classification of Diseases, Tenth Revision (ICD-10): L20. Patients who lived in Beijing were selected for this study.

Air pollution and meteorological data

Daily records of air pollution data (including PM₁₀, PM_{2.5}, SO₂, NO₂) during the study period was obtained from the Beijing Municipal Environmental Monitoring Center. The data represented the daily average concentration from 35 monitoring stations, which were homogenously distributed all over Beijing. Hourly pollutant data was recorded at each site, which we made into daily averages at each site and then for the whole city. Daily mean temperature and relative humidity (relative humidity) data during the same period were collected from the China Meteorological Data Sharing Service System (<http://data.cma.cn/>).

Statistical analysis

We conducted descriptive and spearman's correlation analysis to summarize outpatient visits, air pollution data and meteorological data. Time-series generalized additive models (GAMs) using a quasi-Poisson link function were employed in the main analysis.

Independent model

First, a base model with natural cubic splines was fitted to optimize the control of confounders and was specified as:

$$\log[E(Y_t)] = \alpha + ns(time, df_t = 7/year) + DOW_t + holiday_t = \alpha + COV_s \quad (1),$$

where t is the day of the observation; Y_t is the observed daily outpatient visit counts on day t ; α is the intercept; $ns(time, df_t = 7/year)$ is a natural cubic spline of time with 7 degrees of freedom per year to control for seasonal and long-term trends; DOW_t is day of the week on day t ; $holiday_t$ is a dummy variable indicating public holidays (0 – not a holiday, 1 – holiday). COV_s represent all covariates in the model.

Then, air pollutant concentration as a linear term was added to the base model to study the individual effects of air pollution. To measure the hazard period of air pollution for AD, we

examined the effect of air pollutants with different lag structures: single-day lag from lag0 to lag5 and multi-day lag from lag01 to lag05. In single-day lag models, a lag of 0 day (lag0) corresponds to the current-day pollutant concentration, while in multi-day lag models, lag05 corresponds to 6-day moving average of pollutant concentration of the current and previous 5 days. Daily mean temperature and relative humidity of the same lag structures with pollutants were included in the models as confounders, using the natural cubic spline with 3 degrees of freedom. Degrees of freedom were chosen based on the lowest generalized cross validation (GCV) score.

Third, we used distributed lag non-linear model (DLNM) [23] to observe the individual nonlinear lagged effects of meteorological factors. A cross-basis ($cb(x_t)$) of mean temperature or relative humidity was added to the base model, where x_t is the mean temperature (relative humidity). Natural cubic splines with 3 degrees of freedom were used for the spaces of x_t ; spline knots were placed at quantiles (25%, 50%, 75%) in the log scale of x_t . The median value of x_t were defined as the reference for calculating the cumulative effects. To completely capture the overall effects, we used lags up to 14 days for temperature (relative humidity). We also plotted the lag effects of low and high temperature (relative humidity), respectively. The 5th percentile (-2.6°C/21%) and the 95th percentile (28.8°C/86%) were chosen to represent the low and high temperature (relative humidity).

Based on the lagged effects of air pollutants and meteorological factors, we selected lag 0 for air pollutant concentrations, moving averages over lag 0 to 14 for temperature and relative humidity in the further analysis.

Bivariate response surface model

A nonparametric bivariate response surface model was used to visually explore the joint pattern of air pollutants and temperature (relative humidity) in outpatients for AD. We fitted this model with a thin-plate spline as follows:

$$\log[E(Y_t)] = \alpha + t2(\text{POLL}, T(\text{or } RH)) + ns(RH(\text{or } T), 3) + COVs \quad (3),$$

Where $t2(\dots)$ denotes the thin-plate spline, $t2(\text{POLL}, T(\text{or } RH))$ is the interactive effect of air pollutants and temperature (or relative humidity). The meanings of other variables are the same as above.

Stratification analysis

Finally, we conducted temperature-stratified and relative humidity-stratified parametric analysis and calculated the respective P value for interaction (Pint) in order to see whether the association between air pollutants and AD is significantly different across temperature and relative humidity levels. We defined the temperature strata and relative humidity strata as four levels using quartiles as the cut-off points. Taking temperature-stratified model as an example as follows:

$$\log[E(Y_t)] = \alpha + \sum_{k=1}^4 \beta_k \text{POLL}T_k + ns(T, 3) + ns(RH, 3) + COVs \quad (6),$$

Where T_k denotes the temperature strata (Q1, Q2, Q3, Q4). β_k represent the estimated effects of pollutants at different temperature levels.

The analyses were repeated using multi-pollutant models to assess the stability of pollutants' effect. We stratified outpatient visits by sex (male and female), age (≤ 18 , 18 to 45, 45 to 65 and > 65 years) and repeated the analyses in each subgroup. The estimated health effects were expressed as the increased percentage of daily outpatient visits with per $10\mu\text{g}/\text{m}^3$ increments

in the concentration of air pollutants. The associations were defined as significant if the P-value was < 0.05 . All data analyses were performed using the “mgcv” [24] and “dlnm” [25] packages in statistical software R version 3.4.2.

Results

Characteristics and correlation analysis of subjects, air pollutants and meteorological factors

The descriptive statistics for daily outpatient visits, air pollutants and meteorological factors are shown in Table 1 and Supplementary Table S1. A total of 64,987 outpatient visits for AD were recorded from Jan 1, 2013 to Dec 31, 2017. The daily mean concentrations of $PM_{2.5}$, PM_{10} , NO_2 and SO_2 during the study period were $79.7\mu g/m^3$, $110.5\mu g/m^3$, $50.8\mu g/m^3$ and $16.9\mu g/m^3$, respectively. The average daily temperature and relative humidity were $13.7^\circ C$ and 53.0%, respectively. The four air pollutants were highly positively correlated with each other (Supplementary Table S2). Supplementary Fig.S1 shows the time series of air pollutants, meteorological factors and outpatient visits for AD. The concentrations of all air pollutants were highest in winter. The number of outpatient visits did not show significant seasonal trend.

Individual effect analysis

In Fig.1, all pollutants showed strongest and significant positive associations with outpatient visits for AD on lag0. A $10\mu g/m^3$ increase in $PM_{2.5}$, PM_{10} , NO_2 and SO_2 on lag0 were associated with 0.42% (95%CI: 0.16%-0.67%), 0.34% (95%CI: 0.15%-0.54%), 1.11% (95%CI: 0.38%-1.84%) and 1.06% (0.21%-1.93%) increase in outpatient visits for AD (Table 2). Table 2 shows the effects of pollutants (lag0) in multi-pollutant models. After adjusting

for SO₂, the effect of PMs (PM_{2.5} and PM₁₀) remained statistically significant (percent increase = 0.32 (95% CI: 0.03-0.62) and 0.28 (95% CI: 0.06-0.50), respectively). However, the effects of PMs weakened in multi-pollutant models compared with that in single-pollutant models. For NO₂ and SO₂, their effects turned non-significant after adjusting for other air pollutants in models.

We made sensitivity analysis to test whether the effects from Lag0 to Lag2 and from Lag0-1 to Lag0-2 are stable in the multi-pollutant models. This part is shown in the Fig. S2. The effects of PM (PM_{2.5} and PM₁₀) on Lag0 were still the largest and significant after adjusting SO₂ in the multi-pollutant models. The effects of NO₂ and SO₂ with different lag structures were not significant in multi-pollutant models.

In Fig.2, the cumulative effects of temperature were J-shaped with large comfortable temperature ranges where the relative risks of outpatients were close to 1(a). Cold temperature was generally associated with approximately 10 days-lasting risk after exposure (b). The greatest effect of hot temperature occurred on the day of exposure, after which it decreased rapidly and returned to baseline levels at lag 1 day. For relative humidity, the cumulative effects were non-linear, with risk effects of low relative humidity and protective effects of high relative humidity (d). The effects of low relative humidity fluctuated over lag 0 to 6 and remained stable around baseline after lag 6 (e). High relative humidity showed protective effects from lag 0 to lag4, peaking at lag0 to lag 2 (f).

Bivariate response surface model

Fig.3 show interactive effects between pollutants with mean temperatures and mean relative humidity, respectively. When the temperature was high, pollutants, especially NO₂ and SO₂ showed strong positive associations with outpatients for AD. The associations of PM_{2.5} and NO₂ with outpatient visits for AD changed not so much across different relative humidity

levels, which meant no obvious interactive effects between pollutants with relative humidity. PM₁₀ and SO₂ showed strong positive associations with outpatients for AD when the relative humidity was extremely low.

Stratification analysis

We defined the temperature strata and relative humidity strata as four levels using quartiles of temperature (3.0°C, 15.3°C and 24.0°C) and relative humidity (36.0%, 53.0% and 70.0%) as the cut-off points. The lowest quartile temperature and relative humidity level were chosen as the reference levels when calculating the P value for interaction (P_{int}). As shown in Table 3, enhanced positive associations of pollutants with outpatient visits for AD were found at the highest quartile temperature level. A 10µg/m³ increase in NO₂ and SO₂ were associated with 3.19% (95%CI: 0.18%-6.30%) and 6.96% (95%CI: 0.46%-13.88%) increase in outpatient visits for AD at the highest quartile temperature level. No significant P values for interaction were found between temperature levels and air pollutants. Significant associations between NO₂ and SO₂ with outpatient visits for AD were found at the first and third quartile relative humidity level, respectively. No significant P values for interaction were found between relative humidity levels and air pollutants. These effects were consistent between different age and sex subgroups(Supplementary Fig.S3-S4).

Discussion

The present study used time-series analyses to examine the interactive effects between air pollutants and meteorological factors on outpatient visits for AD in Beijing, China. This study included 64,987 visits for AD over a 5-year period, with an average of 35.6 visits per day. The results of the independent models suggest that temperature, relative humidity, and air pollution are significantly associated with outpatient visits for AD. We revealed

interactions between meteorological factors and air pollution using bivariate response surface model and stratification analysis. We conclude that high temperature facilitates the risk effect of air pollution on AD.

Air pollutants were found to have harmful effects on AD in our study, which was consistent with previous studies [12, 26-29]. We compared our results with a very similar study done in Chengdu, south-western China [30]. As shown in Table 4, both our study and the study in Chengdu investigate the associations between air pollution and outpatients for atopic dermatitis (eczema) during 5 years. Time-series analysis were employed in the analysis of both studies to control the time trend. The daily numbers of outpatient visits were quite the same and even air pollution was similar. However, the meteorological variables were different (mean temperature and especially humidity higher in Chengdu than in Beijing). Significant positive associations between air pollution and outpatients for eczema were found in both studies, but the effects of air pollution in Chengdu were larger than those in Beijing. We suggest that the effects of air pollutants were modified by meteorological factors such as temperature and relative humidity. In our study, we found stronger air pollution effects on hot days, which may explain the larger effects of air pollution in Chengdu, where the temperature is higher than in Beijing.

We found that the harmful effects of air pollutants on AD tend to be enhanced on hot days, although the P values for interaction between temperature levels and air pollutants were not significant (Table 3). The sample size in each exposure quartile may be insufficient to provide a statistically significant power, further studies are still needed to detect the interaction effects. Limited previous studies had reported the effects of air pollution on AD can be modified by meteorological factors and found conflicting results. A recent study in Korea found that the risks of AD symptoms caused by PM_{2.5} and PM₁₀ exposure were significantly increased on dry moderate days, which characterized by mild, dry weather conditions [31,

32]. Considering the diverse demographic, economic and climatic characteristics of the study areas, the temperature, relative humidity and air pollution levels likely vary in different regions, contributing to differences in the direction and magnitude of the modification effects of meteorological factors on air pollution. In the stratification analysis, we found the risk effects of air pollution on AD were much higher in the stratum of the highest quartile temperature level. This stronger effect was biologically plausible, though the definite principle was still unrevealed. Air pollutants may interact with the skin by binding to stratum corneum, or penetrating the epidermis and entering systemic circulation via dermal capillaries [29]. The increased cutaneous blood flow due to vasodilation in hot environments allows more pollutants entering systemic circulation and consequently resulted in increased toxicity of pollutants [33]. In addition, lighter clothing and more time outdoors on hot days increased skin's exposure areas to air pollutants [34, 35]. Overall, our results emphasize the avoidance of exposure to air pollutants, especially on hot days, to reduce the risk of AD.

Strongest associations between air pollutants and AD outpatient visits were found at lag0, suggesting acute effects of air pollution on AD exacerbation and related medical care burdens. Acute effects of air pollution on AD were also found in previous studies. A similar study in Shanghai, China also found the strongest effects between air pollutants and outpatient visits for eczema at lag0 [36]. A panel study in Korea found an increase in PM₁₀ and NO₂ by 10 units increased the risk of eczema symptoms on the same day by 3.2% (95% CI: 1.5%, 4.9%) and 5.0% (95% CI: 1.4%, 8.8%), respectively [26]. Our results, combined with the above previous studies, suggested that AD symptoms worsen and then people go to a clinic immediately. However, different lag effect periods were found in previous studies and for different pollutants. The similar study in Chengdu, China found the greatest effects of air pollution at lag1[30]. The above panel study in Korea found the effects of PM₁₀ were the greatest at lag0-5(moving averages of 5 days) while the effects of NO₂ were the greatest at

lag0 [26]. The lag periods between exposure to air pollution and exacerbation of AD and between exacerbation and visiting a doctor were influenced by lots of factors. Our study suggested that susceptible populations and patients should avoid exposure on the day with high air pollution even the pollution may only last for one day.

Our results on the association between temperature and outpatient visits for AD align with majority of previous findings that cold weather increased the risk of AD [15, 37, 38]. The mechanisms for how lower temperatures might be harmful in AD are unclear. It is possible that ambient temperature directly affects keratinocytes [39]. People living in colder climates use more indoor heating, which may trigger or aggravate AD [34]. Moreover, people living in colder climates may spend less time outdoors and consequently have less UV exposure which may protect against AD [34]. In terms of relative humidity, we found not only the harmful effects of low humidity but also the protective effects of high humidity on AD. Humidity may affect AD by repair or disruption of skin barrier function. A study in murine models showed that low humidity induces epidermal DNA synthesis, causes mast cell degranulation, and leads to epidermal hyperplasia in response to barrier disruption [40]. Higher humidity may have multiple effects on atopic skin. On one hand, higher humidity may offset increased TEWL in AD skin [41]. On the other hand, higher humidity may also provoke perspiration, which can be irritating and aggravate pruritus [16]. Further epidemiologic research on humidity and AD is warranted, particularly because humidifiers are commonly used as an adjunctive treatment by AD patients.

In our multi-pollutant models, the effects of air pollutants were attenuated. These results were consistent with studies applying co-pollutant models in interaction research studies [42, 43]. It was noted that focusing on individual pollutants as the single risk factor is likely not to reflect the effect of combined exposure to multiple air pollutants, and it could be the mixture represents a higher risk than the individual components [44]. These results may suggest that

synergistic effects among air pollutants exist and need to be further explored. In addition, co-linearity between air pollutants ($r \geq 0.5$ between each other) was one factor that should not be neglected in a multi-pollutant model. Further research with advanced methods is needed, such as source apportionment analysis, considering that the chemical component of particles pollutants (PM_{2.5} and PM₁₀) might be responsible for the adverse health effects.

In the present study, the time-series GAM model combined with bivariate response surface model and stratification model were applied to examine the interactive effects of air pollutants and meteorological factors on outpatient visits for AD and has several strengths. The bivariate response surface model could be used to visually examine whether the interaction exists and the stratification model could be used to evaluate the extent to which the observed associations between air pollutants and AD varied by temperature and relative humidity. Beijing has a monsoon-influenced continental climate with four distinct seasons, but the temperature and relative humidity is not often extremely high or low. For example, during our study period, there were only 92 days under -3°C (5th percentile) or above 28.7°C (95th percentile). The effect estimates would be imprecise in such a limited period. Considering this, we stratified the models into quartiles of the distribution of temperature or relative humidity, but not into extremely high or low levels. Different cut-off selection and hierarchical methods have been used in previous stratification analysis exploring the interactive effects between air pollution and climate factors. For example, the median of temperature and visualized turning point were chosen as cut offs to define the temperature strata as two levels [42]. The 5th and 95th percentiles were chosen as cut-off points to define the temperature as three levels [45]. Different cut-off selection and hierarchical methods might result in different observed associations. Overall, more cut-off selection and hierarchical models should be explored in further analysis.

This study was based on a large database in Beijing, China, including a period of 5 years. The dermatology department of PLA is one of the largest and most famous dermatology departments among hospitals in Beijing. Although the hospital selection bias might exist, this hospital has good representativeness on the trend of outpatient visits of the whole city. In addition, high air pollution levels and distinct seasons in Beijing offered ample opportunity to explore the effects of environmental risk factors on skin conditions.

Several limitations in this study should be considered. Firstly, as mentioned above, the cases were only selected from one hospital. Although the patients lived in the same city, we are unable to control their hospital selection. Secondly, this is an ecological study with inevitable bias from measurement. The monitoring results of all stations were averaged and used as the proxy of population exposure level to environmental factors, as lots of previous time-series studies did [36, 42], because data on individual exposure were unavailable.

In conclusion, this study provides further evidence that effects of air pollutants on AD can be modified by meteorological factors, with significant and enhanced effects at hot days.

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Statement of Ethics: This study was carried out by analyzing data from the HIS system of the General Hospital of Air Force of People's Liberation Army (PLA) in Beijing, China.

Patients were not contacted individually for consent. The study was approved by the ethics committee of the hospital.

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Table 1 Summary of daily outpatient visits for atopic dermatitis, air pollutants and meteorological factors in Beijing, China during 2013 to 2017 (n=1826)

Variables	Min	P 25	Median	P75	Max	Mean	Sd
Outpatient visits	0.0	21.0	33.0	44.0	128.0	35.6	20.5
PM _{2.5} (μg/m ³)	5.7	33.4	61.9	104.4	438.1	79.7	65.8
PM ₁₀ (μg/m ³)	5.6	57.7	93.5	139.5	791.0	110.5	75.7
NO ₂ (μg/m ³)	7.8	35.0	45.5	61.8	154.7	50.8	22.5
SO ₂ (μg/m ³)	2.0	4.9	9.6	21.1	176.6	16.9	19.1
Temperature(°C)	-14.3	3.0	15.3	24.0	32.6	13.7	11.1
Relative humidity (%)	8.0	36.0	53.0	70.0	99.0	53.0	20.3

Abbreviations: P25 and P75 represent the percentage; Min: minimal; Max: maximal; Sd: standard deviation;

PM_{2.5}: particulate matter less than 2.5μm in aerodynamic diameter; PM₁₀: particulate matter less than 10μm in aerodynamic diameter; NO₂: nitrogen dioxide; SO₂: sulfur dioxide.

Table 2 Estimates of percent increase (95% CI) in outpatient visits for AD (95%CI) for per 10 μ g/m³ increase in pollutants (lag0) in multi-pollutant models

Pollutant	Percent increase (95%CI)	Pollutant	Percent increase (95%CI)
PM _{2.5}	0.42(0.16-0.67)**	PM ₁₀	0.34(0.15-0.54)***
+NO ₂	0.25(-0.1-0.61)	+NO ₂	0.24(-0.02-0.5)
+SO ₂	0.32(0.03-0.62)*	+SO ₂	0.28(0.06-0.5)*
NO ₂	1.11(0.38-1.84)**	SO ₂	1.06(0.21-1.93)*
+SO ₂	0.9(-0.04-1.86)	+NO ₂	0.51(-0.48-1.5)
+PM _{2.5}	0.6(-0.41-1.61)	+PM _{2.5}	0.49(-0.48-1.46)
+PM ₁₀	0.53(-0.44-1.5)	+PM ₁₀	0.38(-0.73-1.5)

***P<<0.001; ** P<0.01; *P<0.05

Abbreviations: PM_{2.5}: particulate matter less than 2.5 μ m in aerodynamic diameter; PM₁₀: particulate matter less than 10 μ m in aerodynamic diameter; NO₂: nitrogen dioxide; SO₂: sulfur dioxide.

Table 3 Estimates of percent increase (95% CI) in outpatient visits for AD (95%CI) for per 10 μ g/m³ increase in pollutants (lag0) across four temperature levels and relative humidity levels

strata	air pollutant	Percent increase in outpatient visits for AD (95%CI)							
		Q1	Pint	Q2	Pint	Q3	Pint	Q4	Pint
Temperature	PM _{2.5}	-0.06(-0.59-0.48)	`-	0.56(-0.01-1.14)	0.822	0.10(-0.53-0.74)	0.668	0.59(-0.16-1.35)	0.435
	PM ₁₀	0.11(-0.37-0.58)	`-	0.25(-0.21-0.70)	0.555	0.11(-0.28-0.50)	0.89	0.57(-0.12-1.27)	0.521
	NO ₂	-0.15(-1.59-1.31)	`-	1.91(0.49-3.36)**	0.692	-0.31(-2.5-1.94)	0.864	3.19(0.18-6.30)*	0.816
	SO ₂	-0.25(-1.80-1.32)	`-	1.43(-0.01-2.90)	0.657	3.03(-0.33-6.51)	0.309	6.96(0.46-13.88)*	0.102
relative humidity	PM _{2.5}	0.46(-0.08-0.99)	`-	-0.33(-0.93-0.27)	0.569	0.21(-0.32-0.74)	0.316	0.42(-0.12-0.95)	0.505
	PM ₁₀	0.18(-0.16-0.52)	`-	-0.02(-0.50-0.45)	0.746	0.17(-0.26-0.60)	0.483	0.44(-0.04-0.92)	0.699
	NO ₂	1.53(0.08-3.01)*	`-	-0.48(-1.91-0.98)	0.664	0.41(-1.08-1.93)	0.103	1.09(-0.7-2.91)	0.118
	SO ₂	1.73(-0.16-3.66)	`-	0.05(-1.29-1.41)	0.379	2.91(0.13-5.77)*	0.064	1.31(-1.53-4.23)	0.325

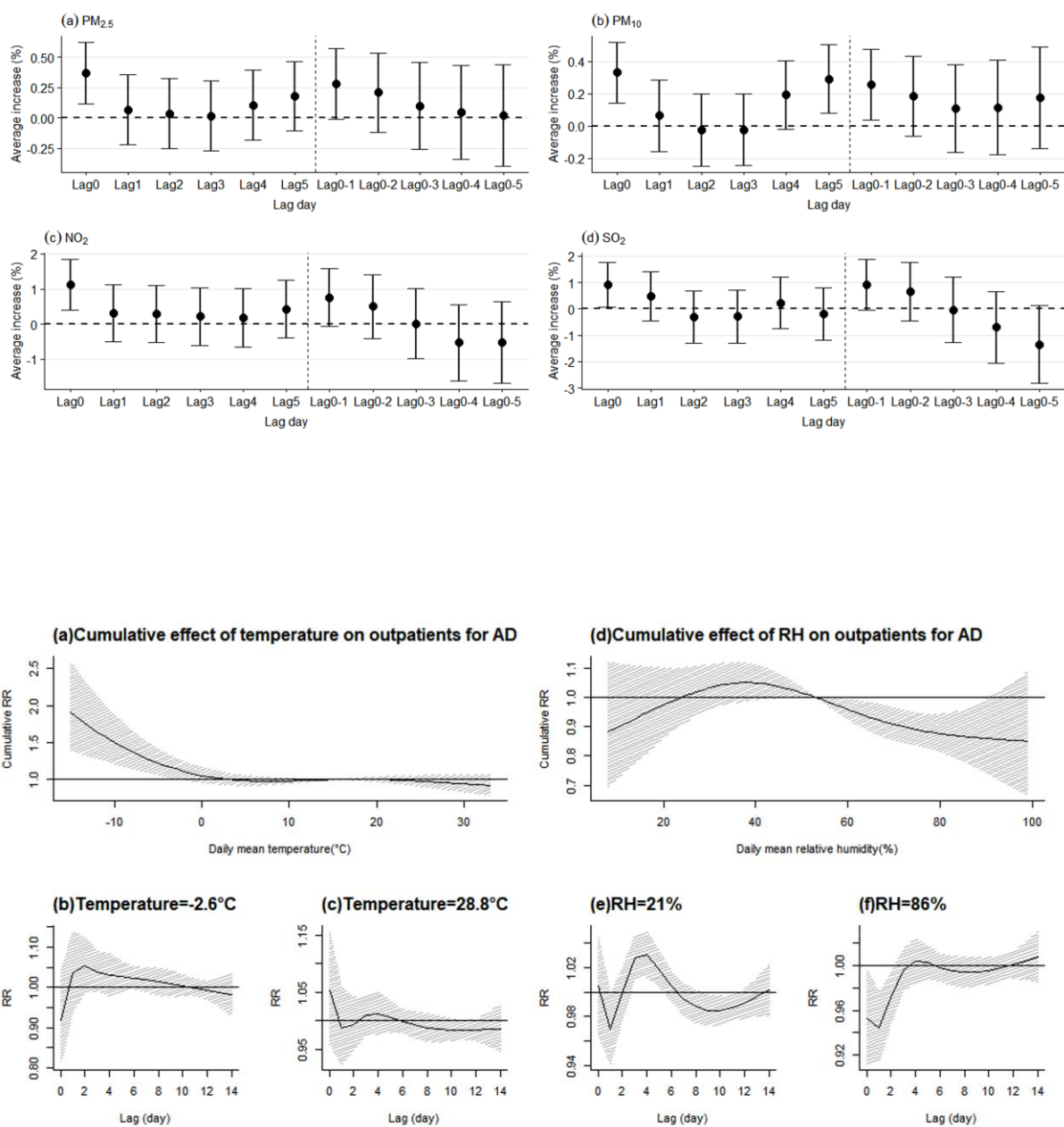
***P<<0.001; ** P<0.01; *P<0.05

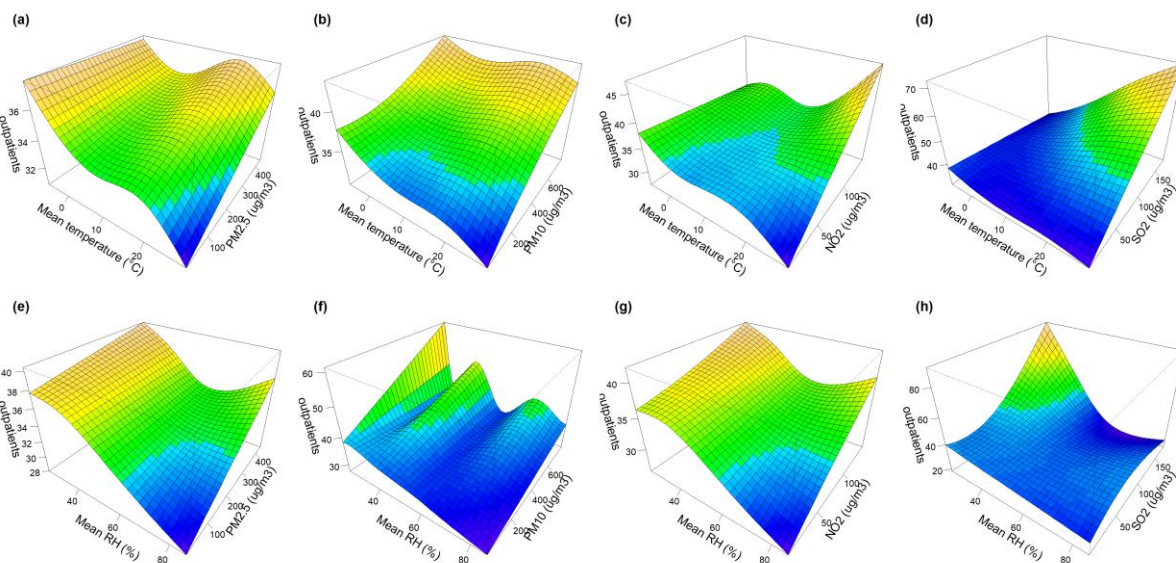
Abbreviations: PM_{2.5}: particulate matter less than 2.5 μ m in aerodynamic diameter; PM₁₀: particulate matter less than 10 μ m in aerodynamic diameter; NO₂: nitrogen dioxide; SO₂: sulfur dioxide; Q1: the first quartile; Q2: the second quartile; Q3: the third quartile; Q4: the fourth quartile.

Table 4 A comparison between the results of our study and the results of a similar study in Chengdu, China.

Variables	Mean±Sd	
	Beijing (2013-2017)	Chengdu (2011-2015)
Outpatient visits	35.6±20.5	40.9±18.1
PM ₁₀ (μg/m ³)	110.5±75.7	119.6±74
NO ₂ (μg/m ³)	50.8±22.5	55.2±18.7
SO ₂ (μg/m ³)	16.9±19.1	25.6±14.5
Temperature (°C)	13.7±11.1	16.3±7.4
Relative humidity (%)	53±20.3	78.5±8.6
	RR (95%CI) per 10μg/m ³	
PM ₁₀	1.0029(1.0053-1.0053)	1.0041(1.0004-1.0078)
NO ₂	1.0100(1.0182-1.0182)	1.0344(1.0012-1.0686)
SO ₂	1.0160(1.0286-1.0286)	1.0530(1.0617-1.1530)

Abbreviations: PM_{2.5}: particulate matter less than 2.5μm in aerodynamic diameter; PM₁₀: particulate matter less than 10μm in aerodynamic diameter; NO₂: nitrogen dioxide; SO₂: sulfur dioxide; Sd: standard deviation.





Supplementary Materials

Table S1 Outpatient visits for atopic dermatitis stratified by gender and age the General Hospital of Air Force of People's Liberation Army (PLA) in Beijing, China during 2013 to 2017

Table S2 Spearman correlation coefficients between air pollutants and weather conditions in Beijing during 2013 to 2017.

Fig.S1 The time series of daily mean air pollution and meteorological factors in Beijing and number of outpatient visits for atopic dermatitis in Hospital of Air Force during 2013 to 2017. The green lines are the trend lines using a smoothing function (cubic-spline) in the time series.

Fig.S2 Association between air pollutants and daily outpatient visits for atopic dermatitis at different lag structures in in single- and two- pollutant models.

Fig.S3 Association between air pollutants and daily outpatient visits for atopic dermatitis in different age groups.

Fig.S4 Association between air pollutants and daily outpatient visits for atopic dermatitis in different sex groups.

Table S1 Outpatient visits for atopic dermatitis stratified by gender and age the General Hospital of Air Force of People's Liberation Army (PLA) in Beijing, China during 2013 to 2017

Variables	N	Proportion (%)
Total	64987	
Gender		
Male	26169	40.27%
Female	38818	59.73%
Age		
age <= 18	5903	9.08%
18< age <=45	29157	44.87%
45< age <=65	21783	33.52%
age > 65	8139	12.52%

Table S2 Spearman correlation coefficients between air pollutants and weather conditions in Beijing during 2013 to 2017

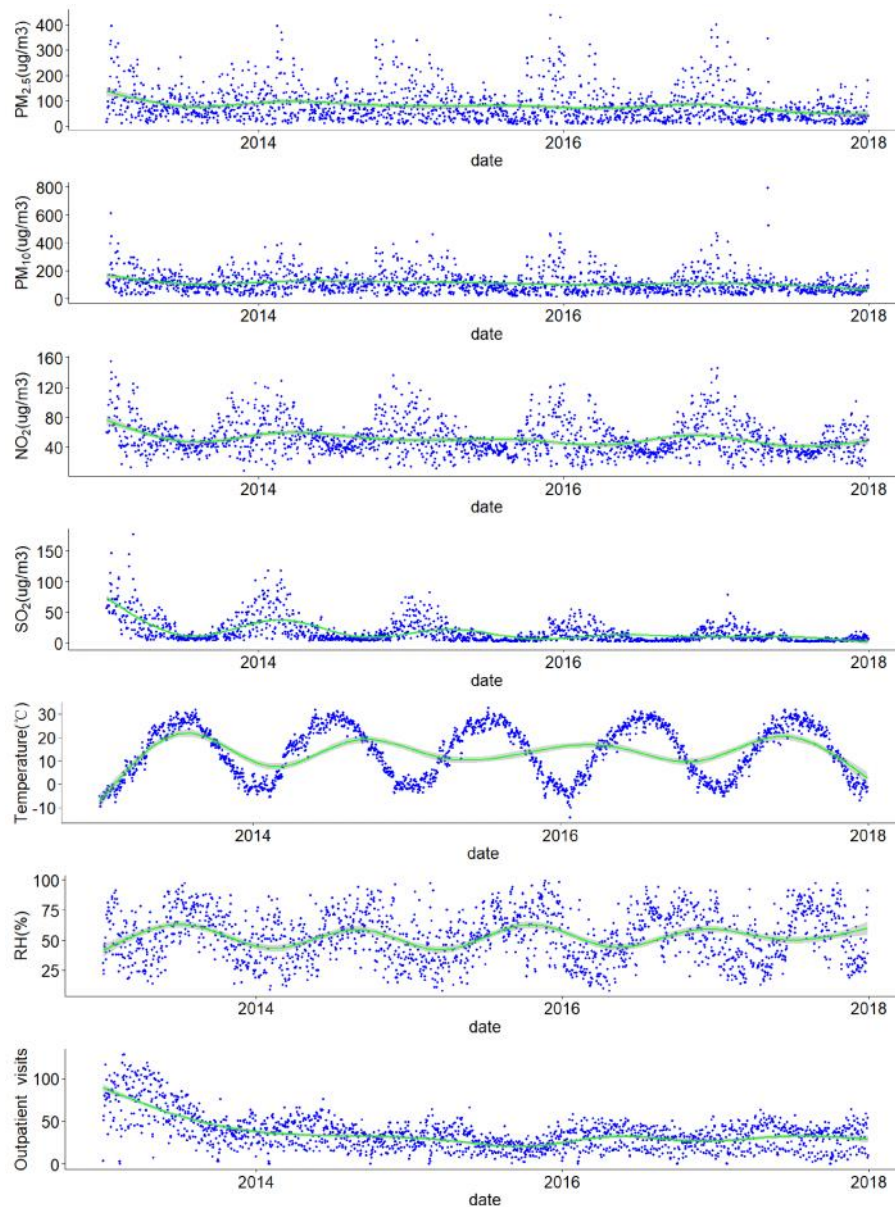
	PM _{2.5}	PM ₁₀	NO ₂	SO ₂	temperature	relative humidity
PM _{2.5}	1					
PM ₁₀	0.9***	1				
NO ₂	0.8***	0.75***	1			
SO ₂	0.56***	0.51***	0.67***	1		
temperature	-0.21***	-0.14***	-0.35***	-0.48	1	
relative humidity	0.43***	0.29***	0.26***	-0.04	0.27***	1

***P<<0.001; ** P<0.01; *P<0.05

Abbreviations: PM_{2.5}: particulate matter less than 2.5 µm in aerodynamic diameter;

PM₁₀: particulate matter less than 10 µm in aerodynamic diameter; SO₂: sulfur dioxide;

NO₂: nitrogen dioxide.



RH: relative humidity

Fig.S1 The time series of daily mean air pollution and meteorological factors in Beijing and number of outpatient visits for atopic dermatitis in Hospital of Air Force during 2013 to 2017. The green lines are the trend lines using a smoothing function (cubic-spline) in the time series.

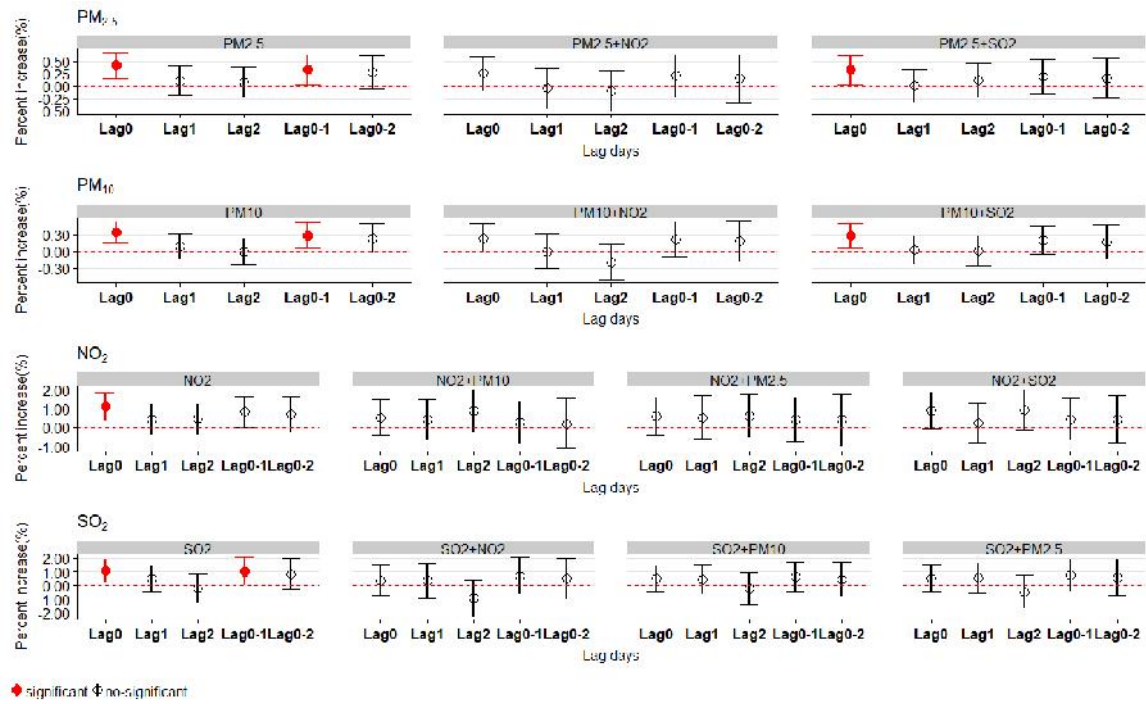
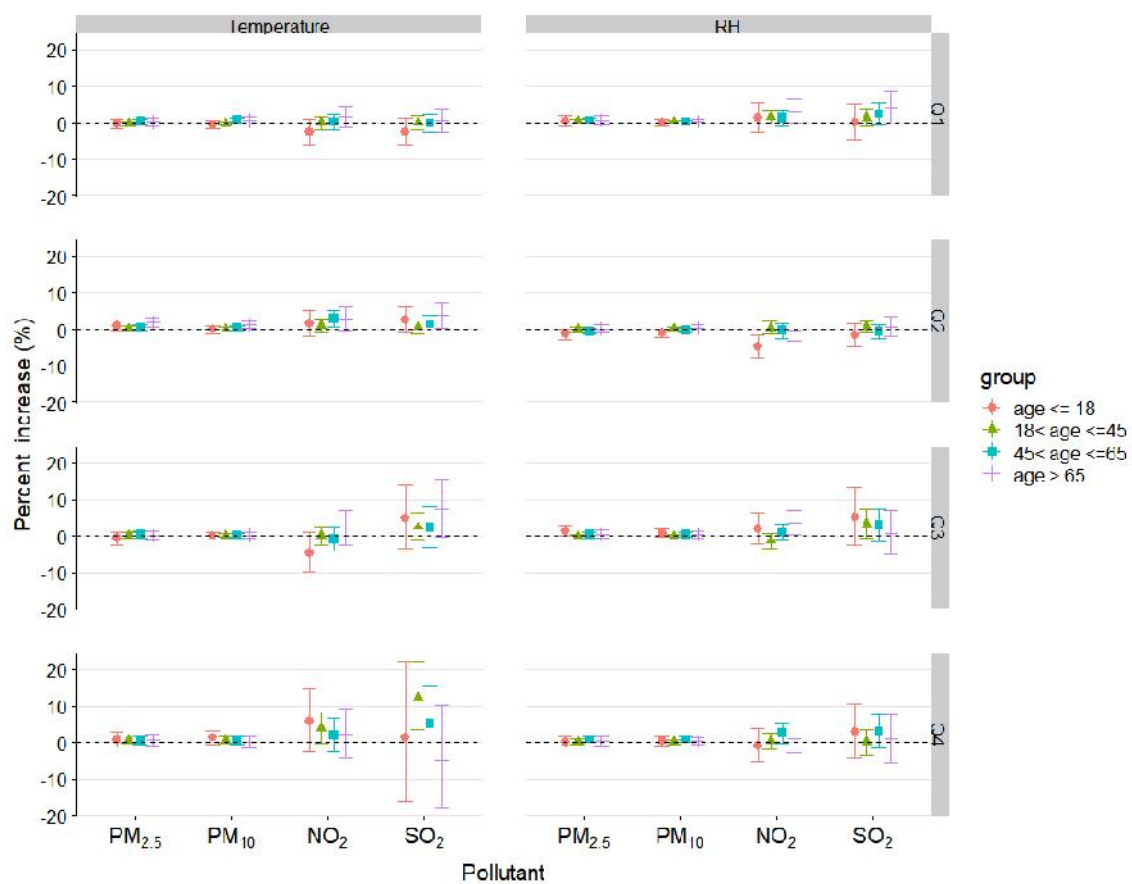
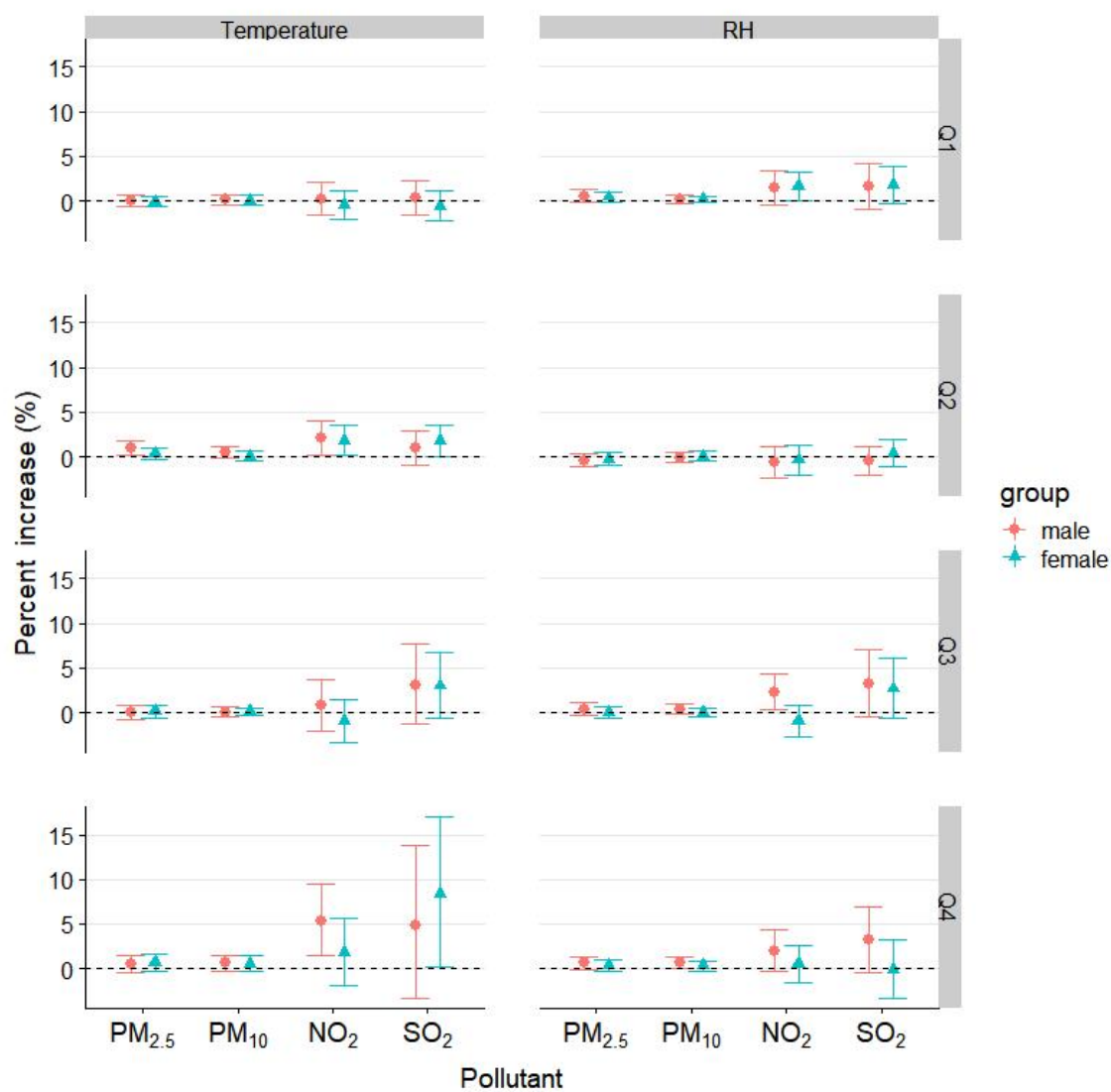


Fig.S2 Association between air pollutants and daily outpatient visits for atopic dermatitis at different lag structures in in single- and two- pollutant models.



RH: relative humidity

Fig.S3 Association between air pollutants and daily outpatient visits for atopic dermatitis in different age groups.



RH: relative humidity

Fig.S4 Association between air pollutants and daily outpatient visits for atopic dermatitis in different sex groups.