

Association between air pollution and atopic dermatitis in Guangzhou, China: modification by age and season*

H.L. Wang¹ J. Sun,² Z.M. Qian,² Y.Q. Gong,¹ J.B. Zhong,¹ R.D. Yang,¹ C.L. Wan,¹ S.Q. Zhang,¹ D.F. Ning,¹ H. Xian,² J.J. Chang,² C.J. Wang,³ E. Shacham,⁴ J.Q. Wang¹ and H.L. Lin⁵ 

¹Guangzhou Institute of Dermatology, Guangzhou, China

²Department of Epidemiology and Biostatistics, College for Public Health & Social Justice, Saint Louis University, St Louis, MO, USA

³Department of Epidemiology and Biostatistics, College of Public Health, Zhengzhou University, Zhengzhou, Henan, China

⁴Department of Behavioral Science and Health Education, College for Public Health & Social Justice, Saint Louis University, St Louis, MO, USA

⁵Department of Epidemiology, School of Public Health, Sun Yat-sen University, Guangzhou, China

Summary

Correspondence

Jian Qin Wang.

Email: jianqinwang@foxmail.com

Hua Liang Lin.

Email: linhualiang@mail.sysu.edu.cn

Accepted for publication

25 October 2020

Funding sources

National Key R&D Program of China (grant no.: 2018YFA0606200) and National Natural

Science Foundation of China (grant no.:

81972993).

Conflicts of interest

The authors declare they have no conflicts of interest.

H.L.W. and J.S. contributed equally to this work.

*Plain language summary available online

DOI 10.1111/bjd.19645

Background The short-term effect of ambient air pollution on atopic dermatitis (AD), along with its effect modifiers, has not been fully addressed.

Objectives To examine the short-term associations between air pollution and AD, and to identify effect modifications by age and season.

Methods We used the generalized additive model to evaluate the short-term effect of ambient air pollution on daily hospital visits for AD, adjusting for potential confounders. Subgroup analyses were performed to identify potential effect modifications by season and age (< 18 years and ≥ 18 years).

Results A total of 29 972 hospital visits for AD were recorded in Guangzhou, China, from 19 January 2013 to 31 December 2017. Among them, 72.8% were visits by children and 51.4% occurred in the cool season. Acute and delayed effects on AD hospital visits were significant for all air pollutants. Stronger effects were seen in the cool season (approximately 1.7–3.0 times higher than effects in the warm season). Stronger effects were also observed in children (approximately 1.3–1.8 times higher than effects in adults). Sensitivity analyses indicated the results were robust.

Conclusions Air pollution might be an important trigger for AD in subtropical Guangzhou, China. Children are more vulnerable than adults, and the effects are stronger in the cool season.

What is already known about this topic?

- Atopic dermatitis (AD) has the highest number of disability-adjusted life-years among skin disorders.
- The acute effect of air pollution on AD has not been well studied in China.

What does this study add?

- We found that air pollution (including ambient fine particulate matter, inhalable particles, sulfur dioxide, nitrogen dioxide and ozone) acutely triggers AD, and that children are more sensitive to this effect.
- The cool season is the vulnerable exposure window for these acute effects.

Atopic dermatitis (AD) is an inflammatory skin disease that has the highest disability-adjusted life-years among skin disorders and is characterized by recurrent eczema with an intractable itch.^{1,2} Although occurring primarily during childhood,³

AD has become more prevalent in Chinese adults in recent years, potentially owing to the interaction between genetics and the environment.^{4–6} Hence, assessing the effect of air pollution on AD hospital admissions would increase

understanding of the causation and may provide insights into the prevention efforts and management of AD.

Multiple studies have shown short-term associations between some air pollutants, meteorological factors and hospital visits due to eczema and AD.^{7–11} However, few studies have thoroughly examined this acute effect for all ambient air pollutants on AD hospital visits by season and age. In the present study, we collected information on all ambient air pollutants, including fine particulate matter (PM_{2.5}), inhalable particles (PM₁₀), nitrogen dioxide (NO₂), sulfur dioxide (SO₂), and ozone (O₃), so we could thoroughly study their correlations with each other and with meteorological factors – information that previous studies have not entirely captured.^{7–11} We also examined the potential effect modification by age by including children and adults. A previous study only examined AD in adults (≥ 18 years);⁷ however, children have been shown to be more vulnerable to air pollution exposure.¹² We chose a study site with an air pollution level much higher than related studies conducted in Korea and Europe^{13–16} but comparatively lower than related studies in China.^{7–9} Lastly, we examined the potential effect modification by season on all ambient air pollutants; a previous study only examined potential effects among particulate matters (PM_{2.5} and PM₁₀).¹⁷ Although temperature and humidity will change moderately between the warm and cool seasons, other seasonal factors such as rainfall and wind speed could interact with temperature and humidity because the association between meteorological factors and AD hospital visits has been shown to differ by region and season, indicating a potential effect of modification by season.¹⁷

The main hypothesis was that ambient PM_{2.5}, PM₁₀, NO₂, SO₂ and O₃ are all positively associated with hospital visits due to AD after controlling for meteorological factors (ambient temperature and humidity). The subhypothesis was that age and season are two effect modifiers of these associations.

Patients and methods

Study location and population

Guangzhou is a subtropical city in China with a typical monsoon climate; it is also an important international transportation hub. In Guangzhou, approximately 12.7 million people reside in a land area of 7434.40 km², with forest coverage of 42.1%.¹⁸

Atopic dermatitis

We obtained de-identified day patient records for the period 19 January 2013–31 December 2017 from the electronic medical system of Guangzhou Municipal Clinical Center for Dermatology. This centre, located in the urban core area of Guangzhou, is one of the highest-level hospitals for the treatment of skin diseases in Guangdong Province and the only municipal clinical centre for dermatology in Guangzhou. The medical records include demographic information, clinical

diagnosis in Chinese and corresponding International Classification of Diseases, 10th Revision (ICD-10) codes. This coding system has been widely used in our clinic, and its operation has been monitored by the centre's strict quality control and quality assurance programmes. Patients of all ages were included in the study, and outpatients with AD with an ICD-10 code of L20.9 were screened.

The study was exempt from Institutional Review Board approval as the data used in the study were de-identified.

Air pollution

The daily 24-h concentrations ($\mu\text{g m}^{-3}$) for PM_{2.5}, PM₁₀, SO₂ and NO₂, and the maximum 8-h concentration for O₃ were collected from 11 Guangzhou Environmental Monitoring Center stations (Figure 1). The daily mean concentrations of each air pollutant from all monitor stations were arithmetically averaged to represent the daily air pollution exposure for the general population. During the study period, there were missing concentration values for < 3% of days, and extremely large concentrations were seen on 10 days. All of these outliers and missing values were replaced by imputed values using the linear interpolation approach ('na.approx' function in R; R Core Team, 2019).¹⁹

Statistical analysis

The time series design is well suited to examining the acute effect of air pollution on hospital visits for AD.²⁰ A hospital visit for AD is a small possibility event, following Poisson distribution. Thus, we used a generalized additive model (GAM) with quasi-Poisson link and specified using an a priori model to estimate the association between air pollution exposure and hospital visits for AD.⁸ Penalized smoothing spline functions were used to account for long-term trends, seasonal patterns, temperature and relative humidity (RH).²¹ In these smoothing functions, degrees of freedom were set according to previous studies.^{22,23}

$$\text{Log}[E(Y_t)] = \alpha + \beta Z_t + S(\text{time}, \text{df}) + S(\text{temperature}_{03}, \text{df}) + S(\text{relative humidity}, \text{df}) + \text{DOW}_t$$

In this equation, t represents the day of observation; $E(Y_t)$ is the expected daily hospital visits for AD on day t ; α is the intercept; β is the coefficient for a pollutant; Z_t represents pollutant concentration at day t ; temperature_{03} is the moving average of daily mean temperatures on the current day and 3 days before the hospital visit for AD;¹⁶ RH is daily mean RH; DOW is a dummy variable for day of the week; and S refers to the smoothing spline function.

We explored the lag effects of air pollution on AD from the current day (lag0) up to 5 days before (lag5). In order to estimate the cumulative effect of air pollutants on the risk of AD, we used the moving averages for the previous one (lag01), three (lag03) and five (lag05) days in the main analysis.^{7,17}

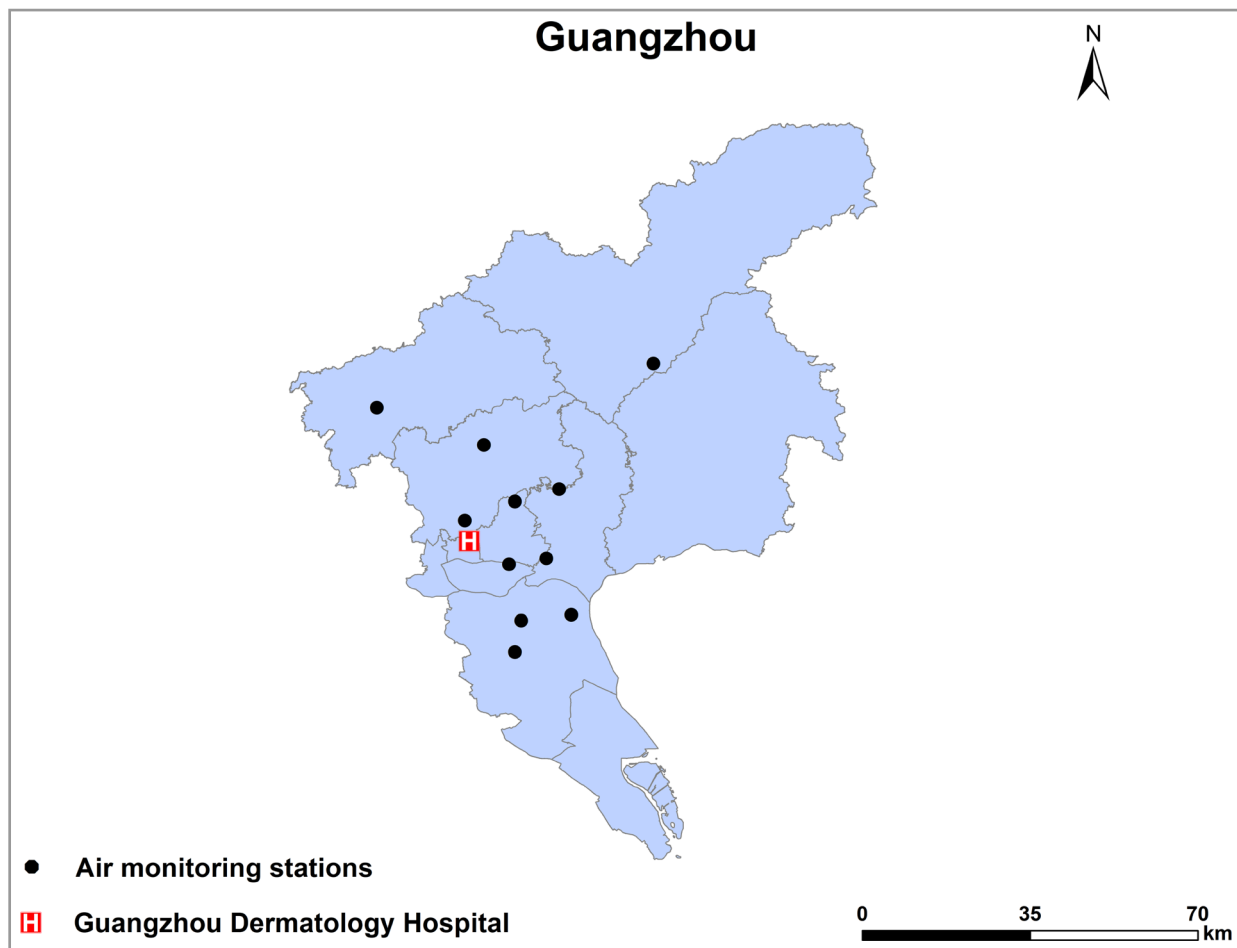


Figure 1 Locations of Guangzhou's 11 ambient air monitoring stations in the period 19 January 2013 to 31 December 2017.

Covariates

Daily temperature (°C) and RH (%) were obtained from the National Weather Data Sharing System (<https://data.cma.cn/>). Spearman's correlation coefficients were used to estimate the correlations between temperature, RH and air pollutants.²⁴

Stratified analysis

The warm season was defined as lasting from 1 May to 30 September, and cool season as lasting from 1 October to 30 April each year. Patients were divided into two groups according to age – children and adults – with children defined as being < 18 years old and adults as being ≥ 18 years old. Patient age and sex were collected from the de-identified medical records. Sex was recorded as either male or female.

In addition, the significance of between-group differences was tested using the 95% confidence interval (CI) of the difference: $(\beta_1 - \beta_2) \pm 1.96 \sqrt{(SE_1)^2 + (SE_2)^2}$, where β_1 and β_2 were the regression coefficient for each subgroup, and SE_1 and SE_2 were the standard errors.²⁵

Two statistical significance levels were used in this study: significant ($P < 0.05$) and highly significant ($P < 0.001$). The

results were reported as excess risks (ERs): $ER = (\text{relative risk} - 1) \times 100\%$ and their 95% CIs. All statistical analyses were conducted in R version 3.5.3 (R Core Team, 2019). The time series analysis was performed using the R package 'mgcv' (version 3.2.3, <http://cran.r-project.org/>).

Sensitivity analyses

A series of sensitivity analyses were performed to evaluate the robustness of the estimated associations by changing the degrees of freedom (df) for the smoothing functions to control for nonlinear covariates (6–9 df/year). In addition, two-pollutant models were conducted. In these two-pollutant models, two different air pollutants were included together on the same lag day.

Results

Descriptive results

Table 1 shows the descriptive results of daily hospital visits associated with AD, air pollution and meteorological data. The mean daily concentrations of $PM_{2.5}$, PM_{10} , SO_2 , NO_2 and O_3

Table 1 Daily air pollution, meteorological data and hospital visits for atopic dermatitis (AD) in Guangzhou, China, from 19 January 2013 to 31 December 2017

	Whole study	Cool season ^a	Warm season ^b	Min.	P ₂₅	P ₅₀	P ₇₅	Max.
Air pollutants								
PM _{2.5} (µg/m ³)	41.4 ± 22.2	49.3 ± 24.0	30.7 ± 13.2	5.8	24.4	36.2	53.7	136.5
PM ₁₀ (µg/m ³)	61.2 ± 28.1	70.1 ± 30.9	49.2 ± 17.8	10.0	39.8	54.4	77.4	174.9
SO ₂ (µg/m ³)	15.4 ± 8.6	16.4 ± 10.3	14.0 ± 5.2	3.8	10.2	13.5	18.4	88.1
NO ₂ (µg/m ³)	46.5 ± 19.0	52.7 ± 21.4	38.1 ± 10.2	3.9	33.1	42.2	56.2	126.6
O ₃ (µg/m ³)	82.1 ± 44.4	72.3 ± 41.3	95.5 ± 45.0	4.8	46.6	79.4	110.1	238.5
Meteorology								
Temperature (°C)	22.0 ± 6.1	18.1 ± 4.9	27.4 ± 2.2	3.5	17.0	23.4	27.3	32.3
RH (%)	80.2 ± 11.0	77.8 ± 12.3	83.5 ± 7.8	31.0	74.0	81.0	88.0	100.0
Outcome (AD)								
Daily admission	16.6 ± 8.5	14.8 ± 7.8	19.0 ± 8.8	0.0	10.0	15.0	22.0	56.0
Daily admission by age (y)								
< 18 (children)	12.1 ± 6.7	10.6 ± 6.1	14.1 ± 7.0	0.0	7.0	11.0	16.0	44.0
≥ 18 (adults)	4.5 ± 3.0	4.3 ± 2.9	5.0 ± 3.1	0.0	2.0	4.0	6.0	19.0
Daily admission by sex								
Female	8.1 ± 4.7	7.0 ± 4.3	9.5 ± 5.0	0.0	5.0	7.0	11.0	27.0
Male	8.5 ± 4.6	7.7 ± 4.3	9.6 ± 4.8	0.0	5.0	8.0	11.0	33.0

Data are mean ± SD unless otherwise indicated. Min., minimal value; P₂₅, the first quartile; P₅₀, the second quartile (median); P₇₅, the third quartile; max., maximal value; PM_{2.5}, particulate matter < 2.5 µm in aerodynamic diameter; PM₁₀, particulate matter < 10 µm in aerodynamic diameter; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; O₃, ozone; RH, relative humidity. ^aCool periods were from 1 October to April 30; ^bwarm period was from 1 May to 30 September.

were 41.4 µg m⁻³, 61.2 µg m⁻³, 15.4 µg m⁻³, 46.5 µg m⁻³ and 82.1 µg m⁻³, respectively. In contrast to the warm season, the cool season had higher mean daily concentrations of all air pollutants, with the exception of O₃. The mean daily temperature in Guangzhou was 22.0 °C, and the mean daily RH was 80.2%. During the study period, a total of 29 972 hospital visits for AD were recorded in the study population. Of these visits, 15 387 were female patients and 21 807 were aged < 18 years (72.8%). The mean daily number of hospital visits associated with AD was 16.6, with a minimum of 0 and a maximum of 56 visits in one day.

Spearman correlation between pollutants and meteorological factors

Table 2 shows the Spearman correlation coefficients between air pollutants and meteorological factors. PM_{2.5}, PM₁₀, SO₂,

NO₂ and O₃ were positively correlated with each other and were all negatively correlated with meteorological factors, except for SO₂ and NO₂. Insignificant correlations were observed between SO₂ and temperature and between NO₂ and RH. PM_{2.5} and PM₁₀ had the strongest correlation with a Spearman's rho of 0.94 ($P < 0.001$).

Short-term effects

Figure 2 shows the ERs of daily AD that were associated with a 10 µg m⁻³ increase of PM_{2.5}, PM₁₀, SO₂, NO₂ and O₃, adjusting for temperature and RH. The single lag days ranged from lag0 to lag5. A 10 µg m⁻³ increase in ambient SO₂, NO₂, PM_{2.5}, PM₁₀ and O₃ corresponded to a 6.1% (95% CI 3.11–9.21), 3.1% (95% CI 2.05–4.26), 2.67% (95% CI 1.67–3.67%), 1.9% (95% CI 1.2–2.7) and 1.1% (95% CI 0.64–1.52) increase in AD hospital visits on the day of

Table 2 Spearman's correlation between daily mean air pollutant concentrations and meteorological factors in Guangzhou, China, from 19 January 2013 to 31 December 2017

	PM _{2.5}	PM ₁₀	SO ₂	NO ₂	O ₃	Temperature	RH
PM _{2.5}	1.00						
PM ₁₀	0.94**	1.00					
SO ₂	0.69**	0.66**	1.00				
NO ₂	0.71**	0.76**	0.50**	1.00			
O ₃	0.30**	0.39**	0.35**	0.08**	1.00		
Temperature	-0.35**	-0.25**	-0.04	-0.35**	0.36**	1.00	
RH	-0.25**	-0.28**	-0.19**	0.04	-0.43**	0.19**	1.00

PM_{2.5}, particulate matter < 2.5 µm in aerodynamic diameter; PM₁₀, particulate matter < 10 µm in aerodynamic diameter; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; O₃, ozone; RH, relative humidity. ** $P < 0.001$.

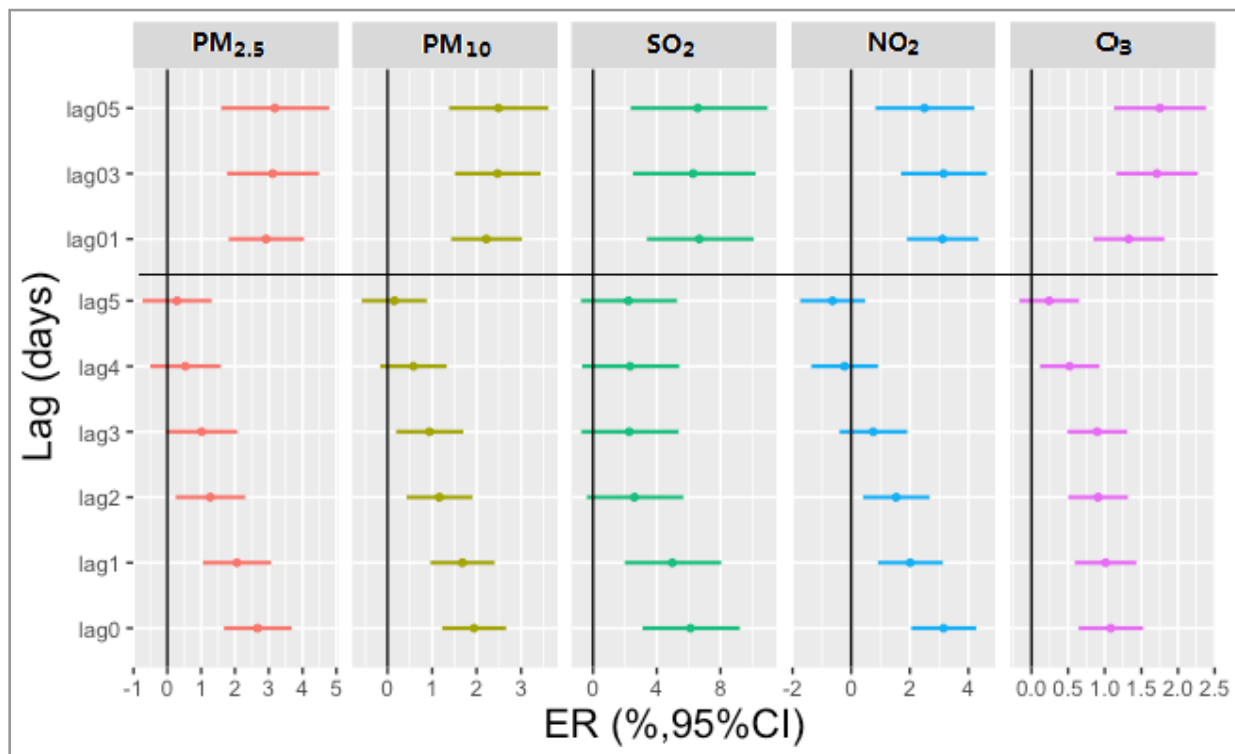


Figure 2 Excess risk (ER; %) and 95% confidence interval (CI) for atopic dermatitis per $10 \mu\text{g m}^{-3}$ increase in the concentration of each air pollutant along different lag days in Guangzhou, China, from 19 January 2013 to 31 December 2017. $\text{PM}_{2.5}$, particulate matter $< 2.5 \mu\text{m}$ in aerodynamic diameter; PM_{10} , particulate matter $< 10 \mu\text{m}$ in aerodynamic diameter; SO_2 , sulfur dioxide; NO_2 , nitrogen dioxide; O_3 , ozone.

exposure, respectively. The delayed effects lasted up to 4 days for O_3 , 3 days for PM_{10} , 2 days for $\text{PM}_{2.5}$ and NO_2 , and 1 day for SO_2 . The cumulative lag days ranged from lag01 to lag05. Cumulative lag days had much stronger effects than single lag days for all pollutants except for NO_2 , indicating higher cumulative effects for air pollutants on the risk of AD hospital visits. The largest cumulative effects occurred on lag03 for $\text{PM}_{2.5}$ (ER 3.1%; 95% CI 1.76–4.49), PM_{10} (ER 2.5%; 95% CI 1.51–3.44), SO_2 (ER 6.3%; 95% CI 2.49–10.21%), NO_2 (ER 3.1%; 95% CI 1.70–4.62) and O_3 (ER 1.7%; 95% CI 1.16–2.27).

Figure 3 shows dose–response curves between each air pollutant and daily hospital visits for AD during the study period in Guangzhou. These curves appear linear from the graph, and the sections where they deviate from the linear relationship have much wider 95% CIs (area between dashed lines), indicating low confidence in the estimates at these sections.

Figure 4 shows the residual plots of associations between air pollutants and daily hospital visits for AD during the study period. All estimation lines appear flat where most spots are located, indicating the assumptions for linearity are generally met for all air pollutants.

Effect modification

Figure 5 shows the estimated ERs of daily hospital visits for AD per $10 \mu\text{g m}^{-3}$ increment in each air pollutant

concentration, stratified by age and season. Stronger effects were seen in children (those aged < 18 years) for each air pollutant, with the exception of SO_2 , which showed an inverse relationship. Stronger and significant effects were seen in the cool season, whereas nonsignificant effects were seen in the warm season.

Sensitivity analysis

Table S1 (see Supporting Information) provides the estimated ERs and 95% CIs using different dfs in the time trend function of the GAM model. The results showed consistent associations between air pollutants and daily hospital visits for AD across different degrees of freedom.

Table S2 (see Supporting Information) provides estimated ERs and 95% CIs using the two-pollutant GAM models. Controlling for a second air pollutant did not change the direction of the significant association in the original one-pollutant model. However, the estimated ERs became much smaller after adding another pollutant into the original one-pollutant model.

Discussion

Our findings indicated that acute exposure to $\text{PM}_{2.5}$, PM_{10} , SO_2 , NO_2 and O_3 was associated with increased daily hospital visits for AD, confirming the main hypothesis that ambient air

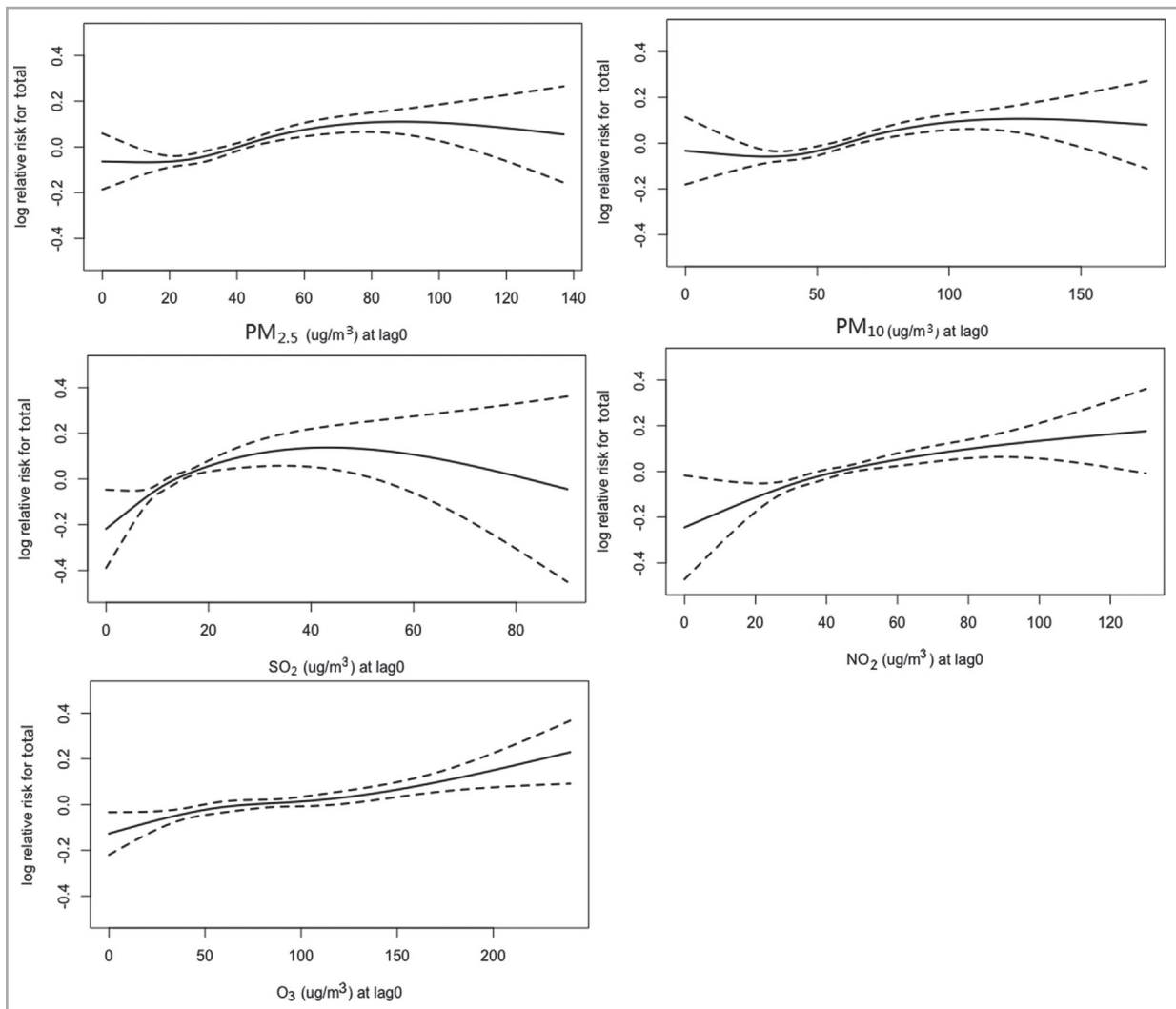


Figure 3 Dose–response curves for different air pollutants in Guangzhou, China, from 19 January 2013 to 31 December 2017. PM_{2.5}, particulate matter < 2.5 µm in aerodynamic diameter; PM₁₀, particulate matter < 10 µm in aerodynamic diameter; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; O₃, ozone.

pollution posed an acute risk on AD hospital visits after controlling for meteorological factors (ambient temperature and humidity). This is consistent with previous time series studies.^{7,8,17} All pollutants had the strongest effects on hospital visits associated with AD on the day of exposure (lag0), which was consistent with previous time series studies in Asia.^{7–11,17} However, the estimated ER of a single pollutant became much smaller after control for another air pollutant, which might be due to the high correlation between the air pollution values. In particular, the effects of SO₂ were no longer significant in two-pollutant models, a finding consistent with previous studies and indicating no independent effect of SO₂ on AD hospital admission.^{8,10}

This study found relatively higher ERs than other Asian time series studies, which might be due to the large forestry coverage of our study site,²⁶ leading to higher allergen exposure and lower wind speeds. However, there could be other

residual confounders that need to be further investigated.^{7–11,17} While studies in Beijing suggested a potential effect modification by ambient temperature, their findings are not consistent with findings from studies in Chengdu and Shanghai,^{7–10} both of which had similar temperatures. However, the study from Chengdu reported much higher effects than the Shanghai study (Table S3; see Supporting Information).^{9,10} Therefore, we support the evidence provided by studies from Korea reporting that weather type, rather than temperature itself, is an effect modifier of the association between air pollution and AD symptoms.^{7–10,17}

Our study showed that season and age modified the short-term association between air pollution and hospital visits for AD, with stronger effects in the cool season and among children. This finding supports our subhypotheses that (i) the cool season shows a stronger effect of air pollution on AD hospital visits than the warm season; and (ii) children are

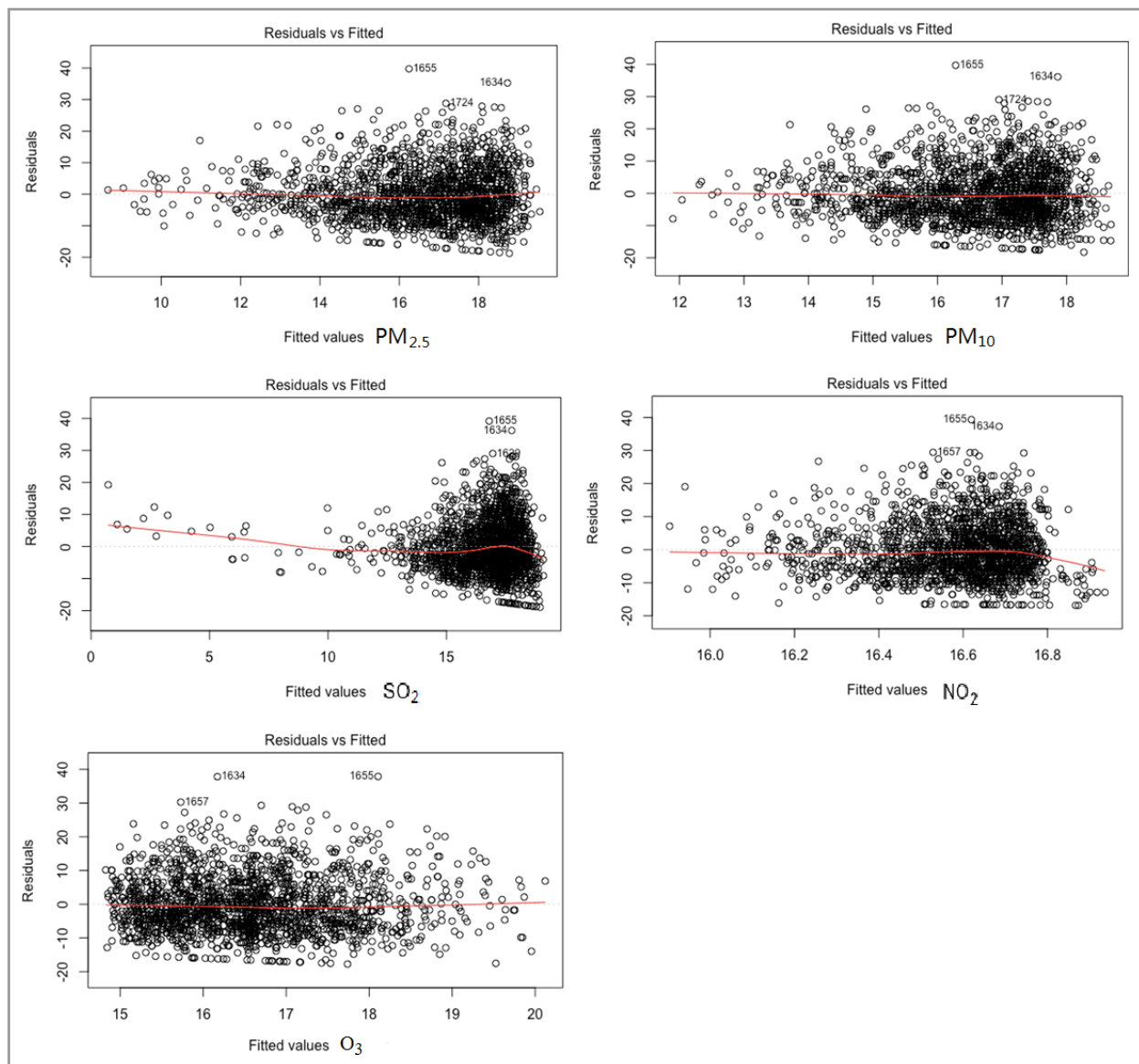


Figure 4 Residual plots of associations between air pollutants and daily hospital visits for atopic dermatitis in Guangzhou, China, from 19 January 2013 to 31 December 2017. PM_{2.5}, particulate matter < 2.5 µm in aerodynamic diameter; PM₁₀, particulate matter < 10 µm in aerodynamic diameter; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; O₃, ozone.

more vulnerable to the acute effect of air pollution on AD hospital visits than adults. These results are consistent with previous studies.^{7,17} Because AD occurs more frequently in children and during the cool season, and we had only 4 years' worth of data from one city, we may not have collected enough data for an analysis of adults and during the warm season. This could partially explain our large 95% CIs for adults and the warm season (Figure 5). The 95% CIs for adults and warm season overlapped with those for children and the cool season, indicating statistically insignificant modifications, which were further confirmed by our between-group difference analyses. However, the patterns of stronger effects among children and in the cool season were consistent across different air pollutants. For example, the effects for all air pollutants in the cool season were

approximately 1.7–3.0 times higher than in the warm season. This seasonality could be explained by the subtropical weather in Guangzhou: in the warm season, the humid weather moisturized skin and eased AD symptoms; in the cool season, the dry weather further aggravated AD symptoms.²⁷ Although inconsistent results have been reported by one study in Beijing,⁸ this discrepancy in findings might be explained by residual confounders that were subject to change of season and that they were unable to control for, such as weather type (cloud cover and wind speed) and ultraviolet radiation.^{10,17,28} Similarly, the effects of PM_{2.5}, PM₁₀, NO₂ and O₃ among children were approximately 1.3–1.8 times higher than among adults, which may be due to the fact that children have thinner stratum corneum than adults. Although children and adults may be

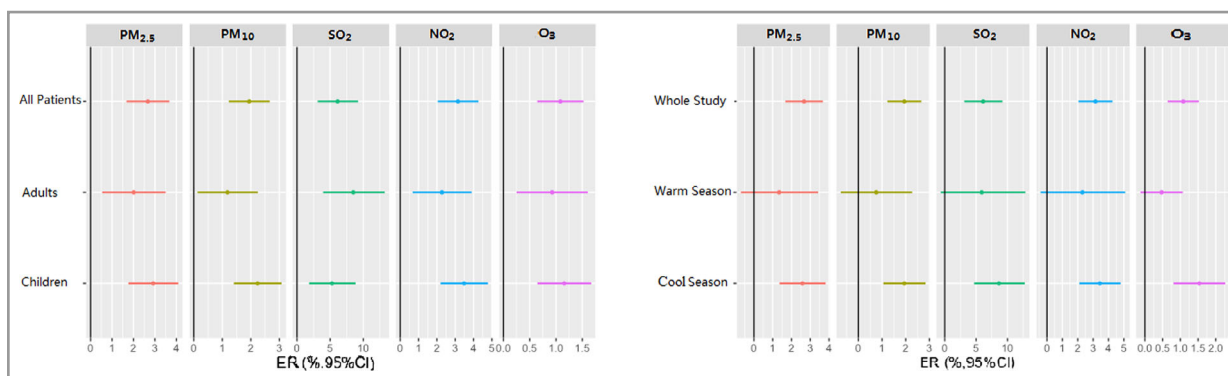


Figure 5 Excess risks (ERs; %) and 95% confidence intervals (CIs) for atopic dermatitis per $10 \mu\text{g m}^{-3}$ increase in air pollutant concentrations, stratified by age (left) and season (right), using lag0, in Guangzhou, China, from 19 January 2013 to 31 December 2017. PM_{2.5}, particulate matter < 2.5 μm in aerodynamic diameter; PM₁₀, particulate matter < 10 μm in aerodynamic diameter; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; O₃, ozone.

exposed to the same level of air pollution, more air pollutants were able to penetrate children's skin. Children also have immature immune systems, leaving them more vulnerable to air pollution exposure.¹² However, the effect of SO₂ in children was relatively lower than in adults, which could be explained by the high correlation between SO₂ and other air pollutants. Therefore, the effects of other air pollutants may mask the effect of SO₂ in our study.

In addition, our study observed a higher effect of O₃ in the cool season than in warm season, although the concentration of O₃ was lower during the cool season. Similar results have been reported in previous study.²⁹ The underlying reason might be that the residents in subtropical Guangzhou tend to have increased outdoor activities on cool days and hence were exposed to more ambient O₃ in the cool season. It is also possible that the correlation with other air pollutants had stronger effects in the cool season with higher concentration levels (Table 2).

There were several limitations to our study. There may have been some prescheduled hospital visits, which could have affected our analysis of the acute effects of air pollution on AD. However, our clinical experience suggested that the number of prescheduled visits was very low and thus the effect on the analysis results would have been negligible.^{30,31} The number of visits for AD did not strictly follow the trend of ambient air pollution concentrations, which may be caused by other AD risk factors that are stronger than air pollution, such as allergens (Figure S1; see Supporting Information).^{7,8,10,27,32} Misclassification of personal exposure and AD cases may have been introduced by our study design owing to the lack of personal exposure data.³³ Misdiagnosis may have been present as there are other diseases that share symptoms with AD, such as eczema and pruritus, which may have led to risk estimates that were lower than reality.^{34,35} The underreporting of AD cases is also likely as individuals with a mild form of AD may choose home remedies instead of seeking medical attention, leading to an underestimation of the association. In addition, we were unable to explain the cluster nature of data by including recurrent cases.

In conclusion, the short-term association between ambient air pollution and AD hospital visits was observed in Guangzhou, China. Children were more vulnerable than adults to the effect and stronger effects were observed in the cooler season. These findings could only be generalized to a city with similar population, social and environmental settings.

References

- 1 Rerksnimitr P, Otsuka A, Nakashima C *et al.* The etiopathogenesis of atopic dermatitis: barrier disruption, immunological derangement, and pruritus. *Inflamm Regen* 2017; **37**:14.
- 2 Silverberg JI. Atopic dermatitis epidemiology: moving beyond cross-sectional studies. *Br J Dermatol* 2019; **181**:883–4.
- 3 Lagrelus M, Wahlgren C-F, Matura M *et al.* Atopic dermatitis at preschool age and contact allergy in adolescence: a population-based cohort study. *Br J Dermatol* 2019; **180**:782–9.
- 4 Tsakok T, Woolf R, Weidinger CHSS *et al.* Atopic dermatitis: the skin barrier and beyond. *Br J Dermatol* 2019; **180**:464–74.
- 5 McAleer MA, Jakasa I, Hurault G *et al.* Systemic and stratum corneum biomarkers of severity in infant atopic dermatitis include markers of innate and T helper cell-related immunity and angiogenesis. *Br J Dermatol* 2019; **180**:586–96.
- 6 Egeberg A, Griffiths CEM, Williams HC *et al.* Clinical characteristics, symptoms and burden of psoriasis and atopic dermatitis in adults. *Br J Dermatol* 2020; **183**:128–38.
- 7 Wang XW, Tian YH, Cao YY *et al.* Association between fine particulate air pollution and outpatient visits for eczema in Beijing, China: a time-series analysis. *Biomed Environ Sci* 2019; **32**:624–7.
- 8 Guo Q, Xiong X, Liang F *et al.* The interactive effects between air pollution and meteorological factors on the hospital outpatient visits for atopic dermatitis in Beijing, China: a time-series analysis. *J Eur Acad Dermatol Venereol* 2019; **33**:2362–70.
- 9 Li Q, Yang Y, Chen R *et al.* Ambient air pollution, meteorological factors and outpatient visits for eczema in Shanghai, China: a time-series analysis. *Int J Environ Res Public Health* 2016; **13**:1106.
- 10 Li A, Fan L, Xie L *et al.* Associations between air pollution, climate factors and outpatient visits for eczema in West China Hospital, Chengdu, south-western China: a time series analysis. *J Eur Acad Dermatol Venereol* 2018; **32**:486–94.

- 11 Kim YM, Kim J, Han Y *et al.* Short-term effects of weather and air pollution on atopic dermatitis symptoms in children: a panel study in Korea. *PLoS One* 2017; **12**:e0175229.
- 12 Simon AK, Hollander GA, McMichael A. Evolution of the immune system in humans from infancy to old age. *Proc Biol Sci* 2015; **282**:20143085.
- 13 Han C, Lim Y-H, Yorifuji T *et al.* Air quality management policy and reduced mortality rates in Seoul Metropolitan Area: a quasi-experimental study. *Environ Int* 2018; **121**:600–9.
- 14 Lee H, Myung W, Cheong H-K *et al.* Ambient air pollution exposure and risk of migraine: synergistic effect with high temperature. *Environ Int* 2018; **121**:383–91.
- 15 Noh SR, Kim JS, Kim EH *et al.* Spectrum of susceptibility to air quality and weather in individual children with atopic dermatitis. *Pediatr Allergy Immunol* 2019; **30**:179–87.
- 16 Lin H, Tao J, Qian Z *et al.* Shipping pollution emission associated with increased cardiovascular mortality: a time series study in Guangzhou, China. *Environ Pollut* 2018; **241**:862–8.
- 17 Kim YM, Kim J, Jung K *et al.* The effects of particulate matter on atopic dermatitis symptoms are influenced by weather type: application of spatial synoptic classification (SSC). *Int J Hyg Environ Health* 2018; **221**:823–9.
- 18 Wang X, Qian Z, Wang X *et al.* Estimating the acute effects of fine and coarse particle pollution on stroke mortality of in six Chinese subtropical cities. *Environ Pollut* 2018; **239**:812–7.
- 19 Zhang L, Yang Y, Li Y *et al.* Short-term and long-term effects of PM_{2.5} on acute nasopharyngitis in 10 communities of Guangdong, China. *Sci Total Environ* 2019; **688**:136–42.
- 20 Qi J, Ruan Z, Qian ZM *et al.* Potential gains in life expectancy by attaining daily ambient fine particulate matter pollution standards in mainland China: a modeling study based on nationwide data. *PLoS Medicine* 2020; **17**:e1003027.
- 21 Song J, Lu J, Wang E *et al.* Short-term effects of ambient temperature on the risk of premature rupture of membranes in Xinxiang, China: a time-series analysis. *Sci Total Environ* 2019; **689**:1329–35.
- 22 Zhao Q, Li S, Coelho M *et al.* The association between heatwaves and risk of hospitalization in Brazil: a nationwide time series study between 2000 and 2015. *PLoS Medicine* 2019; **16**:e1002753.
- 23 Tian Y, Liu H, Wu Y *et al.* Ambient particulate matter pollution and adult hospital admissions for pneumonia in urban China: a national time series analysis for 2014 through 2017. *PLoS Medicine* 2019; **16**:e1003010.
- 24 Liu WY, Yu ZB, Qiu HY *et al.* Association between ambient air pollutants and preterm birth in Ningbo, China: a time-series study. *BMC Pediatr* 2018; **18**:305.
- 25 Lin H, Guo Y, Zheng Y *et al.* Long-term effects of ambient PM_{2.5} on hypertension and blood pressure and attributable risk among older Chinese adults. *Hypertension* 2017; **69**:806–12.
- 26 Li L, Qian J, Ou CQ *et al.* Spatial and temporal analysis of Air Pollution Index and its timescale-dependent relationship with meteorological factors in Guangzhou, China, 2001–2011. *Environ Pollut* 2014; **190**:75–81.
- 27 Kantor R, Silverberg JL. Environmental risk factors and their role in the management of atopic dermatitis. *Expert Rev Clin Immunol* 2017; **13**:15–26.
- 28 Puri P, Nandar SK, Kathuria S *et al.* Effects of air pollution on the skin: a review. *Indian J Dermatol Venereol Leprol* 2017; **83**:415–23.
- 29 Liu T, Li TT, Zhang YH *et al.* The short-term effect of ambient ozone on mortality is modified by temperature in Guangzhou, China. *Atmos Environ* 2013; **76**:65–7.
- 30 Bai L, Su X, Zhao D *et al.* Exposure to traffic-related air pollution and acute bronchitis in children: season and age as modifiers. *J Epidemiol Community Health* 2018; **72**:426–33.
- 31 Eckert L, Gupta S, Gadkari A *et al.* Burden of illness in adults with atopic dermatitis: analysis of National Health and Wellness Survey data from France, Germany, Italy, Spain, and the United Kingdom. *J Am Acad Dermatol* 2019; **81**:187–95.
- 32 Lin Z, Niu Y, Jiang Y *et al.* Protective effects of dietary fish-oil supplementation on skin inflammatory and oxidative stress biomarkers induced by fine particulate air pollution: a pilot randomised, double-blind, placebo-controlled trial. *Br J Dermatol* 2021; **184**:261–9.
- 33 Zhao Q, Li S, Coelho MdSZS *et al.* Ambient heat and hospitalisation for COPD in Brazil: a nationwide case-crossover study. *Thorax* 2019; **74**:1031–6.
- 34 Mancebo SE, Wang SQ. Recognizing the impact of ambient air pollution on skin health. *J Eur Acad Dermatol Venereol* 2015; **29**:2326–32.
- 35 Nakamura T, Haider S, Colicino S *et al.* Different definitions of atopic dermatitis: impact on prevalence estimates and associated risk factors. *Br J Dermatol* 2019; **181**:1272–9.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Figure S1 Proposed mechanisms of ambient air pollutants contributing to hospital visits associated with atopic dermatitis (conceptual model).

Table S1 Excess risks (%) and 95% confidence intervals for atopic dermatitis per 10 $\mu\text{g m}^{-3}$ increase in air pollutant concentrations for different degrees of freedom, using lag0, in Guangzhou, China, from 19 January 2013 to 31 December 2017.

Table S2 Excess risks (%) and 95% confidence intervals for daily hospital visits for atopic dermatitis in two-pollutant models, using lag0, in Guangzhou, China, from 19 January 2013 to 31 December 2017.

Table S3 A comparison between the results of our study and the results of related studies in China.

Powerpoint S1 Journal Club Slide Set.

Video S1 Author video.