

# Temporal cross-correlations between air pollutants and outpatient visits for respiratory and circulatory system diseases in Fuzhou, China

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## Research article

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# Abstract

**Background:** Previous studies have suggested that there is an association between air pollutants and circulatory and respiratory diseases, but relatively few have analyzed the association between air pollutants and outpatient visits considering mortality, hospitalization rates, etc., especially areas with relatively good air quality. Therefore, we conducted this study to research the association between air pollutants and outpatient visits in Fuzhou, China.

**Methods:** We used a generalized linear Poisson model to study the association between air pollution and outpatient visits for respiratory and circulatory diseases during 2016-2018 in Fuzhou, China.

**Results:** In the single pollutant model, nitrogen dioxide (NO<sub>2</sub>) had a significant effect. For lag day 0 to lag day 5, the effect decreased with every 10 µg/L increase in NO<sub>2</sub>. Daily maximum 8-h mean ozone (8-h O<sub>3</sub>) and upper respiratory outpatient visits were positively associated during the cold period [lag2, excess risk (ER) (95% confidence interval (CI)): 1.68% (0.44%-2.94%)], while 8-h O<sub>3</sub> and respiratory disease were positively associated during the warm period [lag5, ER (95% CI): 1.10% (0.11%-2.10%) and lag4, ER (95% CI): 1.02% (0.032%-2.02%)]. Similarly, particulate matter (PM) with an average aerodynamic diameter of less than 10 µm (PM<sub>10</sub>) and lower respiratory diseases were positively associated during the warm period [lag0, ER (95% CI): 1.68% (0.44%-2.94%)]. When the concentration of 8-h O<sub>3</sub> was higher than 100 µg/L, there was a positive effect on circulatory [lag5, ER (95% CI): 2.83% (0.65%-5.06%)], respiratory [lag5, ER (95% CI): 2.47% (0.85%-4.11%)] and upper respiratory [lag5, ER (95% CI): 3.06% (1.38%-4.77%)] outpatient visits. The variation in 8-h O<sub>3</sub> changed slightly when we adjusted for the other air pollutants, and after adjusting for 8-h O<sub>3</sub>, the ERs of the other air pollutants changed slightly. After adjusting for PM with an average aerodynamic diameter of less than 2.5 µm (PM<sub>2.5</sub>), the ERs of the other air pollutants increased, and after adjusting for NO<sub>2</sub>, the ER of PM decreased.

**Conclusion:** Exposure to ambient NO<sub>2</sub>, O<sub>3</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> was associated with an increase in respiratory and circulatory system-related outpatient visits in Fuzhou, China.

## Background

Ambient air pollution is on the rise, with the most marked increases in rapidly developing and industrializing low-income and middle-income countries [1]. As the largest developing country, China has developed increasingly serious air quality problems, and air pollution issues are increasingly prominent. However, few Chinese cities have established citywide morbidity reporting systems, and there are few studies of China's coastal area [2, 3]. Data revealing the association between air pollution and human health are limited in China, and the lack of fine particulate matter (PM<sub>2.5</sub>) and ozone (O<sub>3</sub>) data from most Chinese cities further hinders the value of such studies [2]. According to the World Health Organization's (WHO's) air quality standards, the acceptable daily average concentrations of PM<sub>2.5</sub> and PM<sub>10</sub> are 25

$\mu\text{g}/\text{m}^3$  and  $50 \mu\text{g}/\text{m}^3$ , respectively, and the 8-hour average concentration of  $\text{O}_3$  is  $100 \mu\text{g}/\text{m}^3$ [4]. In China, even areas with relatively good air quality may not meet the WHO's air quality standard.

Previous studies have shown that air pollution and outpatient visits are likely associated with respiratory and circulatory diseases [5, 6]. High pollutant concentrations can even increase the daily cardiovascular/respiratory death rates [7]. For example,  $\text{NO}_2$  may cause lung cancer [8], particulate matter (PM) has been associated with increased blood pressure (BP), and a certain concentration of ozone has been associated with decreased BP [9]. There is an association between  $\text{PM}_{2.5}$  and inflammation [10].  $\text{PM}_{2.5}$  can also increase the incidence of various respiratory and circulatory diseases [11, 12]. Even low air pollution concentrations can increase the risk of emergency department visits [13]. One study in an area with a low level of air pollution found that interquartile range (IQR) increases in  $\text{PM}_{2.5}$ ,  $\text{PM}_{10}$ ,  $\text{NO}_2$  and  $\text{O}_3$  were related to increases in outpatient visits for respiratory conditions [5]. A study that lasted approximately seven years and considered over 4 million emergency department visits in 31 hospitals showed an association between cardiovascular disease and levels of ambient pollutants [14]. Another study conducted over 17 years in Canada reported that ozone is highly associated with circulatory hospitalizations [15]. Some studies have suggested that low-level PM exposure could cause an increased excess risk (ER) of circulatory outpatient visits [11, 16]. Overall, even if the air quality is good in some regions, the effects of air pollution cannot be ignored.

Similar studies may obtain different outcomes because of differences in pollution concentrations and components and different population age structures and sensitivities among different regions [3]. In particular, regarding the concentration of air pollutants, the association between air pollution and health effects in areas with poor air quality was lower than that in areas with good air quality [2, 17]. It is inaccurate to describe the effects of air pollutants by comparisons with analyzes of data from other regions. Thus, research on the association between air pollutants and outpatient visits is necessary to understand the effects of local air pollution.

Modeling is particularly important in such studies. A single air pollutant model is not sufficient; comprehensive air pollutant models that consider synergistic effects are essential for studying the association between air pollutants and outpatient visits [18]. We conducted this study to analyze the associations between air pollutants and outpatient visits in Fuzhou with a comprehensive air pollutant model that considered the synergistic effects of different air pollutants; a total single air pollutant model, a seasonal model (examining the cold season and warm season) and a double pollutant model were constructed.

## Methods

### Data collection

Our daily air pollution monitoring data were based on 3-year data collection from 1 January 2016 to 31 December 2018 from seven air pollution monitoring stations of the Fuzhou Environmental Monitoring

Center Station, and daily meteorological monitoring data were collected through daily monitoring by the Fuzhou Meteorological Bureau, which is part of the nationwide network of monitoring stations and strictly implements relevant national technical requirements. The indicators of air pollution included nitrogen dioxide (NO<sub>2</sub>), daily maximum 8-h mean ozone (8-h O<sub>3</sub>), PM with a particle size less than 10 microns (PM<sub>10</sub>) and fine PM (PM<sub>2.5</sub>). The meteorological indicators included air pressure (AP), relative humidity (RH) and temperature (T). Values of 8-h O<sub>3</sub>, PM<sub>10</sub> and PM<sub>2.5</sub> were evaluated on the basis of the WHO air quality standard (100, 50 and 25 µg/m<sup>3</sup>, respectively), and NO<sub>2</sub> was evaluated on the basis of the China class I air quality standard (80 µg/m<sup>3</sup>). The daily outpatient visits of Jianxin Hospital and Kongjun Hospital were collected by the Fuzhou Center for Disease Control and Prevention, which has been part of the Fuzhou health monitoring network for 3 consecutive years and was subject to strict quality control according to requirements. We identified diseases according to their International Classification of Diseases, 10<sup>th</sup> edition (ICD-10) codes (J00-J99 for respiratory diseases and I00-I99 for circulatory diseases). Among the J00-J99 codes, J00-J06 and J30-J39 represent upper respiratory diseases, and J20-J22, J40-J47, and J85-J86 represent lower respiratory diseases.

In the analysis of the association between outpatient visits and air pollutants, there were meteorological factors and natural fluctuations in daily events over the course of a week that we needed to account for. Ethics approval and consent to participate were not needed for the present study since no individual-level data were used (the study only used publicly available secondary data).

## Statistical analysis

In this study, a generalized linear model (GLM) was used to analyze the association between outpatient visits and the studied air pollutants. The GLM with a time-series regression analysis was based on a Poisson distribution. We introduced meteorological parameters, including T (°C) and RH (%). Because the relationship between meteorology and health is generally nonlinear, we used a natural smoothing spline function to control for this nonlinear hybrid effect. We used 3 degrees of freedom for T and RH [18-20]. The natural spline (ns) function of date was also used in the GLM to address nonlinear trends, sequence correlations and the number of events per day on the time axis. The day of the week (DOW) was considered in this model to control for the natural fluctuation trends over a week. The degrees of freedom (df) for date were 7 df per year [21, 22] {Li, 2015 #64; Chai, 2019 #66; Bhaskaran, 2013 #67}. The model is as follows [23, 24]:

**See formula 1 in the supplementary files.**

where  $E(Y_t)$  is the expected value of the number of outpatient visits on day  $t$ ;  $Z_t$  is the pollutant concentration on day  $t$ ;  $\beta$  is the exposure-response coefficient;  $ns()$  is the natural smoothing spline function;  $df$  is the degrees of freedom;  $time$  is the calendar time variation;  $DOW$  is the weekly variation; and  $X_t$  is the meteorological factor.

The study analyzed the ER of outpatient visits associated with air pollutants and included a total single air pollutant model, seasonal model (cold period and warm season) and exceeding 100  $\mu\text{g}/\text{m}^3$  of ozone mode, double pollutant model. The double air pollutant model considered data from lag0. The seasonal model was divided into a cool period and warm period according to the monthly mean temperature. The months in which the monthly mean temperature exceeded 20°C were considered the warm period (April-October). Otherwise, the months were considered the cool period (November-March of the following year). The ozone model exceeding 100  $\mu\text{g}/\text{m}^3$  did not introduce the ns function of date and DOW because of discontinuity. The model is as follows:

**See formula 2 in the supplementary files.**

where  $E(Y_t)$  is the expected value of the number of outpatient visits on day  $t$ ;  $Z_t$  is the pollutant concentration on day  $t$ ;  $\beta$  is the exposure-response coefficient;  $ns()$  is the natural smoothing spline function; and  $df$  is the degrees of freedom. We also conducted a Wilcoxon paired test to find the significance of the relationship in different seasons. The mgcv package of R 3.5.1 statistical software was used for calculating and painting.

## Results

### Descriptive analyses

Table 1 shows that during the study, the mean pollutant concentrations were 27.38  $\mu\text{g}/\text{m}^3$  for  $\text{NO}_2$ , 89.60  $\mu\text{g}/\text{m}^3$  for daily 8-h  $\text{O}_3$ , 26.07  $\mu\text{g}/\text{m}^3$  for  $\text{PM}_{2.5}$ , and 49.68  $\mu\text{g}/\text{m}^3$  for  $\text{PM}_{10}$ . During the study, the 8-h  $\text{O}_3$  concentration exceeded 100  $\mu\text{g}/\text{m}^3$  for a total of 390 days, the  $\text{NO}_2$  concentration exceeded 80  $\mu\text{g}/\text{m}^3$  for a total of 0 days, the  $\text{PM}_{2.5}$  concentration exceeded 25  $\mu\text{g}/\text{m}^3$  for a total of 509 days, and the  $\text{PM}_{10}$  concentration exceeded 50  $\mu\text{g}/\text{m}^3$  for a total of 478 days. The mean daily average T, RH and AP were 21.54 °C, 72% and 1010 hpa, respectively.

### Association between air pollution and meteorological factors

Fig. 1A shows that except for temperature and  $\text{PM}_{10}$ , meteorological factors were significantly correlated with air pollutants. RH was positively correlated with  $\text{NO}_2$  and negatively correlated with 8-h  $\text{O}_3$ ,  $\text{PM}_{2.5}$  and  $\text{PM}_{10}$ . T was positively correlated with 8-h  $\text{O}_3$  and negatively correlated with  $\text{NO}_2$ ,  $\text{PM}_{2.5}$  and  $\text{PM}_{10}$ . AP was positively correlated with  $\text{PM}_{10}$ ,  $\text{NO}_2$  and  $\text{PM}_{2.5}$  and negatively correlated with 8-h  $\text{O}_3$ .

### Time series distribution of air pollutants and outpatient visits

Fig. 2A shows that  $\text{NO}_2$ ,  $\text{PM}_{10}$  and  $\text{PM}_{2.5}$  had higher concentrations during the cold season than during the warm season, but 8-h  $\text{O}_3$  had a higher concentration during the warm season than during the cold season. Fig. 2B shows that respiratory diseases, including upper and lower respiratory diseases, resulted in more outpatient visits during the cold season than during the warm season.

## Association between air pollutants and outpatient visits

In Fig. 3A, the single air pollutant model shows that NO<sub>2</sub> had a significant effect on the ER of total respiratory, lower respiratory, upper respiratory and circulatory diseases. There was a single-day lag effect that was most obvious at lag0 and increased by 5.11% (95% CI: 3.31%-6.95%) for total respiratory visits, 6.04% (95% CI: 3.91%-8.21%) for upper respiratory visits, 3.23% (95% CI: 0.46%-6.08%) for lower respiratory visits, and 4.75% (95% CI: 6.81%-2.73%) for circulatory outpatient visits. The cumulative lag effect was the most obvious at lag0-5, increasing by 9.43% (95% CI: 6.31%-12.65%) for total respiratory disease, 10.96% (95% CI: 7.22%-14.84%) for upper respiratory disease, 7.69% (95% CI: 2.96%-12.64%) for lower respiratory disease, and 8.14% (95% CI: 4.74%-11.65%) for circulatory diseases.

As shown in Fig. 3B, after adjusting for the three other air pollutants, the ER of 8-h O<sub>3</sub> did not obviously change. NO<sub>2</sub>, after adjusting for PM<sub>2.5</sub> and PM<sub>10</sub>, increased greatly. Because of the possible collinearity of PM<sub>10</sub> and PM<sub>2.5</sub>, we did not introduce them into our model, but after adjusting for NO<sub>2</sub>, the ERs of PM<sub>10</sub> and PM<sub>2.5</sub> decreased.

Fig. 4A shows the association between the different air pollutants and outpatient visits during the cold and warm seasons. During the cold season, NO<sub>2</sub> appeared to have an obvious effect, but its effect was less than that during the warm season. Eight-hour O<sub>3</sub> had a significant impact on outpatient visits for upper respiratory diseases at lag2 during the cold season; the ER was 1.68% (2.94%-0.44%).

Fig. 5 shows that when the concentration of 8-h O<sub>3</sub> was higher than 100 µg/L, there was a positive effect on circulatory [lag5, ER (95% CI): 2.83% (0.65%-5.06%)], respiratory [lag5, ER (95% CI): 2.47% (0.85%-4.11%)] and upper respiratory [lag5, ER (95% CI): 3.06% (1.38%-4.77%)] outpatient visits.

## Discussion

In this study, NO<sub>2</sub> presented a more obvious effect than the other three air pollutants in Fuzhou. We explored the relationship between air pollutants and outpatient visits for different diseases and in different seasons. During the cold season, there were more outpatient visits for respiratory, upper respiratory and circulatory diseases in association with the effects of 8-h O<sub>3</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> than during the warm season, but during the warm season, there were more outpatient visits for lower respiratory diseases in association with those three air pollutants than there were during the cold season. In the double pollutant model, after adjusting for NO<sub>2</sub>, the effects of the other three air pollutants decreased. After adjusting for PM<sub>2.5</sub>, PM<sub>10</sub> showed a significant effect. After adjusting for the other three air pollutants, the ER of 8-h O<sub>3</sub> changed only slightly. Different air pollutants presented different effects because of different conditions.

Our study showed the association between meteorological factors and the air pollutants NO<sub>2</sub>, 8-h O<sub>3</sub>, PM<sub>10</sub> and PM<sub>2.5</sub>. We found that the action of AP, RH and T caused high concentrations of air pollutants. Other studies showed that meteorological factors had an effect on the concentrations of air pollutants,

similar to the findings of our study [25, 26]. RH is known to increase haze, possibly because RH is positively correlated with  $\text{NO}_2$ , which converts from the gas phase of  $\text{NO}_x$  to the particulate phase in relatively low-visibility conditions [27]. We did not find a positive association between PM and RH in the Spearman correlation model, but in the contour plot, the correlation between RH and  $\text{PM}_{10}$  and  $\text{PM}_{2.5}$  first increased and then decreased at a certain AP and T. The joint action of meteorological factors had seemingly obvious effects on PM.  $\text{O}_3$  had a positive association with T and a negative association with RH because sunshine might be the main promoter of  $\text{O}_3$ , as  $\text{O}_3$  is enhanced by photochemical factors, and RH can affect sunshine duration [28]. Meteorological factors can influence air pollution, thus impacting health. Therefore, meteorological factors were introduced into the GLM. The time series diagram shows that during the cold season, all the air pollutants except ozone had higher concentrations than during the warm season. This discrepancy is due to the negative association between T and air pollutants and the positive association between AP and air pollutants other than ozone. In addition to meteorological factors, emissions also increase pollutant concentrations [29]. During the cold season, people in Fuzhou do not keep warm with coal but usually light fires, leading to increased PM emissions. The time series diagram also shows that there were more outpatient visits for respiratory diseases, including upper and lower respiratory diseases, during the cold season than during the warm season, which may be different from the findings for other regions; for example, the spring dust storm season in Lanzhou may increase emergency room visits for respiratory diseases [30].

The GLM reflected different aspects, including the total situation, different seasons and double air pollutant model. Because of the significant effects of the different air pollutants, we conducted a comprehensive study to evaluate the ERs of  $\text{NO}_2$ ,  $\text{O}_3$ ,  $\text{PM}_{2.5}$  and  $\text{PM}_{10}$  [31, 32]. In the overall model, we found that  $\text{NO}_2$  had a more obvious effect than the other three air pollutants on the ER of outpatient visits, especially considering the cumulative lag effect. Some studies also found that  $\text{NO}_2$  was strongly associated with hospital admissions for both respiratory and cardiovascular diseases [33, 34]. In China, the Sixth National Population Census showed that coastal areas had become old-age societies, and a systematic review and meta-analysis reported that the effect of  $\text{NO}_2$  exhibited regional differences because of differences in the proportions of elderly people with increased susceptibility to  $\text{NO}_2$ , which may be the cause of the high ER associated with  $\text{NO}_2$  [35]. Even when air quality is not poor, the elderly may still be susceptible to air pollutants.

However, when we examined the results according to seasons, the effect of  $\text{NO}_2$  was less significant than that of the total situation, and the ER of  $\text{NO}_2$  was lower during the warm season than during the cold season; more specifically, it lost all significance during the warm season. In addition to T, the concentrations of air pollutants differed between the cold season and the warm season. During the cold season, the concentration of  $\text{NO}_2$  was  $33.11 \mu\text{g}/\text{m}^3$ , while during the warm season, it was  $23.32 \mu\text{g}/\text{m}^3$ . There is a dose-dependent relationship between pulmonary injuries and ambient  $\text{NO}_2$  [36], but for circulatory injuries, there is a lack of research. Interestingly,  $\text{NO}_2$ ,  $\text{O}_3$ ,  $\text{PM}_{2.5}$  and  $\text{PM}_{10}$  had similar results in terms of their influences on outpatient visits for upper and lower respiratory diseases. Generally,  $\text{PM}_{10}$

has a greater impact on the upper respiratory tract than on the lower respiratory tract, while  $PM_{2.5}$  and  $O_3$  exhibit the opposite effect. During the cold season, the increase in outpatient visits for upper respiratory disease was greater than that during the warm season, while the opposite results were observed for lower respiratory disease-related visits, except in the case of  $NO_2$ . Nitrogen dioxide, ozone and  $PM_{2.5}$  caused more ERs for upper respiratory-related outpatient visits than for lower respiratory-related outpatient visits during the cold period, but nitrogen dioxide, ozone,  $PM_{2.5}$  and  $PM_{10}$  caused more ERs for lower respiratory-related outpatient visits during the warm season. T and AP were 14.66 °C and 1016.65 hPa, respectively, during the cold season and 26.40°C and 1004.66 hPa, respectively, during the warm season. Some studies reported that low AP and warm Ts increased susceptibility to respiratory-related diseases [37, 38]. A study pointed out that a greater diurnal temperature range caused more outpatient visits for the common cold [39]. Similarly, greater temperature change affects the number of hospital admissions for chronic obstructive pulmonary disease [40]. Fuzhou often experiences a high diurnal temperature range during cold periods. However, PM and  $O_3$  had greater effects on upper respiratory-related outpatient visits during the cold season and greater effects on lower respiratory-related outpatient visits during the warm season, possibly because the depths of the respiratory tract that pollutants are able to reach are impacted by T and AP; however, this theory needs further study. Regarding circulatory diseases, in our study, we found that during the cold season, air pollutants increased the number of outpatient visits for circulatory diseases. Some studies presented similar outcomes [34, 41]. However, a study conducted over a 17-year period in Canada reported that 1-day lagged ozone had a greater association with the three examined circulatory hospitalization causes (ischemic heart disease, other heart disease and cerebrovascular disease) during the warm season than during the cold season [15]. A study in Hong Kong reported that PM and  $NO_2$  increased emergency hospital admissions during the warm season [42]. During our study, increased concentrations of PM and  $NO_2$  were observed during the cold season, but an increased concentration of  $O_3$  was not. In addition to the increased concentrations of air pollutants, heat waves and other extreme high-temperature events were more likely to occur on low-temperature days, which may cause more outpatient visits for circulatory diseases [43]. We found that during the warm season of high temperatures ( $> 30$  °C), pollutants cause greater damage to the cardiovascular system than when temperature are less than 30 °C. Studies have reported that under high temperature conditions, the risk of ozone-related cardiovascular death increases, and PM has a greater impact on the cardiovascular system; thus, temperature and pollutants may have a synergistic effect on cardiovascular disease [18, 46]. However, a study in low-pollution areas found that the effects of  $PM_{2.5}$  were more obvious during the cool season than during the warm season[5].

We also conducted analyses of ozone concentrations exceeding 100  $\mu g/m^3$  because ozone pollution is serious. The model with ozone exceeding 100  $\mu g/m^3$  did not introduce the ns function of date and DOW because of discontinuity. Ozone exceeded 100  $\mu g/m^3$  for a total of 390 days during the study period (total study period, 1096 days), and during the warm season, ozone exceeded 100  $\mu g/m^3$  for a total of 315 days. The warm season model showed that high ozone levels had a significant effect on respiratory outpatient visits at lag4 and lag5. The time at which the significant effect appeared was the same in the

warm period model and the model with ozone exceeding 100  $\mu\text{g}/\text{m}^3$ , but the predominant diseases were different. The difference may be due to the increased concentration of  $\text{O}_3$  in the 100  $\mu\text{g}/\text{m}^3$  ozone model [8-h  $\text{O}_3$  average (standard 8-h  $\text{O}_3$  concentration model): 126.36  $\mu\text{g}/\text{m}^3$  vs 8-h  $\text{O}_3$  average (the warm season average): 100.48  $\mu\text{g}/\text{m}^3$ ].

In the double model, at lag0, after adjusting for  $\text{PM}_{2.5}$ ,  $\text{NO}_2$  and 8-h  $\text{O}_3$  presented increased ERs. In contrast, after adjusting for  $\text{NO}_2$ , the three other pollutants, especially PM ( $\text{PM}_{2.5}$  and  $\text{PM}_{10}$ ), presented decreased ERs. There was a strong correlation between PM and  $\text{NO}_2$ . The ER of ozone did not fluctuate considerably after adjusting for the three other pollutants. The interaction between PM and  $\text{NO}_2$  was strong, and the effect of 8-h  $\text{O}_3$  was independent. Previous studies also found a strong correlation between PM and gaseous air pollution, with the exception of  $\text{O}_3$ , which did not change much after the other air pollutants were added to the model [6, 18]. Some mechanics studies noted that inflammation, oxidative stress, changes in systemic coagulation functioning and reduced cardiac autonomic control occurred after exposure to gaseous air pollutants and PM [44, 45], which may trigger respiratory and cardiovascular events as well as high concentrations of air pollutants, except 8-h  $\text{O}_3$ , during the same period (the cold season). These factors may cause high correlations among air pollutants. Therefore, it is difficult to evaluate the independent effects of PM or  $\text{NO}_2$  because of their high correlations [17].

There are several limitations. In coastal areas, ozone pollution is more serious than PM and  $\text{NO}_2$  pollution, but in this study,  $\text{NO}_2$  increased the number of outpatient visits. Eight-hour  $\text{O}_3$  and  $\text{NO}_2$  are related to photochemical smog, and they promote one another; it is possible that they exhibit joint action. However, we could not find obvious interactions in the double model; therefore, further research is required.  $\text{PM}_{2.5}$  increased the outpatient visit risk rate in many studies, even in areas with better air quality than Fuzhou, which may indicate that there are regional differences in the effect of  $\text{PM}_{2.5}$  exposure in China [47]. In our study, we did not observe a significant effect of  $\text{PM}_{2.5}$ . If we stratify the results by different ages and diseases, we may obtain significant outcomes. Overall, our study comprised a comprehensive analysis of the association between air pollutants and outpatient visits. In some comprehensive studies of large cohorts in other regions, even low exposure to air pollutants can have health effects [48, 49]. However, there is a lack of studies on the association between specific respiratory and circulatory diseases and different air pollutants. The effects observed in this study were short-term effects. Studies of long-term effects still need to be conducted in coastal areas in China.

## Conclusions

There was an association between air pollutants and respiratory and circulatory outpatient visits. During the cold season, the ER of  $\text{NO}_2$  was higher than that during the warm season for both respiratory- (both upper and lower) and circulatory-related outpatient visits. However, during the cold season, 8-h  $\text{O}_3$ ,  $\text{NO}_2$  and  $\text{PM}_{2.5}$  had greater ERs for upper respiratory-related outpatient visits than for lower respiratory-related

outpatient visits, and during the warm season, 8-h O<sub>3</sub>, NO<sub>2</sub>, PM<sub>10</sub> and PM<sub>2.5</sub> had greater ERs for lower respiratory-related outpatient visits. In the double air pollutant model, PM and NO<sub>2</sub> had high correlations.

## Declarations

### Ethics approval and consent to participate

We only collected the total number of outpatient visits, and the selection was not related to outpatients' personal privacy (i.e., not including personal name, gender, ethnicity, body weight, etc.), and the data belong to de-identification.

### Consent to publish

Not applicable.

### Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

### Competing interests

All authors declare that they have no competing interests.

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**Authors' Contributions:** YJ, CW, XZ and BL: study concept and design; YJ, XL, QZ, SJ, XZ: data collection and supervision; JC and YJ: drafting of the manuscript; JC, CW and SY: analysis and interpretation of data; XZ and BL: critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

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## Abbreviations

AP: air pressure; DOW: day of the week; 8-h O<sub>3</sub>: daily maximum 8-h mean ozone; ERs: excess risks; df: degrees of freedom; GLM: generalized linear model; ICD-10: 10th edition of the International Classification of Diseases; NO<sub>2</sub>: nitrogen dioxide; ns: natural spline; PM<sub>10</sub>: particulate matter with an aerodynamic diameter less than 10 µg<sup>-3</sup>; PM<sub>2.5</sub>: particulate matter with an aerodynamic diameter less than 2.5 µg<sup>-3</sup>; RH: relative humidity; T: temperature

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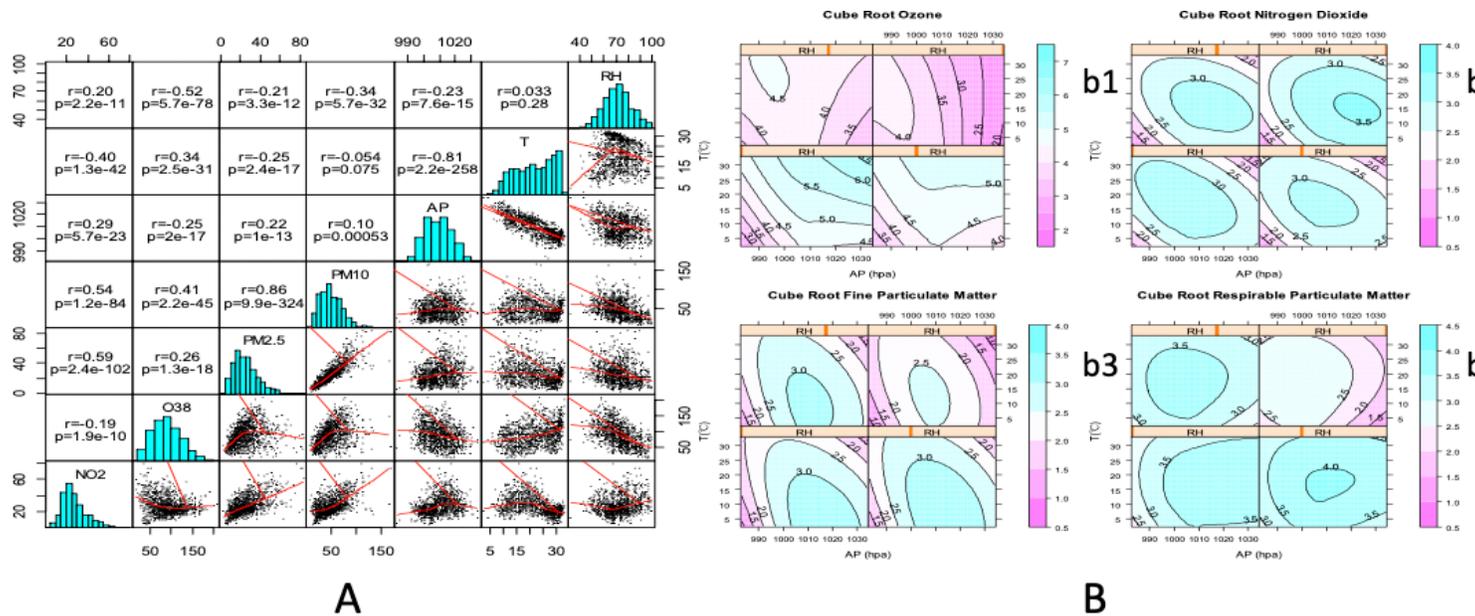
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## Table

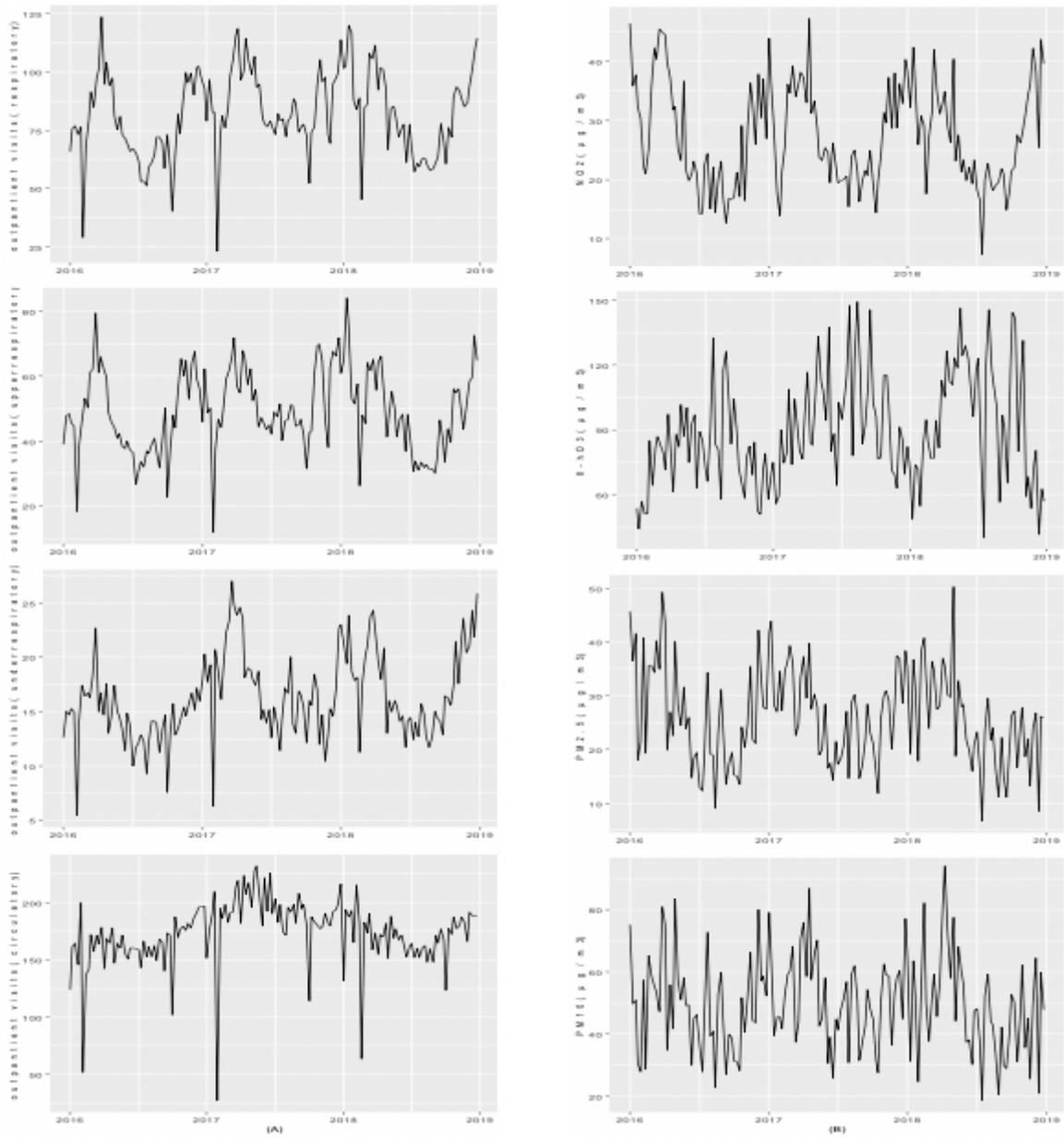
**Table 1** Statistical summary of daily air pollutants, meteorological factors and outpatient visits in Fujian, China, 2016-2018

## Figures



**Figure 1**

Spearman correlations (left) between air pollutants and meteorological factors from 2016 to 2018. (RH, relative humidity; T, temperature; AP, air pressure; PM10, respirable particulate matter; PM2.5, fine particulate matter; 8-h O3, daily maximum 8-h mean ozone; NO2, nitrogen dioxide).



**Figure 2**

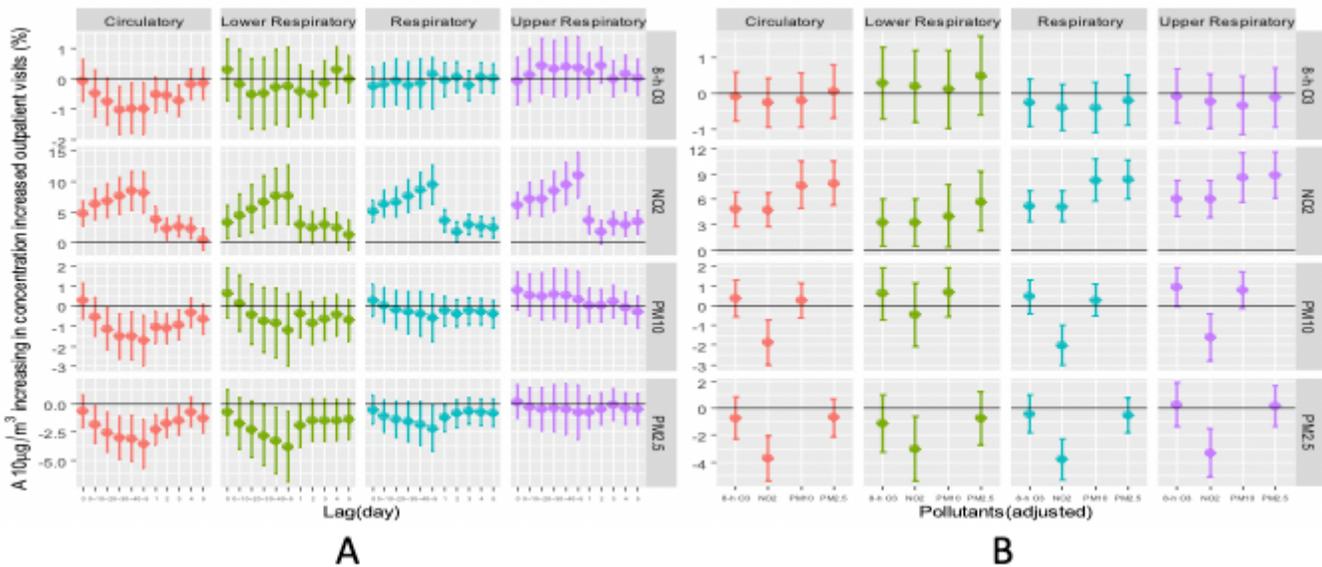
Time series graphs of weekly air pollutants (A) and outpatient visits (B) for respiratory and circulatory diseases

Variable	Mean ± SD	Minimum	Percentile			Maximum
			25th	50th	75th	
<b>Total</b>						
Respiratory disease	82±32	1	60	83	104	180
Upper respiratory disease	49±20	0	35	49	63	113
Lower respiratory disease	16±8	0	10	16	22	47
Circulatory disease	174±83	0	105	191	231	382
NO <sub>2</sub> (µg/m <sup>3</sup> )	27.38±11.18	3.83	19.55	25.14	33.14	79.57
8-h O <sub>3</sub> (µg/m <sup>3</sup> )	89.60±33.94	16.71	64.02	87.36	112.00	208.43
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	26.07±13.14	2.43	16.57	23.86	32.71	83.57
PM <sub>10</sub> (µg/m <sup>3</sup> )	49.68±22.62	7.43	33.33	46.49	63.89	167.57
Temperature (°C)	21.54±7.08	2.60	15.60	22.00	28.00	32.80
Relative humidity (%)	72±11	33	65	72	79	99
Air pressure (hpa)	1,010±8	983	1003	1009	1016	1034
<b>Cold season</b>						
Respiratory disease	91±34	1	70	96	114	166
Upper respiratory disease	55±22	0	43	56	70	106
Under respiratory disease	18±9	0	12	19	25	46
Circulatory disease	175±84	0	108	195	236	367
NO <sub>2</sub> (µg/m <sup>3</sup> )	33.11±11.55	10.43	24.57	31.72	41.34	79.57
8-h O <sub>3</sub> (µg/m <sup>3</sup> )	74.21±26.59	16.71	53.66	73.72	92.97	168.14
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	30.42±14.44	2.43	19.86	28.14	38.50	82.14
PM <sub>10</sub> (µg/m <sup>3</sup> )	52.28±23.48	7.43	33.72	50.79	68.54	134.14
Temperature (°C)	14.66±4.11	2.60	11.60	14.30	14.30	24.70
Relative humidity (%)	72±12	33	63	73	80	98
Air pressure (hpa)	1,017±6	1001	1013	1016	1021	1034
<b>Warm season</b>						
Respiratory disease	76±29	11	56	77	95	180
Upper respiratory disease	45±18	5	33	44	56	113
Under respiratory disease	15±8	0	10	15	20	47
Circulatory disease	173±81	13	103	189	229	382
	23.32±8.92	3.83	17.74	22.00	27.20	73.29

NO <sub>2</sub> (µg/m <sup>3</sup> )						
8-h O <sub>3</sub> (µg/m <sup>3</sup> )	100.48±34.39	30.00	75.04	99.24	124.14	208.43
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	22.99±11.17	4.86	15.14	21.00	28.86	83.57
PM <sub>10</sub> (µg/m <sup>3</sup> )	47.84±21.82	10.29	33.04	44.14	60.03	167.57
Temperature (°C)	26±4	14.50	23.53	27.10	27.10	32.80
Relative humidity (%)	72±11	41	65	72	79	99
Air pressure (hpa)	1,005±6	983	1001	1004	1008	1022

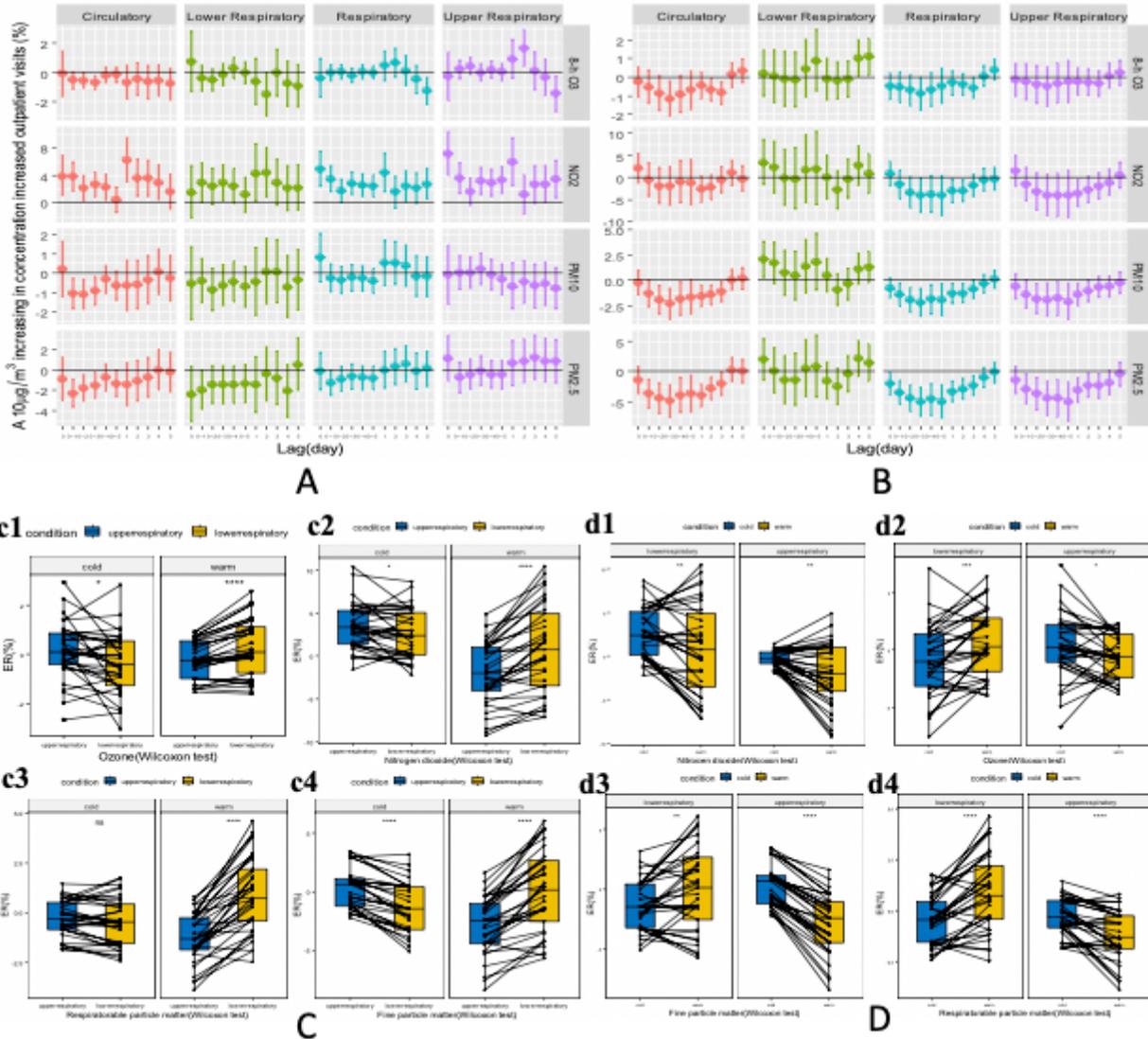
**O<sub>3</sub> concentrations exceeding 100 µg/m<sup>3</sup>**

Respiratory disease	82±30	12	61	84	102	163
Upper respiratory disease	49±19	7	36	47	62	103
Lower respiratory disease	17±8	0	11	17	23	47
Circulatory disease	181±81	18	115.5	194.5	238.75	382
NO <sub>2</sub> (µg/m <sup>3</sup> )	25.16±7.56	10.14	20.14	23.745	28.2825	56.14
8-h O <sub>3</sub> (µg/m <sup>3</sup> )	126.36±20.89	100.14	109.86	121.71	136.66	208.43
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	29.81±10.97	6.43	21.74	27.86	35.57	70.43
PM <sub>10</sub> (µg/m <sup>3</sup> )	59.81±19.55	15.29	45.895	57.43	70.86	164.14
Temperature (°C)	24.36±6.46	8.5	19.75	26	26	32.8
Relative humidity (%)	66±9	41	60	66	72	96
Air pressure (hpa)	1,007±7	992	1002	1006	1013	1031



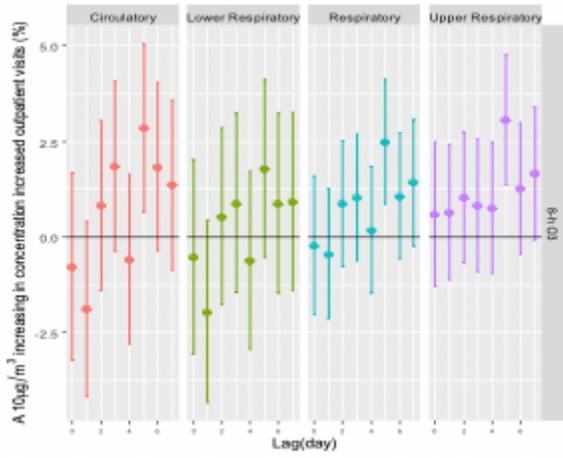
**Figure 3**

ERs of outpatient visits for total respiratory, lower respiratory, upper respiratory and circulatory diseases in the single air pollutant models (A) and double air pollutant models (B) (The ER (%) of the y-axis indicates that a 10  $\mu\text{g}/\text{m}^3$  increase in the concentration of air pollutants increases outpatient visits; "01, 02, 03, 04, 05" represent the cumulative lag effect, same as below). See also Tables S1 and S4.



**Figure 4**

ERs of outpatient visits for total respiratory, lower respiratory, upper respiratory and circulatory diseases in the cold period (A) and warm period (B). See also Tables S2 and S3. The Wilcoxon paired test of ERs between the upper respiratory and lower respiratory periods in different periods and between the cold period and warm period in the upper and lower respiratory periods (C) ( $p > 0.05$ : 'ns';  $0.01 < p < 0.05$ : '\*';  $0.001 < p < 0.01$ : '\*\*';  $0.0001 < p < 0.001$ : '\*\*\*';  $p < 0.0001$ : '\*\*\*\*')



**Figure 5**

The ERs of outpatient visits when the ozone concentration was over  $100 \mu\text{g}/\text{m}^3$ . See also Table S5.

## Supplementary Files

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