Temporal Cross-Correlations between air pollutants and outpatient visits for respiratory and circulatory system diseases in coastal area of China

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Research article

Keywords: Air pollution, coastal area, time-series analysis, season

Posted Date: October 18th, 2019

DOI: https://doi.org/10.21203/rs.2.16198/v1

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Version of Record: A version of this preprint was published on July 20th, 2020. See the published version at https://doi.org/10.1186/s12889-020-08915-y.
Abstract

Background Some previous studies have suggested that there is an association between air pollutants and circulatory and respiratory diseases. However, the association of air pollutants and outpatient visits considering mortality, hospitalization rates, etc. has been analyzed in relatively few studies.

Methods We used a generalized linear Poisson model was constructed to study the association between air pollution and outpatient visits for respiratory and circulatory diseases during 2016-2018 in coastal area of China.

Results In the single pollutant model, NO$_2$ had a significant effect. For lag day 0 to lag day 5, the effect decreased with every 10 µg/L increase in NO$_2$. O$_3$ and upper respiratory outpatient visits were positively associated in the cold period [lag2, ER (95%CI): 1.68% (0.44%-2.94%)], while O$_3$ and respiratory disease were positively associated in 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, PM$_{10}$ and lower respiratory diseases were positively associated in the warm period [lag0, ER (95%CI): 1.68% (0.44%-2.94%)]. When the concentration of O$_3$ 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 O$_3$ changed slightly when we adjusted for the other air pollutants, and after adjusting for O$_3$, the ERs of the other air pollutants changed slightly. After adjusting for PM$_{2.5}$, the ER of the other air pollutants increased, and after adjusting for NO$_2$, the ER of particulate matter (PM) decreased.

Conclusion Exposure to ambient NO$_2$, O$_3$, PM$_{2.5}$ and PM$_{10}$ was associated with an increase in respiratory and circulatory system outpatient visits in coastal area of 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, air quality in China has become increasingly serious, and air pollution issues are increasingly prominent. However, few Chinese cities have established city-wide morbidity reporting systems, and there are few studies in China's coastal area [2, 3]. Data revealing the association between air pollution and human health are limited in China, and the lack of PM$_{2.5}$ and O$_3$ 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$_{2.5}$ and PM$_{10}$ are 25 µg/m$^3$ and 50 µg/m$^3$, respectively, and the 8-hour average concentration of O$_3$ is 100 µg/m$^3$[4]. In China, even areas with relatively good air quality may not achieve 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]. For example, NO$_2$ may cause lung cancer development [7]. Particulate matter (PM) has been associated with increased blood pressure (BP), and a certain concentration of ozone has been associated with decreased BP [8]. There exists an association between PM$_{2.5}$ and inflammation [9]. PM$_{2.5}$ can increase the incidence of various respiratory and circulatory diseases [10,
Even low air pollution concentrations can increase the risk of emergency department visits [12]. One study in an area with a low level of air pollution found that interquartile range (IQR) increases in PM$_{2.5}$, PM$_{10}$, NO$_2$ and O$_3$ were related to increases in outpatient visits for respiratory conditions [5]. A study that lasted approximately seven years showed an association between cardiovascular disease and the levels of ambient pollutants considering over 4 million emergency department visits in 31 hospitals [13]. Another study conducted over 17 years in Canada reported that ozone is highly associated with circulatory hospitalizations [14]. Some studies have suggested that low-level PM exposure could cause an increased excess risk (ER) of circulatory outpatient visits [10, 15]. Overall, even if air quality is good in some regions, the effects of air pollution cannot be ignored.

Similar studies may obtain distinct outcomes because of different 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, 16]. It is inaccurate to describe the effects of air pollutants by analyzing 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 [17]. We conducted this study to analyze the associations between air pollutants and outpatient visits in China's coastal area with a comprehensive air pollutant model considering the synergistic effects of different air pollutants; a total single air pollutant model, seasonal model (cold period and warm season) and double pollutant model were constructed.

**Methods**

**Data collection**

We collected meteorological monitoring data and air pollution monitoring data from 1 January 2016 to 31 December 2018 from the Fuzhou Environmental Monitoring Center Station. The indicators of air pollution included nitrogen dioxide (NO$_2$), daily maximum 8-h mean ozone (8-h O$_3$ or O$_3$8), PM with particle size less than 10 microns (PM$_{10}$) and fine PM (PM$_{2.5}$). The meteorological indicators included air pressure (AP), relative humidity (RH) and temperature (T). Values of 8-h O$_3$, PM$_{10}$ and PM$_{2.5}$ were evaluated on the basis of the WHO air quality standard (100, 50 and 25 µg/m$^3$, respectively), and NO$_2$ was evaluated on the basis of the China class I air quality standard (80 µg/m$^3$). Outpatient visit data were obtained from Jianxin Hospital and Kongjun Hospital. We identified diseases according to their 10th edition of the International Classification of Diseases (ICD-10) codes (J00-J99 for respiratory diseases and I00-I99 for circulatory diseases). Among the J00-J99 codes, J00-J06 and J30-J39 represented upper respiratory diseases, and J20-J22, J40-J47, and J85-J86 represented 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 or consent to participate was not needed for the present study since no data on individual level was used (only the secondary data for public access).

**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 $T$ ($^\circ$C) and RH (%). Because the relationship between meteorology and health is generally nonlinear, we used a natural spline smoothing function to control for this nonlinear hybrid effect. We used 3 degrees of freedom for $T$ and RH\[17, 18\]. 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. Day of the week (DOW) was considered in this model to control for the natural fluctuation trends in a week. The degrees of freedom for date were 7 df per year\[19, 20\]\{Li, 2015 \#64;Chai, 2019 \#66;Bhaskaran, 2013 \#67\}. The model is as follows\[21, 22\]:

$$\log E(Y_t) = \beta Z_t + \text{ns}(\text{time}, 7 \ast 3) + \text{DOW} + \text{ns}(X_t, 3) + \text{intercept}$$

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 $\mu$g/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$^\circ$C were considered the warm period (April-October). Otherwise, the months were considered the cool period (November-March of the following year). The exceeding 100 $\mu$g/m$^3$ of ozone model did not introduce the ns function of date and DOW because of discontinuity. The model is as follows:

$$\log E(Y_t) = \beta Z_t + \text{ns}(X_t, 3) + \text{intercept}$$
where E(Yt) is the expected value of the number of outpatient visits on day t; Zt 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. We also conducted Wilcoxon paired test to find significance in different season.

**Results**

**Descriptive analyses**

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

**Association of air pollution and meteorological factors**

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

Fig. 1B shows that Contour plot considers each air pollutant and three meteorological factors (AP*T*RH). In the case of joint action by the three meteorological factors, a peak concentration appears in the contour plot of PM\(_{2.5}\), PM\(_{10}\) and NO\(_2\) at a certain RH. A suspicious peak appears in the O\(_3\) figure at 2/3 the maximum RH.

The peak represents the strongest correlation between the air pollutants and meteorological factors, leading to high concentrations of air pollutants at certain RHs. Among them, PM\(_{10}\) appeared to peak at 1/3 of the maximum RH (Fig. 1b4). In particular, NO\(_2\) appears to peak at the maximum RH. At a certain RH, the peak concentration occurred at approximately 15\( ^\circ \)C and 1010 hpa, except O\(_3\).

**The time series distribution of air pollutants and outpatient visits**
Fig. 2A shows that NO\textsubscript{2}, PM\textsubscript{10} and PM\textsubscript{2.5} had higher concentrations in the cold period than in the warm period, but O\textsubscript{3} had a higher concentration in the warm period than in the cold period. Fig. 2B presents that respiratory, including upper and lower respiratory, diseases resulted in more outpatient visits in the cold period than in the warm period.

**Association of air pollutants and outpatient visits**

At Fig.3A, single air pollutant model shows that NO\textsubscript{2} 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 is most obvious at lag0, increasing by 5.11\% (95\%CI: 3.31\%-6.95\%) for total respiratory, 6.04\% (95\%CI: 3.91\%-8.21\%) for upper respiratory 3.23\% (95\%CI: 0.46\%-6.08\%) for lower respiratory, and 4.75\% (95\%CI: 6.81\%-2.73\%) for circulatory outpatient visits. The cumulative lag effect is the most obvious at lag0-5, increasing by 9.43\% (95\%CI: 6.31\%-12.65\%) for total respiratory, 10.96\% (95\%CI: 7.22\%-14.84\%) for upper respiratory, 7.69\% (95\%CI: 2.96\%-12.64\%) for lower respiratory, and 8.14\% (95\%CI: 4.74\%-11.65\%) for circulatory diseases.

At Fig. 3B, after adjusting for the three other air pollutants, the ER of O\textsubscript{3} did not obviously change. NO\textsubscript{2}, after adjusting for PM\textsubscript{2.5} and PM\textsubscript{10}, increased greatly. Because of the possible collinearity of PM\textsubscript{10} and PM\textsubscript{2.5}, we did not introduce them into our model, but after adjusting for NO\textsubscript{2}, the ERs of PM\textsubscript{10} and PM\textsubscript{2.5} decreased.

Fig. 4A shows the association between the different air pollutants and outpatient visits in the cold and warm period. In cold period, NO\textsubscript{2} appeared to have an obvious effect, but its effect was less than that in warm period. O\textsubscript{3} had a significant impact on outpatient visits for upper respiratory diseases at lag2 in cold period; the ER was 1.68\% (2.94\%-0.44\%).

Fig. 4B shows the association between the different air pollutants and outpatient visits in the warm period. In warm period, NO\textsubscript{2} had no significant association with outpatient visits. O\textsubscript{3} had a significant effect on outpatient visits for respiratory conditions at lag4 (1.02\%, 95\%CI: 0.032\%-2.02\%) and lag5 (1.10\%, 95\%CI: 0.11\%-2.11\%), and PM\textsubscript{10} had a significant impact on outpatient visits for respiratory conditions at lag0 (2.05\%, CI: 0.27\%-3.86\%). Fig.4C and Fig.4D show that we conducted Wilcoxon paired test for lower and upper respiratory in different seasons to test significance.

Fig.5 shows that when the concentration of O\textsubscript{3} was higher than 100 \(\mu\text{g}/\text{L}\), 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\textsubscript{2} presented a more obvious effect than the other three air pollutants in coastal area. We explored outpatient visits for different diseases and in different seasons. In the cold period, there were more outpatient visits for respiratory, upper respiratory and circulatory diseases under the effects of O\textsubscript{3}, PM\textsubscript{2.5} and PM\textsubscript{10} than in the warm period, but in the warm period, there were more outpatient visits for lower respiratory diseases under that three air pollutants than in the cold period. In the double pollutant model, after adjusting for NO\textsubscript{2}, the effect of the other three air pollutants decreased. After adjusting for PM\textsubscript{2.5}, PM\textsubscript{10} expressed a significant effect. After adjusting for the other three air pollutants, the ER of O\textsubscript{3} 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\textsubscript{2}, O\textsubscript{3}, PM\textsubscript{10} and PM\textsubscript{2.5}. 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 our study [23, 24]. RH is known to increase haze, possibly because RH is positively correlated with NO\textsubscript{2}, which converts from the gas phase of NO\textsubscript{x} to the particulate phase in relatively low visibility conditions [25]. 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 PM\textsubscript{10} and PM\textsubscript{2.5} first increased and then decreased between at a certain AP and T. The joint action of meteorological factors was seemingly obvious for PM. O\textsubscript{3} had a positive association with T and a negative association with RH because sunshine might be the main promoter of O\textsubscript{3}, as O\textsubscript{3} is enhanced by photochemical factors, and RH could affect sunshine duration [26]. Meteorological factors could influence air pollution, thus impacting health. Therefore, meteorological factors were introduced into the GLM. The time series diagram shows that in the cold period, the air pollutants, except ozone, had higher concentrations than those in the warm period. This is due to the negative association between T and air pollutants and the positive association between AP and air pollutants, except ozone. In addition to meteorological factors, emissions also increase pollutant concentrations [27]. In the cold period, 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, in the cold period than in the warm period.

The GLM showed the 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 NO\textsubscript{2}, O\textsubscript{3}, PM\textsubscript{2.5} and PM\textsubscript{10} [28, 29]. In the overall model, we found that NO\textsubscript{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 NO\textsubscript{2} was strongly associated with hospital admissions for both respiratory and cardiovascular diseases [30, 31]. In China, the Sixth National Population Census showed that coastal area had become an old-age society, and a systematic review and meta-analysis reported that the effect of NO\textsubscript{2} exhibited regional differences because of different proportions of elderly persons with increased susceptibility to NO\textsubscript{2}, which may be the
cause of the high ER associated with NO₂ [32]. Although air quality is not bad, the elderly may be still susceptible to air pollutants.

However, once we studied the different seasons, the effect of NO₂ was less significant than that of the total situation, and the ER of NO₂ was lower in the warm period than in the cold period; moreover, it lost all significance in the warm period. In addition to T, the concentrations of air pollutants were different between the cold period and warm period. In the cold period, the concentration of NO₂ was 33.11 μg/m³, while in the warm period, it was 23.32 μg/m³. There is a dose-dependent relationship between pulmonary injuries and ambient NO₂ [33], but for circulatory injuries, there is a lack of research. Interestingly, NO₂, O₃, PM₂.₅ and PM₁₀ had similar results, in term of influences on upper and lower respiratory outpatient visits. Generally, PM₁₀ has a greater impact on the upper respiratory tract than on the lower respiratory tract, while PM₂.₅ and O₃ exhibit the opposite. In the cold period, the increase in upper respiratory outpatient visits was greater than that in the warm period, while the results for lower respiratory were in direct contradiction with the above mentioned situation, except NO₂. And nitrogen dioxide, ozone and fine particle matter caused more ERs for upper respiratory outpatient visits than lower respiratory outpatient visits in cold period, but nitrogen dioxide, ozone, respiratorable and fine particle matter caused more ERs for lower respiratory outpatient visits in warm period. T and AP were 14.66°C and 1016.65 hpa in the cold period and 26.40°C and 1004.66 hpa in the warm period. Some studies reported that low AP and warm Ts increased susceptibility to respiratory-related diseases [34, 35]. However, PM and O₃ had greater effects on upper respiratory outpatient visits in the cold period and greater effects on lower respiratory outpatient visits in the warm period, possibly because the depths of the pollutants entering the respiratory tract are impacted by T and AP; however, this theory needs further study. Regarding circulatory diseases, in our study, we found that in the cold period, air pollutants increased the number of outpatient visits for circulatory diseases. Some studies presented similar outcomes [31, 36]. However, a study over 17 years in Canada reported that warm season 1-day lagged ozone had a greater association with the three examined circulatory hospitalization causes (ischemic heart disease, other heart disease and cerebrovascular disease) than cold season ozone [14]. A study in Hong Kong reported that PM and NO₂ increased emergency hospital admissions during the warm period [37]. During our study, increased concentrations of PM and NO₂ were observed in the cold period, but an increased concentration of O₃ was not. In addition to the increased concentrations of air pollutants, heat waves and the other extreme high-temperature events were more likely to occur on low-temperature days, which may cause more outpatient visits for circulatory diseases [38].

We also conducted exceeding 100 μg/m³ of ozone model, because ozone pollution is serious. the exceeding 100 μg/m³ of ozone model did not introduce the ns function of date and DOW because of discontinuity. Ozone exceeded 100 μg/m3 for a total of 390 days during the study period (total study period, 1096 days) and in the warm period, ozone exceeded 100 μg/m3 for a total of 315 days, and the warm period model showed 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 exceeding 100
µg/m³ of ozone model, but the diseases were different. The difference may be due to the increased concentration of O₃ in the 100 µg/m³ ozone model [O₃ average (standard O₃ concentration model): 126.36µg/m³ vs O₃ average (the warm period average): 100.48µg/m³].

In the double model, at lag0, after adjusting for PM_{2.5}, NO₂ and O₃ presented increased ERs. In contrast, after adjusting for NO₂, the three other pollutants, especially particulate matter (PM_{2.5} and PM_{10}), presented decreased ERs. There was a strong correlation between PM and NO₂. The ER of ozone did not fluctuate considerably after adjusting for the three other pollutants. The interaction between PM and NO₂ was strong, and the effect of O₃ was independent. Previous studies also found that there was a strong correlation between PM and gaseous air pollution, with the exception of O₃, which did not change much after adding the other air pollutants into the model [6, 17]. Some mechanics studies noted that inflammation, oxidative stress, changes in systemic coagulation functioning and reduced cardiac autonomic control appeared after exposure to gaseous air pollutants and PM [39, 40], which may trigger respiratory and cardiovascular events as well as high concentrations of air pollutants, except O₃, in the same period (cold period). These factors may cause high correlations among air pollutants. Therefore, it is difficult to evaluate the independent effects of PM or NO₂ because of their high correlations [17].

There are several limitations. In coastal area, ozone pollution is more serious than PM and NO₂ pollution, but in this study, NO₂ increased the number of outpatient visits. O₃ and NO₂ are relative to photochemical smog, and they promote one another; perhaps they exhibit joint action. However, we could not find obvious interactions in the double model; therefore, further research is required. PM_{2.5} increased the outpatient visit risk rate in many studies, even in areas with better air quality than Fuzhou. In our study, we did not observe a significant effect of PM_{2.5}. If we stratify the results by different ages and diseases, we may obtain significant outcomes. Overall, our study comprised comprehensive analysis to investigate the association between air pollutants and outpatient visits. 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 on 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, in the cold period, the ER of NO₂ was higher than that in the warm period, regardless of respiratory (both upper and lower) or circulatory outpatient visits. However, in the cold period, O₃, NO₂ and PM_{2.5} had greater ERs for upper respiratory outpatient visits than lower respiratory outpatient visits, and in the warm period, O₃, NO₂ PM_{10} and PM_{2.5} had greater ERs for lower respiratory outpatient visits. In the double air pollutant model, PM and NO₂ had high correlations.

**Abbreviations**
AP: air pressure; DOW: day of the week; 8h-O₃ or O₃8: 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; NO₂: nitrogen dioxide; ns: natural spline; PM₁₀: Particle matter with an aerodynamic diameter less than 10 μg⁻³; PM₂.₅: Particle matter with an aerodynamic diameter less than 2.5μg⁻³; RH: relative humidity; T: temperature

Declarations

Acknowledgments

Not applicable

Author 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: involved in the critical revision of the manuscript for important intellectual content. All the authors read and approved this paper.

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Funding

This work was funded by Startup Fund for scientific research, Fujian Medical University (Grant numbers 2018QH1008) and Fujian Medical University’s Research Foundation for Talented Scholars (Grant number XRCZX2018011).

Availability of data and materials

Please contact author for data requests.

Ethics approval and consent to participate

Ethics approval or consent to participate was not needed for the present study since no data on individual level was used (only the number of visits per day).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 Statistical summary of the daily air pollutants, meteorological factors and outpatient visits in Fujian, China, 2016-2018
| Variable                      | Mean ± SD | Minimum | Percentile | Maximum |
|-------------------------------|-----------|---------|------------|---------|
|                               |           | 25th    | 50th       | 75th    |
| **Total**                     |           |         |            |         |
| Respiratory disease           | 82±32     | 1       | 60         | 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     |
| \(\text{NO}_2\) (\(\mu g/m^3\)) | 27.38±11.18 | 3.83   | 19.55      | 25.14   | 33.14   | 79.57   |
| \(\text{O}_3\) (\(\mu g/m^3\)) | 89.60±33.94 | 16.71  | 64.02      | 87.36   | 112.00  | 208.43  |
| \(\text{PM}_{2.5}\) (\(\mu g/m^3\)) | 26.07±13.14 | 2.43   | 16.57      | 23.86   | 32.71   | 83.57   |
| \(\text{PM}_{10}\) (\(\mu g/m^3\)) | 49.68±22.62 | 7.43   | 33.33      | 46.49   | 63.89   | 167.57  |
| Temperature (\(\degree C\)) | 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    |
| **Cold period**               |           |         |            |         |
| 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     |
| \(\text{NO}_2\) (\(\mu g/m^3\)) | 33.11±11.55 | 10.43  | 24.57      | 31.72   | 41.34   | 79.57   |
| \(\text{O}_3\) (\(\mu g/m^3\)) | 74.21±26.59 | 16.71  | 53.66      | 73.72   | 92.97   | 168.14  |
| \(\text{PM}_{2.5}\) (\(\mu g/m^3\)) | 30.42±14.44 | 2.43   | 19.86      | 28.14   | 38.50   | 82.14   |
| \(\text{PM}_{10}\) (\(\mu g/m^3\)) | 52.28±23.48 | 7.43   | 33.72      | 50.79   | 68.54   | 134.14  |
| Temperature (\(\degree C\)) | 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    | 1003       | 1016    | 1021    | 1034    |
| **Warm period**               |           |         |            |         |
| 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     |
| \(\text{NO}_2\) (\(\mu g/m^3\)) | 23.32±8.92  | 3.83   | 17.74      | 22.00   | 27.20   | 73.29   |
| \(\text{O}_3\) (\(\mu g/m^3\)) | 100.48±34.39 | 30.00  | 75.04      | 99.24   | 124.14  | 208.43  |
| \(\text{PM}_{2.5}\) (\(\mu g/m^3\)) | 22.99±11.17 | 4.86   | 15.14      | 21.00   | 28.86   | 83.57   |
| \(\text{PM}_{10}\) (\(\mu g/m^3\)) | 47.84±21.82 | 10.29  | 33.04      | 44.14   | 60.03   | 167.57  |
| Temperature (\(\degree C\)) | 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    |
| **Exceeding 100 \(\mu g/m^3\) of ozone** | | | | |
| 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     |
| \(\text{NO}_2\) (\(\mu g/m^3\)) | 25.16±7.56 | 10.14  | 20.14      | 23.74   | 28.28   | 56.14   |
| \(\text{O}_3\) (\(\mu g/m^3\)) | 126.36±20.89 | 100.14 | 109.86     | 121.71  | 136.66  | 208.43  |
|                                | 29.81±10.97 | 6.43   | 21.74      | 27.86   | 35.57   | 70.43   |
|                | PM$_{2.5}$ (μg/m³) | PM$_{10}$ (μg/m³) |
|----------------|---------------------|--------------------|
|                | 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                 |

Figures

**Figure 1**

Association of air pollution and meteorological factors. (A) The Spearman correlations (left) between the 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; O38, daily maximum 8-h mean ozone; NO2, nitrogen dioxide). (B) Contour plot (right) of the association between air pollutants and meteorological parameters.
Figure 2

Time series graphs of weekly air pollutants (B) and outpatient visits (A) for respiratory and circulatory diseases
Figure 3

ERs of outpatient visits for total respiratory, lower respiratory, upper respiratory and circulatory diseases in single air pollutant modes(A) and double air pollutant modes(B). See also Table 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 Table S2 and S3. You can see that Wilcoxon paired test of ERs between upper respiratory and lower respiratory in different period (C) and between cold period and warm period in upper and lower respiratory (D) (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 µg/m₃. See also Table S5

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