

# Analysis of the Association between environmental-meteorological factors and Acute Suppurative Otitis Media: Further Epidemiological Evidence from Lanzhou, Northwestern China

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## Research article

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# Abstract

## Objective

To investigate the possible associations, lag effects and pathogenic characteristics of urban air quality on acute suppurative otitis media (ASOM) in Lanzhou, a city in Northwestern China.

## Methods

SPSS software was used to analyze Spearman correlation between ambient environment-meteorological factors and the daily number of patient ASOM visits. The GAM of time series was used to analyze the exposure-response curve, and R software was used to calculate RR. Using above results to discuss the relationship of air pollutions, meteorological factors and morbidity of ASOM.

## Results

The number of patients with ASOM in 2014, 2015 and 2016 were 916, 875 and 1023 respectively. There was no significant difference in three years ( $P=0.85$ ). The annual visits peaked in December, the lowest in August, followed by February, Summer was less than the other three seasons. The morbidity of ASOM had a largest peak within 14 years old (53.84%), and the number of male patients 1514 (53.6%) is 1.16 times that of female patients 1309 (46.4%). Spearman correlation analysis showed that the correlation between air pollutions and environmental variables. As for single-day lag effects, there were positive correlations between PM<sub>2.5</sub>, PM<sub>10</sub>, CO, NO<sub>2</sub>, SO<sub>2</sub> and the daily number of ASOM visits, but the correlation between O<sub>3</sub> and ASOM did not pass the significance test. As for multi-day lag effects, PM<sub>2.5</sub>, PM<sub>10</sub>, CO, NO<sub>2</sub> had lagging effects on the daily number of ASOM visits, but the correlation between SO<sub>2</sub> and O<sub>3</sub> did not pass the significant test. There was a positive correlation between ATM and the daily number of patient ASOM visits, and negative correlation between T and the daily number of patient ASOM visits, while the correlation between W, RH and ASOM was weak.

## Conclusions

The incidence of ASOM has obvious age and seasonal characteristics. There may be some correlation between environmental-meteorological factors and the incidence of ASOM. Therefore, it is of great significance to strengthen environmental control and public health strategy in order to reduce and prevent the occurrence of ASOM diseases.

## 1. Introduction

Along with the rapid economic growth and urbanization, environmental pollution has become a serious problem due to the extensive use of fossil fuels. Especially in Lanzhou and other areas where heavy industry development is an important support. The impact of environmental change on health has become a sensitive topic for the public, the media and even the Chinese government and adjacent countries[1].

Globally, scholars used cohort studies, case-control studies, cross-case studies and cross-sectional studies to analyze the correlation between air pollutants and otitis media (OM). There is growing evidence that air pollution exposure is associated with OM, and all studies investigating this association found evidence that exposure to at least one pollutant increased the risk of OM [2]. MacIntyre et al. reported a significant positive correlation between NO<sub>2</sub> and OM in the largest birth cohort of 10 European cohorts [3]. Brauer et al. found that there was a correlation between children's exposure to nitrogen dioxide (NO<sub>2</sub>), PM<sub>2.5</sub> and OM [4]. However, A systematic review by Jones et al. reported in 2012 that living with a smoker increased the risk of people's OM by 62% [5]. Zemek et al. reported lag effects between NO<sub>2</sub>, PM<sub>10</sub>, O<sub>3</sub> and the hospital OM visits[6].

However, for environmental pollutants, only a few studies have reported the effects of air pollutants on the incidence of AOM in China, and the research object is children. Lu[7] and Zhang[8] studied the correlation between air pollution and children's AOM in Beijing. The results showed that air pollutants increased the incidence of AOM in children, especially SO<sub>2</sub> and NO<sub>2</sub>.

Although there is convincing evidence for an association between environmental tobacco smoke exposure and OM [9], the relationship between ASOM and ambient air pollution exposure is not yet established, and the impact of meteorological factors on ASOM is rarely reported. As one of the most common diseases in children, ASOM mostly secondary to respiratory tract infections, and is the most common cause of antibiotic use in people. It is clinically characterized by earache, ear purulence, tympanic membrane congestion and perforation. If the treatment is not timely, it may lead to tympanic membrane perforation, hearing loss, and even chronic suppurative otitis media, which will bring great economic and social burden to families and health care systems [10, 11]. Therefore, it is of great significance to explore the pathogenesis, early prevention and treatment of ASOM. To provide reference for reducing and preventing the occurrence of diseases and rationally arranging medical resources.

In this study, we collected data of ASOM from 2014 to 2016 in Lanzhou, and used time series analysis method to analyze the relationship between environmental-meteorological factors and the daily number of ASOM visits.

## 2. Materials And Methods

### 2.1. Air Pollutant and Meteorological Data

#### 2.1.1 Air Pollutant Data

Air quality data for the daily PM<sub>2.5</sub>, PM<sub>10</sub>, CO, NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub> concentrations between 1 January 2014 and 31 December 2016 were provided by the Lanzhou Municipal Environmental Protection Monitoring Center, continuous monitoring data and regional average are provided. The daily data was obtained as average values derived from the hourly data of 4 state-controlled monitoring stations distributed across Lanzhou.

### 2.1.2 Meteorological Monitoring Data

Meteorological data collected from Lanzhou Meteorological Bureau include the daily observation data of Lanzhou Station from January 1, 2014 to December 31, 2016. Including average temperature (T, °C), relative humidity ((RH, %), atmospheric pressure (ATM, hPa), wind speed (W, m/s), etc.

### 2.1.3 Medical Record Data

Daily numbers of outpatients for ASOM symptoms between 1st January 2014 and 31st December 2016 were extracted from the Department of Otolaryngology-Head and Neck Surgery, The 940th Hospital of the Joint Logistics Support Unit of the Chinese PLA and Second Affiliated Hospital of Lanzhou University. Both hospitals are Class-Three, and have advanced inspection equipment, experienced clinicians and perfect electronic medical record system. The most important is undertake a large part of the diagnosis and treatment of Otolaryngology diseases in Lanzhou, which ensures sufficient sample size and the reliability of medical record data. They are both comprehensive teaching and researching medical centers.

The principal diagnosis of ASOM was based on medical history, physical examination, auxiliary examination. Case data included patient's medical record number, first name, last name, sex, age, date of birth, diagnosis, and excluded ANSOM according to international disease diagnostic criteria. In order to avoid repeated counting, only one visit per individual patient per day was used as daily visit counts. Subsequent follow-ups within 30 days of the initial visit were excluded. All patients have given written consent to participate in the study. All medical interviewers (general practitioners or nurses) were trained to use uniform examination protocols. Medical records and the respective results were confirmed by the supervisors at each hospital. This study was approved by the Gansu Provincial Ethics Committee and the Human Research Ethics Committee of the Ministry of Health.

## 2.2 Data Analysis

### 2.2.1 Descriptive Statistics

Frequency distribution characteristics of meteorological data, air pollution data and disease data were analyzed, including mean, SD, Minimum and Maximum, and 25, 50 and 75 percentiles (P25, Median and P75, respectively). The characteristics of annual and monthly changes of disease data were analyzed. In addition, the disease data were stratified, taking into account the distribution characteristics of different ages (0–14 years old, 15–64 years old and over 64 years old) .

### 2.2.2 Correlation Analysis

SPSS version 24.0 was used to analyze spearman correlation between ambient environment-meteorological factors and the daily number of patient ASOM visits.

### 2.2.3 Generalized Additive Model

Generalized additive model(GAM)has become one of the most widely used methods in studying the effects of meteorological and environmental factors on human health. It is more flexible than other statistical models and has greater advantages in dealing with the complex non-linear relationship between independent variables and strain variables. Due to the daily number of ASOM visits was sparse and typically followed a Poisson distribution [9], the core analysis was a GAM with log link and Poisson error that accounted for smooth fluctuations in daily number of consultations for ASOM patient. A detailed introduction of the GAM has been previously described [10]. GAM was used to analyze the influence of meteorological factors and air pollutants on the daily number of patients with ASOM. Due to the number of hospitalized patients changes nonlinearly with time, spline smoothing function is used to control the long-term trend. At the same time, weekend and holiday effects are taken as dumb variables to control. The degree of freedom of model parameters is judged by Akaike's Information Criterion(AIC). The basic model is:

$$\text{Log}[E Y_t]=\alpha + \beta x_{t-l}+ H +W + S(\text{time},df)+S(\text{factors}, df)$$

Y<sub>t</sub> refers to the number of ASOM visits on day t; E (Y) refers to the expected number of ASOM visits on day t; X<sub>t</sub> refers to the average daily concentration of pollutants on day t; l is the lag day of air pollutant exposure, which is a commonly used concept in time series analysis. Its meaning is to use the health effect index of that day and the pollutants of the previous n days. Regression analysis was used to study the influence of pollutant concentration on the number of patients visiting ASOM in the past few days. α was residual; β was regression coefficient, which indicated that the relative variable of natural logarithm of the number of patients visiting ASOM was spline level for each unit of pollutant concentration (PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub>:10 μg/m<sup>3</sup>; CO:1 mg/m<sup>3</sup>). S is a spline smoothing function; df is a degree of freedom, W is a weekly effect; H is a holiday variable. Time is a calendar time to control long-term effects. Factors refer to the corresponding values of air pollutants (PM<sub>2.5</sub>, PM<sub>10</sub>, CO, NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub>) and meteorological factors (T, RH, W, ATM).

For seasonal analysis, seasonality was differentiated on the basis of heating/non-heating periods. This study divides the seasons according to the meteorological characteristics of Northwest China, it is defined that spring is from February to April(2–5), the summer is from May to August(5–8), the autumn is from September to November(9–11), and the winter is from December to next year January(12 – 2).

For the lag effects model, we examined the effect of air pollutants with different lag (L) structures of single-day lag (distributed lag; from L0 to L7) and multi-day lag (moving average lag; L0-1 to L0-14). In this study ,a lag of 0 day (L0) corresponds to the current-day pollution, and a lag of 1 day refers to the previous-

day concentration. In multi-day lag models, L0-14 corresponds to 15 day moving average of pollutant concentration of the current and the previous 14 days [12]. The data of meteorological factors used in the lag model are similar to those of atmospheric pollution.

In this study, R software (version 3.5.0) with mgcv package was used to analyze the exposure-response relationship between atmospheric pollutants and meteorological factors and the daily number of ASOM visits. The results obtained were expressed as the relative risk (RR) percentage change in the daily number of ASOM visits for per 10 µg/m<sup>3</sup>(1 mg/m<sup>3</sup>) increases of air pollutant concentrations. Relative risk (RR) and 95% confidence interval (95% CI) were calculated. The test level was 0.05 (P < 0.05 test had statistical significance, p < 0.01 test had statistical significance).

### 2.3 Regional Survey Of Research

Lanzhou is located in the western part of the Loess Plateau and the eastern part of the Qinghai-Tibet Plateau. Its geographical location is 35°34'–37°07', 102°36'–104°34', high in the West and south, low in the East and north. The Yellow River runs through the whole city from southwest to northeast, forming typical geomorphological features of the valley basins. The urban area is about 35 kilometers long from east to west and 8 kilometers wide from north to south. It is located in the Inland hinterland, in the transition zone between monsoon area and non-monsoon area, and belongs to temperate semi-arid climate.

### 2.4 Quality Control

Medical records are managed and checked in accordance with the national standards of the third-class and first-class hospitals. Personnel are responsible for the entry and management of medical records and excluding cases with incomplete information, unclear diagnosis and non-acute suppurative otitis media. Air pollution data and meteorological data are from the national certified automatic atmospheric monitoring system and meteorological observation system. Personnel are responsible for inspection, identification and management. In this study, the data used are aggregated and calculated through data management software, and the analysis, statistics and management of data are strictly controlled.

## 3. Results

### 3.1 General Statistical Analysis

#### 3.1.1 Characteristics of Air Pollutants and Meteorological Factors

Table 1 summarizes the distribution of the annual mean air pollutant concentrations of Lanzhou during the study period. The results show that the average concentrations of PM<sub>10</sub>, PM<sub>2.5</sub> were 119.78 µg/m<sup>3</sup> and 52.01 µg/m<sup>3</sup>, respectively. The average concentrations of NO<sub>2</sub>, SO<sub>2</sub> and O<sub>3</sub> were 46.50 µg/m<sup>3</sup>, 25.30 µg/m<sup>3</sup> and 44.82 µg/m<sup>3</sup>, and the average concentration of CO was 1.342 mg/m<sup>3</sup>.

Table 1  
Characteristics of Air Pollutants

	<b>M ± SD</b>	<b>Min</b>	<b>P25</b>	<b>P50</b>	<b>P75</b>	<b>Max</b>
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	52.01 ± 25.58	13	34.67	44.89	63.22	266
PM <sub>10</sub> (µg/m <sup>3</sup> )	119.78 ± 71.80	23	81.00	104.91	140.62	972
CO(mg/m <sup>3</sup> )	1.342 ± 0.650	0.462	0.892	1.114	1.610	4.245
NO <sub>2</sub> (µg/m <sup>3</sup> )	46.50 ± 18.66	11	32.98	44.24	56.64	120
SO <sub>2</sub> (µg/m <sup>3</sup> )	25.30 ± 15.91	4	11.59	21.18	37.45	78
O <sub>3</sub> (µg/m <sup>3</sup> )	44.82 ± 22.54	6	26.83	42.65	60.14	130
M ± SD: Mean ± standard deviation; Min: minimum; P25: 25th percentile; P50: Median; P75: 75th percentile; Max: maximum						

Table 2 summarizes the distribution of the annual mean atmospheric pressure, temperature, relative humidity and other meteorological factors of Lanzhou during the study period.

During our study period, the average atmospheric pressure was 811.3 hPa and the average wind speed was 1.99 m/s. The relative humidity ranged from 21–100%, the mean value was 60.56%, the temperature ranged from –17°C to 25 °C, and the average value was 7.74 C. The average maximum temperature was 18.13 C, the minimum temperature was 5.81 C, and the average daily temperature difference was 12.32 C.

Table 2  
Characteristics of Meteorological Factors

	<b>M + SD</b>	<b>Min</b>	<b>P25</b>	<b>P50</b>	<b>P75</b>	<b>Max</b>
ATM (hPa)	811.33 ± 4.28	797.4	808.3	811.1	814.2	825.1
W (m/s)	1.99 ± 0.74	0.5	1.5	1.8	2.3	6.3
RH (%)	60.47 ± 15.99	21	48	61	72	100
T (°C)	7.74 ± 9.68	-17	-0.9	9.2	16.3	25
Max T (°C)	18.13 ± 10.17	-7	9	20	27	38
Min T (°C)	5.81 ± 9.44	-17	-3	7	14	24
Diu T difference (°C)	12.32 ± 3.21	3	10	13	14	22
M ± SD: Mean ± standard deviation; Min: minimum; P25: 25th percentile; P50: Median; P75: 25th percentile; Max: maximum; ATM: average atmospheric pressure; W: average Wind Speed; RH: average relative humidity; T: average temperature; Max T:Maximum Temperature; Min T:Minimum temperature; Diu T difference: Diurnal temperature difference						

### 3.1.2 Characteristics of ASOM patients

In this study, 2 823 patients with ASOM were collected from two first-class hospitals in Lanzhou from 2014 to 2016. Among them, 1 514 (53.6%) were males and 1 309(46.4%) were females. The number of male patients was 1.16 times that of female patients. There were 1520(53.84%) children aged 0–14, 1205(42.69%) patients aged 15–64, and only 98(3.47%) elderly patients. The average number of daily visits was 2.66, and the maximum number of daily visits was 12. The average number of male patients was 1.42, the maximum was 8, the average number of female patients was 1.23, the maximum was 8. The daily average number of children under 14 years old, 15–64 years old and older persons over 64 years old were 1.43, 1.13 and 0.09 respectively, the maximum were 9, 5 and 2 respectively, and the minimum number of patients per day for all different groups was 0. Characteristics of ASOM patients are also summarized in Table 3.

Table 3  
Characteristics of ASOM patients

	<b>M ± SD</b>	<b>Mix</b>	<b>P25</b>	<b>P50</b>	<b>P75</b>	<b>Max</b>
Total	2.66 ± 2.05	0	1	2	4	12
Male	1.42 ± 1.40	0	1	2	3	8
Female	1.23 ± 1.13	0	1	2	3	8
≤ 14	1.43 ± 0.75	0	1	2	2	9
15–64	1.13 ± 1.04	0	1	1	2	5
≥ 65	0.09 ± 0.24	0	0	0	1	2
M ± SD: Mean ± standard deviation; Min: minimum; P25: 25th percentile; P50: Median; P75: 25th percentile; Max: Maximum						

#### 3.1.2.1 Age Composition

The age distribution of patients with ASOM showed that the proportion of children under 14 years old was the highest (53.84%).The second was the age of 15–64(42.69%), and the elderly over 64 years old had the least number of visits, accounting for 3.47%. To some extent, it can also be explained that the number of ASOM visits decreases with the increase of age.

#### 3.1.2.2 Seasonal Effect

Annual morbidity of ASOM was 916, 875 and 1023 respectively. The results showed that the number of patients in Summer was less than the other three seasons(Fig. 2), The number of patients was the largest in winter, and there was no significant difference between spring and autumn( $p = 0.65$ ).

#### 3.1.2.3 Monthly Effect

The distribution of monthly visits in ASOM showed that the number of visits increased gradually from September to December, but there was an episode in November 2015. It was noted that peak could be seen in December, and a valley in August (168), followed by February (171), and the medium level in March to May, as shown in Fig. 3.

### 3.2 Associations between Air Pollutants and Meteorological Variables

Table 4 presents the Spearman correlation coefficients between different air pollutants and meteorological variables. Generally, the correlation coefficients between  $PM_{10}$ , CO,  $NO_2$ ,  $SO_2$  and  $PM_{2.5}$  were high and positive ( $p \leq 0.01$ ), whereas  $O_3$ , T, W had significant negative correlation with the other environmental variables. Daily atmospheric press showed a positive relationship with all air pollutants except for  $PM_{2.5}$  and  $PM_{10}$ . Humidity was negatively correlated with all pollutants except for T.

Table 4  
Spearman correlation coefficients among environmental variables in Lanzhou ,2014–2016

	PM <sub>2.5</sub>	PM <sub>10</sub>	CO	NO <sub>2</sub>	SO <sub>2</sub>	O <sub>3</sub>	T	RH	W	ATM
PM <sub>2.5</sub>	1.0									
PM <sub>10</sub>	0.804**	1.0								
CO	0.697**	0.485**	1.0							
NO <sub>2</sub>	0.583**	0.563**	0.650**	1.0						
SO <sub>2</sub>	0.507**	0.351**	0.539**	0.270**	1.0					
O <sub>3</sub>	-0.374**	-0.139**	-0.401**	-0.123**	-0.752**	1.0				
T	-0.419**	-0.320**	-0.528**	-0.241**	-0.338**	0.247**	1.0			
RH	-0.146**	-0.415**	-0.116**	-0.250**	-0.188**	-0.246**	0.024	1.0		
W	-0.182**	-0.182**	-0.405**	-0.343**	-0.206**	0.216**	0.321**	-0.091**	1.0	
ATM	0.048	0.027	0.165**	0.085**	0.105**	-0.170**	-0.532**	0.121**	-0.286**	1.0

\*\* Correlation is significant at the 0.01 level (2-tailed)

### 3.3 Lag Effects

#### 3.3.1 Single-day lag effects on ASOM

Table 5 represents the single-lag effects of air pollutions and meteorological factors on the daily number of patient ASOM visits, while *Italic value* were the strongest lag days.

The results showed that atmospheric factors PM<sub>2.5</sub>, PM<sub>10</sub>, CO and NO<sub>2</sub> had single-day lag effects on the daily number of patients with ASOM, the lag days were mainly concentrated in 3–7 days. Among them, the largest single-lag effect of NO<sub>2</sub> on day 7 (L7), the strongest single-lag effects of PM<sub>2.5</sub>, PM<sub>10</sub> on day 6 (L6) and day 3 (L3), respectively. The single-day lag effects of CO were on day 1, 3, 4, 5 and 6 (L1,3,4,5,6). SO<sub>2</sub> has lag effect only on day 3 (L3), while O<sub>3</sub> had no lag effect. As for meteorological factors, only T has single lag effect on the daily number of ASOM visits, lag 4, 5, 6 days (L4,5,6). Other factors W, RH and ATM have no single lag effect on the number of daily visits of ASOM patients.

Table 5  
Spearman analysis of single-day lag effects on ASOM by environmental variables

Factors	L1	L2	L3	L4	L5	L6	L7
PM <sub>2.5</sub>	0.082**	0.067*	0.107**	0.102**	0.115**	0.122**	0.052
PM <sub>10</sub>	0.071*	0.060*	0.136**	0.121**	0.110**	0.110**	0.050
SO <sub>2</sub>	0.049	0.048	0.064*	0.057	0.037	0.051	0.040
CO	0.075*	0.051	0.062*	0.070*	0.080**	0.104**	0.053
NO <sub>2</sub>	0.084**	0.074*	0.109**	0.107**	0.113**	0.154**	0.156**
O <sub>3</sub>	-0.025	-0.023	-0.032	-0.019	-0.028	-0.027	0.005
T	-0.046	-0.048	-0.051	-0.060	-0.062*	-0.069*	-0.068*
ATM	-0.036	-0.026	-0.015	0.026	0.033	0.029	0.024
RH	-0.054	-0.039	-0.049	-0.043	-0.039	-0.020	-0.020
W	0.007	0.018	-0.045	-0.015	-0.030	-0.030	-0.035

\*Correlation is significant at the 0.05 level (2-tailed),\*\* Correlation is significant at the 0.01 level (2-tailed); *Italic value* are the strongest correlation coefficients

#### 3.3.2 Multi-day lag effects on ASOM

Table 6 shows the multi-day lag effects of environmental variables on the daily number of patient ASOM visits. *Italic value* represents the strongest multi-day lag effect days.

The results of this study showed that the multi-day lag effects of environmental- meteorological factors were mainly concentrated in 3–6 days. The environmental factors PM<sub>2.5</sub>, PM<sub>10</sub>, CO and NO<sub>2</sub> we selected were positively correlated with the daily number of ASOM visits, and had the multi-day lag effects on the daily number of ASOM visits. Among them, PM<sub>2.5</sub> and PM<sub>10</sub> had the strongest multi-day lag effects on day 13 (L0-13) and day 14 (L0-14) respectively, the strongest multi-day lag effects of NO<sub>2</sub> and CO were on the same day (L0-6), SO<sub>2</sub> and O<sub>3</sub> did not pass the significance test ( $P > 0.05$ ). The meteorological factor ATM was positively correlated with the daily number of ASOM visits, while there were negatively correlated with RH, W and T. And ATM, T, W had the multi-day lag effects on the daily number of ASOM visits, the strongest multi-day lag effects of ATM, W, and T were on day 6 (L0-6), day 3 (L0-3) and day 5 (L0-5), respectively. RH passed the significance test only on the 11th day(L0-11).

Table 6  
Spearman analysis of multi-day lag effects on ASOM by environmental variables

Factors	L0-1	L0-2	L0-3	L0-4	L0-5	L0-6	L0-7	L0-8	L0-9	L0-10	L0-11	L0-12	L0-13	L
PM <sub>2.5</sub>	0.090**	0.094**	0.108**	0.116**	0.127**	0.135**	0.133**	0.133**	0.136**	0.135**	0.130**	0.136**	0.137**	0
PM <sub>10</sub>	0.072*	0.075*	0.099**	0.106**	0.119**	0.127**	0.126**	0.127**	0.132**	0.132**	0.130**	0.138**	0.141**	0
NO <sub>2</sub>	0.076*	0.086**	0.102**	0.112**	0.122**	0.142**	0.137**	0.130**	0.132**	0.132**	0.129**	0.133**	0.133**	0
SO <sub>2</sub>	0.046	0.050	0.058	0.056	0.057	0.054	0.053	0.050	0.048	0.047	0.049	0.048	0.045	0
CO	0.071*	0.073*	0.077*	0.083**	0.085**	0.094**	0.092**	0.092**	0.094**	0.092**	0.091**	0.091**	0.090**	0
O <sub>3</sub>	-0.028	-0.028	-0.031	-0.029	-0.031	-0.031	-0.031	-0.027	-0.026	-0.025	-0.026	-0.029	-0.029	0
ATM	0.054	0.036	0.048	0.076*	0.065*	0.079**	0.076*	0.075*	0.046	0.076*	0.076*	0.048	0.065*	0
RH	-0.006	-0.015	-0.014	-0.013	-0.011	-0.007	-0.007	-0.006	-0.013	-0.007	-0.007*	-0.007	-0.007	0
W	-0.034	-0.083**	-0.087**	-0.059*	-0.078**	-0.077*	-0.075*	-0.080**	-0.059*	-0.055*	-0.068	-0.034*	-0.075*	0
T	-0.107**	-0.107**	-0.107**	-0.107**	-0.109**	-0.108**	-0.106**	-0.106**	-0.109**	-0.107**	-0.108**	-0.108**	-0.109**	0

\*Correlation is significant at the 0.05 level (2-tailed);\*\* Correlation is significant at the 0.01 level (2-tailed); Italic value are the strongest correlation coefficients

### 3.4 Exposure-response Associations

After controlling the long-term trend, weekend effect and mixed meteorological factors, we use the nonparametric generalized addition model (GAM) to analyze the exposure-response relationship. Relative risk (RR) was expressed as a change in the number of counseling sessions for ASOM patients with an increase of air pollutant concentration of 10 µg/m<sup>3</sup> and 1 mg/m<sup>3</sup> (95% CI).

Figure 4 presents the Single-lag exposure-response relationships between air pollutions and meteorological factors on the daily number of ASOM visits.

In this study, we found generally linear relationships (monotonic trends) for daily number of ASOM visits associated with CO, NO<sub>2</sub> and T. In addition, we observed basically monotonic increased RR for both CO and NO<sub>2</sub> within these ranges of concentrations (Fig. 4), indicating that CO and NO<sub>2</sub> are significantly associated with the daily number of ASOM visits. we also observed basically monotonic increased RR for NO<sub>2</sub>, but there is a turning point in the process of increasing. RR increased slightly while the concentration of NO<sub>2</sub> was less than 50 µg/m<sup>3</sup>, and increased more while the concentration of NO<sub>2</sub> was more than 50 µg/m<sup>3</sup>. The daily number of ASOM patients was negatively correlated with CO concentration (CO < 1 mg/m<sup>3</sup>), however, with the increase of CO concentration (> 1 mg/m<sup>3</sup>), the number of ASOM patients increased. Temperature was negatively correlated with the daily number of ASOM patients.

The curve of PM<sub>10</sub> and O<sub>3</sub> are "N". When the concentration of PM<sub>10</sub> is between 250 µg/m<sup>3</sup> and 600 µg/m<sup>3</sup>, the RR decreases gradually. When the concentration of PM<sub>10</sub> is less than 250 µg/m<sup>3</sup> or more than 600 µg/m<sup>3</sup>, the RR increases gradually.

Moreover, we observed basically monotonic increased RR for both RH and PM<sub>2.5</sub>, within these ranges (Fig. 4), indicating that PM<sub>2.5</sub> and RH are significantly associated with increased hospital visits of ASOM.

Figure 5 shows the exposure-response relationships for multi-day lag exposure-response relationships between air pollutions and meteorological factors on the daily number of ASOM visits. We can draw the following conclusions:

The increase of concentration of PM<sub>2.5</sub>, PM<sub>10</sub>, CO, SO<sub>2</sub>, NO<sub>2</sub>, RH and ATM were positively correlated with the daily number of ASOM visits (monotonous increasing trend), while the increase of concentration of O<sub>3</sub>, W and T was negatively correlated with the daily number of ASOM visits.

The change curves of CO, NO<sub>2</sub>, PM<sub>2.5</sub> and ATM are similar with single-lag exposure-response curves. The curve of SO<sub>2</sub> was "M" type with two peak threshold ranges. The first RR peak appeared at the concentration of SO<sub>2</sub> of 20 µg/m<sup>3</sup>, and the second peak appeared at the concentration of NO<sub>2</sub> of 55 µg/m<sup>3</sup>, that means when the SO<sub>2</sub> concentration is higher or lower, the risk of seeing a doctor for ASOM is reduced. The RR was minimum when the NO<sub>2</sub> concentration was 35 µg/m<sup>3</sup>. The curve of PM<sub>10</sub> and RH were "S" and there was a dangerous threshold concentration. ATM was positively correlated with the daily number of ASOM visits. RR increases with the increase of ATM. With the increase of T, the RR value increases first and then decreases. That means when the T is higher or lower, the risk of patients with ASOM will decrease.

### 3.5 Relative Risk

Table 7 shows the RRs of air pollutants for single-day and multi-day lag effects on ASOM visits.

It is obvious that high level of PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, CO and SO<sub>2</sub> were associated with increased daily number of ASOM visits. Among these pollutants, CO showed higher risk on the daily number of ASOM visits than PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub>. The largest RRs and 95% confidence interval of PM<sub>2.5</sub>, PM<sub>10</sub>, CO, NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub> for single-day lags were (1.0064, 1.0050–1.0078), (1.0027, 1.0012–1.0042), (1.3807, 1.2242–1.5372.), (1.0085, 1.0062–1.0108), (1.0095, 1.0061–1.0129), (1.0043, 1.0023–1.0063), respectively. The largest RRs and 95% confidence interval of PM<sub>2.5</sub>, PM<sub>10</sub>, CO, NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub> for multi-day lags were (1.0112, 1.0094–1.0134), (1.0035, 1.0021–1.0049), (1.3059, 1.2017–1.4101), (1.0135, 1.0103–1.0157), (1.0111, 1.0083–1.0140), (0.9959, 0.9933–0.9985) respectively. The single-day lags and multi-day lags effect of PM<sub>10</sub> showed the largest RR on day 3. The effect magnitude of CO for both single-day and multi-day lags showed an increasing trend. RRs of NO<sub>2</sub> for multi-day lags had similar time trends to that of CO, and the largest associations were for L0-14. The single-day lags and multi-day lags effect of O<sub>3</sub> showed the largest RR on day 1.

**Due to technical limitations, Tables 7-8 are provided in the Supplementary Files section.**

Table 8 shows the associations between meteorological factors and the prevalence of ASOM in Lanzhou. It also shows the change of RRs of meteorological factors for single-day and multi-day lag effects on daily number of ASOM visits. From the table, we can conclude that the largest RRs of T, W, RH, and ATM for single-day lags were found for the 7th day (L7), 2nd day (L2), 6th day (L6), 7th day (L7), respectively. The effect of RH showed an increasing trend from L0 to L7. The effect of ATM for both single-day and multi-day lags showed an increasing trend. The greatest RRs of T, RH, W and ATM were found on 12-day cumulative measures (L0-12), 2-day cumulative measures (L0-2), 11-day cumulative measures (L0-11), 14-day cumulative measures (L0-14), respectively

## 4. Discussion

This study utilized environmental and epidemiological data to focus on the air quality with temporal variation and its health effects on ASOM in Lanzhou during 2014–2016. Our study was based on medical records from the two major hospitals in Lanzhou. All patients in our study were diagnosed by health professionals of the Department of Otolaryngology-Head and Neck Surgery of Lanzhou hospital, and all documentations were completed under the supervision of doctors. After controlling for long term trends, the 'day of the week' effect and confounding meteorological factors, non-parametric generalized additive model (GAM) was used to analyze the highly non-linear or non-monotonic exposure–response relationship between air pollutants and daily patients clinic for ASOM. Although there are some limitations, it still reflects the acute health effects of air pollution and meteorological factors on the incidence of ASOM in exposed population in Lanzhou.

### 4.1 Characteristics Of Environmental-meteorological Factors

The World Health Organization (WHO 2005) suggests standard levels of PM<sub>2.5</sub>, PM<sub>10</sub>, CO, NO<sub>2</sub>, SO<sub>2</sub> and O<sub>3</sub> in air quality standards. The mean concentration of PM<sub>10</sub> as determined in this study was 119.78 µg/m<sup>3</sup>, which is higher than the standard value suggested by WHO (AQG value, 50 µg/m<sup>3</sup> /24 h). The mean concentration of PM<sub>2.5</sub> was 52.01 µg/m<sup>3</sup>, which is lower than China atmosphere environmental standard (24 h, 75 µg/m<sup>3</sup>), but it exceeded the standard value suggested by WHO (AQG value, 24 h, 25 µg/m<sup>3</sup>). The mean concentration of CO was 1.34 mg/m<sup>3</sup>, which was lower than the EPA standard value (10 mg/m<sup>3</sup>/8 h). The mean concentration of NO<sub>2</sub> was 46.5 µg/m<sup>3</sup>, which was lower than the suggested by the WHO (AQG value, 200 µg/m<sup>3</sup> / h). This was similar to the results of a study conducted in China that reported between 53 and 73 µg/m<sup>3</sup>. The mean concentration of O<sub>3</sub> was 44.82 µg/m<sup>3</sup>, which was lower than the WHO standard values (AQG value, 100 µg/m<sup>3</sup> /8 h). The mean concentration of SO<sub>2</sub> was 25.3 µg/m<sup>3</sup>, which was higher than the standard suggested by the WHO (AQG value, 20 µg/m<sup>3</sup>/24 h). Overall, this study showed that the air quality was at a moderate pollution level in Lanzhou, which is similar with the research of Hu et al[14].

Over the 3 years studied, daily atmospheric pressure ranged from 797.4 to 825.1 hPa, with an average concentration of 811.3 hPa. The relative humidity ranged from 21–100%, with the mean value of 60.56%. The average wind speed was 1.99 m/s. And the temperature ranged from –17°C to 25°C, with the average value of 7.74°C. The average maximum temperature was 18.13°C, the minimum temperature was 5.81°C, and the average daily temperature difference was 12.32°C. Lanzhou is located in the geometric center of China's land plate, in the Yellow River Valley Basin on the Northwestern side of the Qinghai-Tibet Plateau, facing three mountains and narrow east-west, which forms the unique landform and meteorological conditions. Thus, the diffusivity of air pollutants are greatly reduced. In addition, the petrochemical industry, the rapid growth of car ownership and the surrounding fragile ecological environment make air pollution gradually worsen in Lanzhou.

### 4.2 Pathogenic Characteristics Of ASOM

Our study demonstrated that ASOM patients were mainly concentrated in children under 14 years old in Lanzhou. This can be attributed to the anatomical features of the middle ear in children are smaller and shorter than that in adults, and more horizontally aligned Eustachian tubes, and frequent upper respiratory tract infections [13]. The upper respiratory tract plays an important role in filtering and regulating inhaled air. Air is inhaled through the mouth and nose and connected through the nasopharynx. The nasopharynx is connected to the middle ear through the eustachian tube located at the back of the nasopharynx. This direct connection with the middle ear makes the connection between air and the middle ear. As a continuation of the upper respiratory tract, the middle ear mucosa is closely related to respiratory diseases, so the occurrence of ASOM is directly related to respiratory diseases. Many studies have showed that with the aggravation of air pollution, the probability of children suffering from respiratory diseases also increases[17]. Furthermore, air pollution can lead to changes in children's immune function and more prone to inflammation. Meanwhile, we also found that there were more male ASOM patients than female ASOM patients, and male patients were 1.16 times as many as female patients, this is consistent with the literature report[15]. Which may be related to

the higher incidence of acute respiratory infections in male patients, or to the sex ratio of infants born in China. Further large-scale epidemiological studies are needed to determine what factors contribute to this difference. The incidence of respiratory tract infection in children mentioned in some literatures is higher in males than in females.

Seasonal distribution showed that the daily number of ASOM visits in summer was significantly less than that in other three seasons, which is consistent with other findings that OM is more common in winter than in summer[16]. The reason may be that there is more rain in summer, nasal mucosa is wet and eustachian tube cilia are moving well, which cause the incidence of ASOM is relatively low. We also found the largest number of ASOM visits occur in December of each year. One important reason is the cold weather in winter, a large number of coal combustion heating and heavy industry operation lead to more serious air pollution, and  $PM_{2.5}$ ,  $PM_{10}$ ,  $CO$ ,  $NO_2$ ,  $SO_2$  are higher than other three seasons, bad climate conditions and human susceptibility body, air pollutants with bacteria and (or) viruses will speed up the invasion of the human body. Moreover, the weather is dry in winter, the respiratory mucosa, especially the eustachian tube and nasal mucosa loses water, and the human resistance decreases in winter, air pollutants such as particulate matter  $PM_{2.5}$  and  $PM_{10}$  will adhere to the respiratory mucosa, they will act as allergens to increase the risk of respiratory infection, and the number of ASOM patients is also higher than other seasons[17]. In addition, people mainly live indoors in winter, creating favorable conditions for the spread of the virus, while influenza mainly spreads through the air. Therefore, low winter temperature and upper respiratory tract infection are risk factors for ASOM.

We can also learned that the lowest number of patients in August, followed by February. On the one hand, the air quality from June to August is better. On the other hand, the students have summer vacation in August. February is the next lowest month for ASOM visits, which is contrary to what we think is the visits increase in winter. We believe that this result is in line with the characteristics of big cities in China. February is usually the Chinese Lunar New Year and the winter vacation for students. A large number of people who usually work in big cities return home for the New Year or go out for tourism, the number of people in the city and the total number of hospital visits have been reduced, which makes the high incidence month of ASOM become a relative low throughout the year.

#### 4.3 Ambient Air Pollution And ASOM

The current research reports that there is a significant statistical correlation between the improvement of air quality and the reduction of ear infection rate. Deng et al. [18] reported that the incidence of OM in urban was higher than that in rural, and urban pollution was more serious than that in rural areas. Heinrich et al think that tobacco exposure and air pollution are both important environmental risk factors for OM, while cdcers and others think that air pollution and low socioeconomic status are more likely to be risk factors for AOM than parents smoking[19]. Although prior studies have demonstrated associations between high ambient air pollutants and OM, these have been small, short-term studies of population cohorts outside the Chinese, and there is no report on the impact of air pollution on the incidence of ASOM and which pollutants can cause or aggravate ASOM. This study We found  $PM_{2.5}$ ,  $PM_{10}$ ,  $CO$ ,  $NO_2$ ,  $SO_2$  have positive correlations with the daily number of ASOM visits. The nasopharynx is connected to the middle ear through the eustachian tube located at the back of the nasopharynx. This direct connection with the middle ear is linked to the blast and the middle ear. Larger airborne particles( $PM_{10}$ ) are dissolved or otherwise trapped by the nasal mucosa and transported to the back of the nasopharynx, where they are either swallowed or expectorated[20]. However, other pollutants in the air, such as gases ( $NO_2$ ,  $CO$ ) and particles less than  $2.5 \mu m$  in diameter ( $PM_{2.5}$ ) can enter the airways and lungs through the nasopharyngeal cavity. In view of the direct connection between the nasopharynx and middle ear, these pollutants may interact with Eustachian tube epithelium. These epithelial cells includes columnar ciliated cells whose hairy appendages are called cilia, which beat rhythmically along the nasopharynx and participate in mucociliary clearance and middle ear fluid drainage. Animal studies provide evidence that air pollutants, such as sulfur dioxide ( $SO_2$ ), impair the mucociliary function of the eustachian tube and increase mucus secretion in the middle ear [21]. Similarly, epidemiological evidence supports the link between air pollution and ASOM. Many studies have reported health effects of  $O_3$  has a strong potentially adverse health effects on various respiratory symptoms such as, dyspnea, upper airway irritation, coughing, and chest tightness[22]. However, no significant association between  $O_3$  and the prevalence of ASOM was observed in Lanzhou. Research on harmful effects of  $O_3$  is rare in China, so further studies are needed.

To identify possible time-delay on air pollutant health effect in the clinical manifestation of symptoms, we analyzed the lag effects of air pollutants and meteorological factors on the daily number of ASOM visits. Single lag days were selected for 1–14 days (Lags 1–14, L1-L14). There was no statistical significance after the 7th day, so Table 5 only showed lag 1–7 data. The multi-day were selected for 1–14 days (Lags01-014, L01-L014). When running the model, we also consider the data of each factor after 14 days, but the correlation is very small. Therefore, the lag results of more than 14 days are not included in Table 6. As for single lag effects, there was a positive correlation between  $PM_{2.5}$ ,  $PM_{10}$ ,  $CO$ ,  $NO_2$ ,  $SO_2$  and the daily number of ASOM visits, but the correlation between  $O_3$  and ASOM did not pass the significance test. The strongest lag effects of  $PM_{2.5}$ ,  $PM_{10}$ ,  $SO_2$ ,  $CO$ ,  $NO_2$  were at lag6, lag3, lag3, lag6 and lag7. In an Canadian study, Zemek et al. reported associations between exposure to  $NO_2$ ,  $PM_{10}$ ,  $O_3$  and OM, and  $NO_2$  (lag 2 and 3 days),  $PM_{10}$  (lag 2 and 4 days), and  $O_3$  (lag 1 day) [6]. And the largest effect RRs and 95% confidence interval of  $PM_{2.5}$ ,  $PM_{10}$ ,  $CO$ ,  $NO_2$ ,  $SO_2$  were(1.0064,1.0050–1.0078), (1.0027,1.0012–1.0042),(1.3807,1.2242–1.5372),(1.0085,1.0062–1.0108),

(1.0095,1.0061–1.0129) respectively. As for cumulative lag effects,  $PM_{2.5}$ ,  $PM_{10}$ ,  $CO$ ,  $NO_2$  had lagging effects on the daily number of ASOM visits, but the correlation between  $SO_2$  and  $O_3$  did not pass the significant test. The largest associations of  $PM_{2.5}$ ,  $PM_{10}$ ,  $CO$ ,  $NO_2$  were observed at lag0-13, lag0-14, lag0-6 and lag0-6. A study conducted in Beijing, China, showed that the best fits for  $PM_{2.5}$ ,  $PM_{10}$ ,  $CO$  and  $NO_2$  were same day visit (lag 0–3)[8]. The largest RRs and 95% confidence interval of  $PM_{2.5}$ ,  $PM_{10}$ ,  $CO$ ,  $NO_2$  for multi-day lags were(1.0112,1.0094–1.0134),(1.0035,1.0021–1.0049),(1.3059,1.2017–1.4101), (1.0135,1.0103–1.0157), respectively. Generally speaking, environmental and meteorological factors had single-day and multi-day lag effects on the daily number of ASOM visits, and the impact of single-day lag effects are greater than that of multi-day lag effects ( $P < 0.01$ ).

We also found that the daily number of ASOM visits were negatively correlated with temperature. That means the lower the temperature, the higher the incidence of ASOM. The common pathogens causing ASOM include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, respiratory

syncytial virus and rhinovirus. Numminen et al. found that dry and cold season is more conducive to the spread of *Streptococcus pneumoniae*, so the incidence of AOM increases at low temperature[24]. Old thorium studies such as Kim also found that there was a significant positive correlation between *Streptococcus pneumoniae* infection and temperature below 24°C, and the incidence of respiratory syncytial virus infection was higher in winter than in other seasons[25]. In addition, we also found that the incidence of ASOM had a positive correlation with ATM, the reason may be that the Eustachian tube also allows air exchange and pressure balance. When inflammatory agents such as viral or bacterial pathogens, allergens, pollutants and other irritants interact with the nasal mucosa, resulting inflammation can narrow or block the Eustachian tube. Dysfunction in the Eustachian tube can lead to middle ear fluid stasis and subsequent ASOM. The increase of external pressure will cause the increase of pressure in the middle ear cavity, which will induce and aggravate the occurrence of ASOM. The single-day lag effects showed that there is no lag effect between W, RH, ATM and daily number of ASOM visits, but the Multi-day lag effects showed that there has lag effect between W, ATM and daily number of ASOM visits, which has no reasonable explanation and needs further study. The results of single lag and cumulative lag showed that there was no correlation between O3 and the number of visits per day in ASOM. Overall, meteorological factors have less impact on the daily number of ASOM visits than air pollutants.

The shape of exposure-response correlation reflects the potential health effects of atmospheric pollutants and meteorological factors on ASOM. In this study, In this study, we found different exposure-response curves of air pollutants and meteorological factors to the daily number of ASOM visits. At present, no scholar has studied the exposure-reaction relationship between air pollutants and meteorological factors to ASOM, which needs further research to prove.

#### 4.4 Biological Mechanism Of ASOM

Although the specific mechanism of air pollutants causing ASOM is unclear, animal studies have shown that air pollutants can inhibit mucociliary clearance of respiratory epithelium, which may have similar effects due to the similar histology of middle ear mucosa. On the one hand, air pollutants can destroy the nasal mucosal epithelial barrier, increase the contact opportunity and time between pollutants and upper respiratory mucosa, and induce and aggravate the occurrence of ASOM. For example, SO<sub>2</sub> stimulates mucus secretion in the proximal exposed part of the middle ear and impairs ciliary body function in the distal exposed part. On the other hand, air pollutants are small in volume, easy to combine with mucosal water to produce various products, enhance the permeability of respiratory epithelium, and improve the sensitivity and contact opportunity of mucosal epithelial cells with allergens. In addition, contaminants adhere to the cell surface, resulting in disordered cell arrangement and the destruction of the structure of ciliated cells. It can reduce the activity of mucosal epithelial cells, induce the synthesis and release of inflammatory cytokines, induce apoptosis through oxidative stress, and destroy the barrier function of mucosal epithelial cells. The incidence of allergic rhinitis increases, which indirectly affects the incidence of ASOM. On the other hand, it has been reported that air pollutants can increase the incidence of rhinitis and sinusitis [26]. Sinusitis is one of the main causes of otitis media. The retrograde transport of purulent secretions by nasal cilia leads to eustachian tube edema and nasopharyngeal infection into the middle ear, which leads to the irremovable secretions of the middle ear cavity. It is the mechanism of otitis media caused by sinusitis. Therefore, the increase of air pollutant concentration can indirectly increase the incidence of ASOM. Mostly, exposure to air pollution can lead to immune and inflammatory dysfunction and increase the risk of allergic rhinitis [23]. Andrianifahanana et al. [27] showed that the incidence of OM in patients with allergic rhinitis was high, because nasal lesions such as inflammation and allergy were the main causes of dysfunction of eustachian tube, and dysventilation and drainage of eustachian tube were also directly related to the occurrence of ASOM. However, not only in low income countries, wood heaters or fire places are also common in some developed countries. Studies have shown that the results of increased exposure to wood smoke and OM risk are consistent with the toxicological effects of wood smoke on respiratory epithelial cells [28,29]. In the experimental study, the composition of wood smoke increased oxidative stress in epithelial cells [30]. Recent experimental studies have shown that human respiratory cells exposed to particulate matter from beech sawdust smoke have cytotoxic and genotoxic effects comparable to those produced by diesel engines [31]. As true upper respiratory mucosa, middle ear mucosa has similar mechanism of causing ASOM.

## 5. Conclusions

This study provided evidence of the adverse effect of ambient air pollution on ASOM in Northwestern China. We analyzed the distribution characteristics of air pollutants and meteorological factors in Lanzhou from 2014 to 2016, and the correlation between air pollutants and meteorological factors. We also examined the lag effects of air pollutants, meteorological factors and the possible differences of air pollutants, meteorological factors on the daily number of ASOM visits that were consulting the hospital for treatment for ASOM over a period of 3 years. The results showed that the daily number of ASOM visits had obvious seasonal differences. The air pollutants positively correlated with the daily number of ASOM visits, and had lag effects on the daily number of ASOM visits, temperature is negatively correlated with the daily number of ASOM visits. RR in the number of ASOM visits increased with air pollution level. There are also some limitations to our study. The data at the moment are so sparse that we are not in a position to provide any far-reaching conclusion yet. Further experimental studies are needed to prove. With the continuous rapid urbanization process, more people are becoming exposed to high levels of air pollution. Environmental control and public health strategies should be enforced by the health service policy makers to address this increasingly challenging problem. During haze events, both the health care provider and the public should be given real-time alerts on air quality. The affected population should be appropriately advised and treated. Winter is the most important season when alerts need to be raised regarding the cost of health systems for ASOM and air pollution from straw burning in Northwestern China.

## Declarations

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## Figures

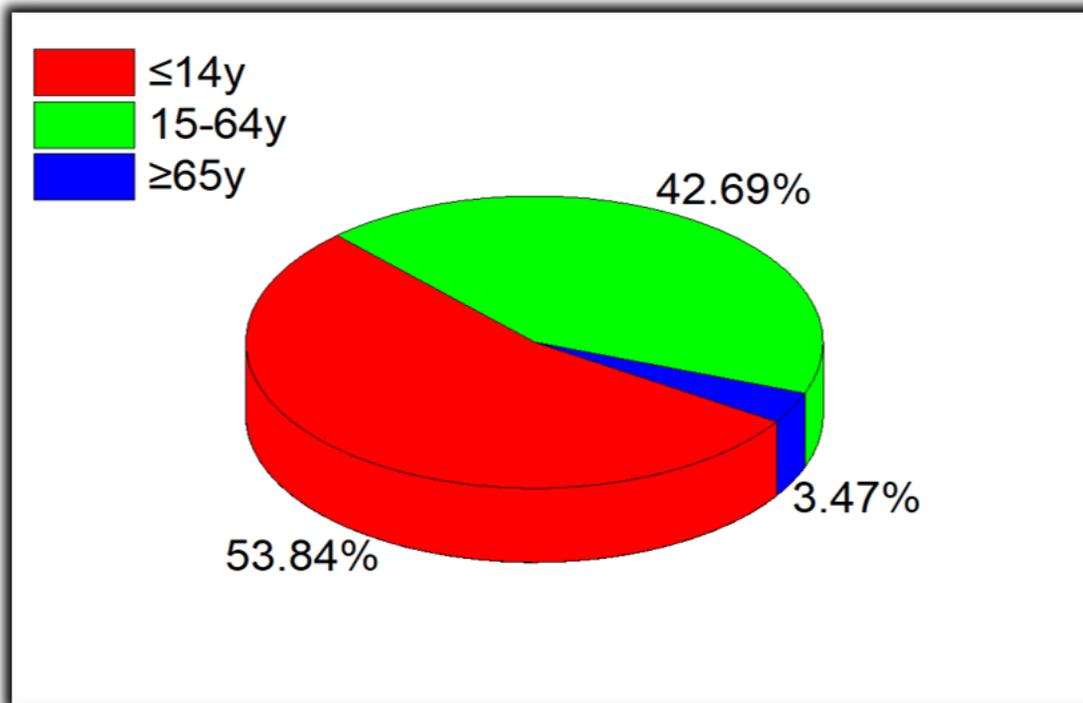


Figure 1

Age distribution of ASOM from 2014 to 2016 in Lanzhou

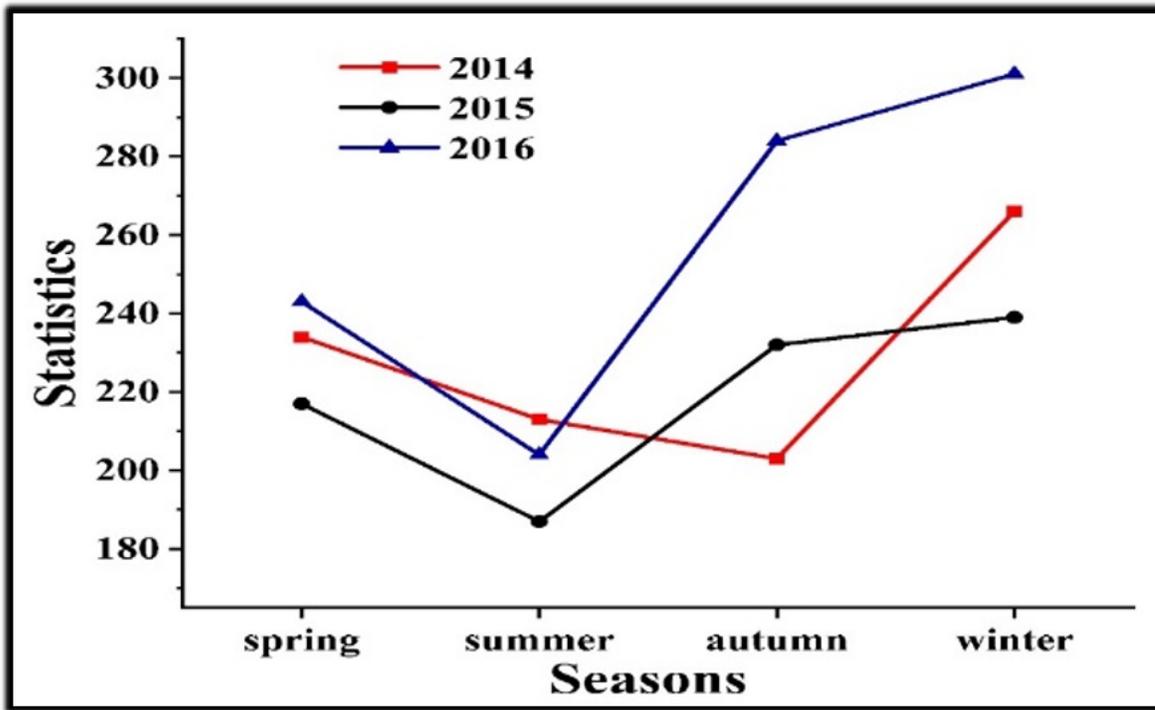


Figure 2

Different seasons ASOM visits during 2014-2016 period in Lanzhou

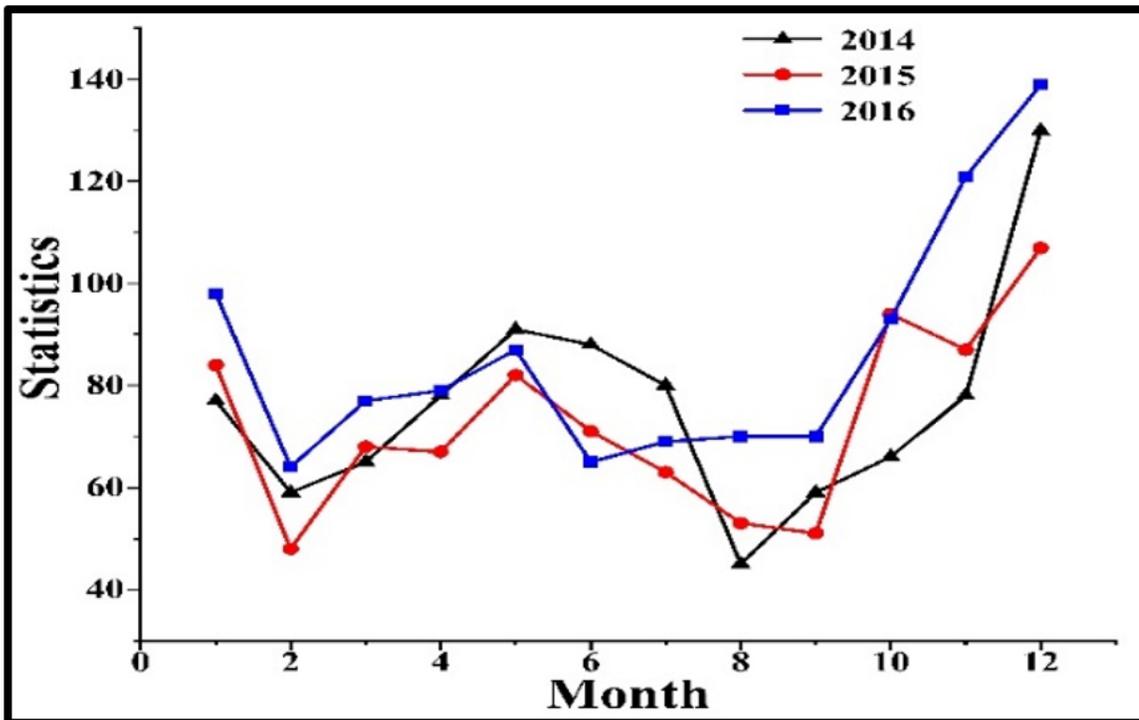
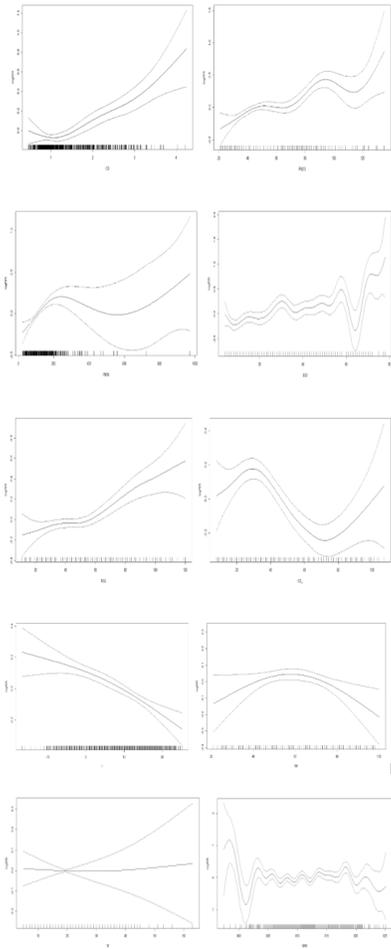
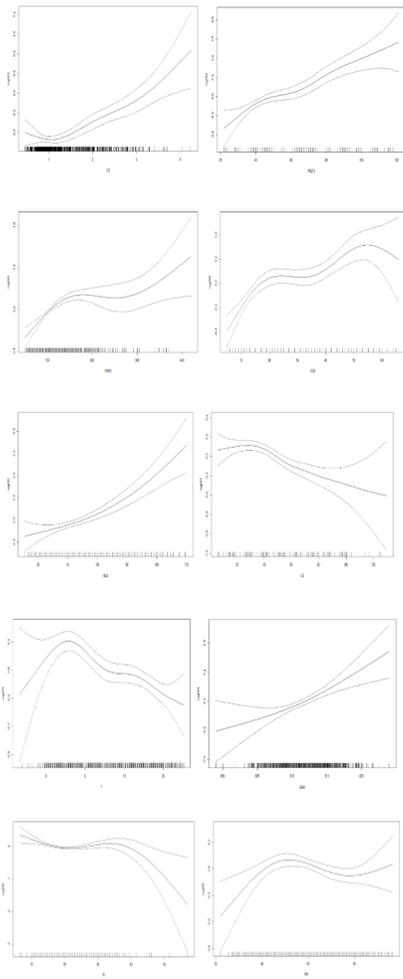


Figure 3

Distribution of ASOM visits in different months from 2014 to 2016 in Lanzhou



**Figure 4**  
 Presents the Single-lag exposure-response relationships for air pollutants and meteorological factors with hospital visits for ASOM , the solid line represents logarithmic relative risk (log RR) and the dashed line represents 95% confidence interval (CI). [BAR=ATM]



**Figure 5**  
 Presents the cumulative lag exposure-response relationships for air pollutants and meteorological factors with outpatient visits for ASOM in Lanzhou, China (2014–2016), the solid line represents logarithmic relative risk (log RR) and the dashed line represents 95% confidence interval (CI). BAR(=ATM) 3.5 Relative risk

### Supplementary Files

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- [Tables78.docx](#)