

RESEARCH ARTICLE

Risk of temperature, humidity and concentrations of air pollutants on the hospitalization of AECOPD

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Data Availability Statement: Fine particulate matter (PM_{2.5}), sulfur dioxide (SO₂), nitrogen dioxide (NO₂), ozone (O₃) and inhalable particle (PM₁₀) were collected from Shenyang Environmental Protective Bureau. Daily average temperature, daily average wind speed and daily average relative humidity were attained from the Shenyang Meteorology Bureau. Meteorological and air pollution data are available as Supporting Information files. The hospitalization record was obtained from the Shenyang Medical Insurance Bureau and cannot be publicly shared by the

Abstract

Aim

To investigate the effect of temperature, humidity and the concentration of ambient air pollution on the hospitalization of AECOPD.

Method

Hospitalization record was obtained from Shenyang Medical Insurance Bureau, concluding patient's age, gender, income hospital time, outcome hospital; Generalized additive model was used to analyze the relationship between temperature, humidity, the concentration of ambient air pollution and the hospitalization of AECOPD.

Result

The effect of ozone on admission rate in male group was higher than that in female group. Ambient air pollution had a weak influence on age \leq 50 group. It was found that the optimal lag day for daily relative 40 humidity to age \leq 50 group, 50 $<$ age \leq 60, 60 $<$ age \leq 70 group and age $>$ 70 group was on lag5, lag4, lag4 and lag5, respectively.

Conclusion

Air pollution, relative humidity and temperature can increase the risk of admission for acute exacerbation of COPD, and in this process there was a lag effect.

authors. Interested researchers may contact the Shenyang Medical Insurance Bureau through the website: ybj.shenyang.gov.cn/.

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Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; CI, confidence interval; NO₂, nitrogen dioxide; O₃, Ozone; PM, particulate matter; RR, relative risk; SO₂, sulfur dioxide.

Introduction

Environmental problems has become one of public problems in the world, ambient air pollution has been put closer attention to, which has aroused public's health and environmental awareness. More epidemiological investigations have proved that ambient air pollution such as particulate matter (PM_{2.5} and PM₁₀), sulfur dioxide (SO₂), nitrogen dioxide (NO₂) and ozone (O₃), can cause acute inflammatory injury of respiratory tract and exacerbate pulmonary chronic diseases[1–3]. One study showed that fine particulate matter (PM_{2.5}) with oxidized organic material was associated with a greater inflammatory response, which increased the amount of neutrophil and the level of CXCL-1 and TNF- α protein[4]. The published research proved that after the particulate matter (PM) was engulfed by alveolar macrophages, the airway inflammatory mediators increased, such as interleukin (IL)-6 and IL-18, which could lead to more inflammatory cell infiltration and airway mucus secretion[5]. A study showed that when Sprague-Dawley rats exposed to SO₂ acutely, acute inflammation with neutrophil and macrophage airway infiltration was presented and inflammatory infiltrates remained in lung tissue for at least 14 days[6]. Previous research has established that NO₂ exposure could induce pulmonary inflammatory response, mucus formation, and Th1/Th2 imbalance in control group [7]. It was reported that sex differences in acute O₃-induced airway physiology responses and airspace influx without significant difference in other injury and inflammation measures[8].

Another research has demonstrated that per 10ug/m³ increase for SO₂ was linked to -3.37 (95% confidence interval, CI, -5.39- -1.30) percent variation for forced expiratory volume after one second[9]

Furthermore, published reports have shown that meteorological factors such as temperature and barometric pressure, have a negative influence on respiratory diseases[10,11]. A study conducted in Hong Kong demonstrated that per 1 °C increase in wintertime was associated with 1.20% (95% CI, 1.08–1.32) increase for total respiratory diseases hospitalization and 1.41% (95% CI, 1.15–1.71) increase for COPD hospitalization[12].

Shenyang, located in northeast China (123.38E, 41.8N), is the economic, cultural and transportation center in northeast China, which has suffered from severe air pollution for many years. In recent years, the minimum temperature in Shenyang Winter was below -20 degrees Celsius and the maximum temperature in summer was over 35 degrees Celsius. This paper purposed to estimate the effect of ambient air pollution and meteorological factors on AECOPD hospitalization in Shenyang.

Materials and methods

Hospitalization record was obtained from Shenyang Medical Insurance Bureau, concluding patient's age, gender, income hospital time, outcome hospital, work place and residence place. All this hospitalization data was only used to explore the effect of air pollution on AECOPD. And we had signed a confidentiality agreement, and this part of the data will not be disclosed. Fine particulate matter (PM_{2.5}), sulfur dioxide (SO₂), nitrogen dioxide (NO₂), ozone (O₃) and inhalable particle (PM₁₀) were collected from Shenyang Environmental Protective Bureau. Daily average temperature, daily average wind speed and daily average relative humidity were attained from Shenyang Meteorology Bureau.

In this paper, generalized additive model with the link function of Poisson distribution was used to estimate the influence of air pollution on relative risk (RR) of hospitalization for acute exacerbations of chronic obstructive pulmonary disease (AECOPD)[13]. Patients who met the following criteria were included: (1) resided and worked in the study area during study period and (2) were admitted for AECOPD. People who met the following were excluded (1) not

resided and worked in Shenyang during study period; (2) patients with duplicate records; and (3) patients admission within more than once among a week.

Stratification analysis based on age was divided to four group (age ≤ 50 group, 50 < age ≤ 60 group, 60 < age ≤ 70 group and age > 70 group), considering the sensitivity and tolerance to different group for temperature change, humidity change and air pollution were different. Stratification analysis based on gender was divided to two group: male group and female group.

$$\text{Log}[E(y_t)] = \alpha + \beta_1 x_i + ns(\text{Temperature}, 3) + ns(\text{Humidity}, 3) + ns(\text{Wind}, 5) + ns(\text{Time}, 4) + ns(\text{Pressure}, 5) + \beta_2 \text{factor}(\text{DOW}) + \beta_3 \text{factor}(\text{Holidays}) \tag{1}$$

where α is the intercept value; β_1 , β_2 and β_3 are regression correlations; $E(y_t)$ represents the expected number of daily hospital admissions at day t ; x_i is the daily air pollutant concentration; Temperature is daily average temperature; Humidity is the daily relative humidity; Pressure is the daily average pressure; Wind is the daily average wind speed; DOW is a dummy variable for the day of the week; ns represents a smoothed function [14,15]. Results are displayed as percentage change in relative risk (RR) of hospitalization and its 95% confidence intervals (CI) for a 10 $\mu\text{g}/\text{m}^3$ increase in daily ambient air pollution concentration. Furthermore, we investigate the relationship between AECOPD and daily average temperature and relative humidity. Where X_i represents daily average temperature and relative humidity. (2)

$$\text{Log}[E(y_t)] = \alpha + \beta_1 X_i + ns(\text{Wind}, 5) + ns(\text{Time}, 4) + ns(\text{Pressure}, 5) + \beta_2 \text{factor}(\text{DOW}) + \beta_3 \text{factor}(\text{Holidays}) \tag{2}$$

Results

Descriptive statistical results of daily ambient air pollution and meteorological factors from 2014 to 2018 were showed in Tables 1 and 2. Table 3 demonstrated the population amount of

Table 1. Descriptive statistics for daily air pollution in Shenyang, China from 2014 to 2017.

Variable($\mu\text{g}/\text{m}^3$)	X±S	Min	P ₂₅	P ₅₀	P ₇₅	Max	IQR
PM _{2.5}	60±50	4	30	46	77	848	47
PM ₁₀	102±67	8	59	87	126	912	67
SO ₂	52±55	3	15	133	146	333	131
NO ₂	43±17	13	30	39	52	125	22
O ₃	58±33	9	32	53	78	218	46

Min: minimum; Max: maximum; IQR: inter quartile range; X: mean value; S: standard deviation

<https://doi.org/10.1371/journal.pone.0225307.t001>

Table 2. Descriptive statistics for daily meteorological factors in Shenyang, China from 2014 to 2017.

Meteorological Factors	X±S	Min	P ₂₅	P ₅₀	P ₇₅	Max	IQR
Temperature (°C)	9±13	-25	-3	11	21	30	24
Humidity (%)	46±26	2	17	51	67	98	50
Pressure (hPa)	1017±71	987	1008	1016	1025	1041	17
Wind Speed(Km/h)	8±3	2	6	8	10	26	4

Min: minimum; Max: maximum; IQR: inter quartile range; X: mean value; S: standard deviation

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Table 3. The amount of AECOPD hospitalization based on the stratification of age and gender.

AECOPD		
Total		17592
Gender	Male	9196
	Female	8396
Age(X±S)	age≤50	265
	50<age≤60	1709
	60<age≤70	3742
	Age>70	11876

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AECOPD based on the stratification of age and gender. Fig 1 shows boxplot of daily AECOPD hospitalization during research period. It was found that the amount of group age≤50 was less than the other group. The amount of male group for AECOPD hospitalization was larger than that among female group.

The influence of PM_{2.5}, PM₁₀, SO₂, NO₂ and O₃ on the relative risk of AECOPD hospitalization based on the stratification of gender was shown in Figs 2–6. It was seen from Figs 2 and 3 that there was an obvious lag effect, which was that PM_{2.5} and PM₁₀ had the highest impact on AECOPD admission on lag3 and lag4 compared to the other lag days.

Fig 4 shown that both male group and female group was influenced by SO₂ concentration on the day of admission and female group was more sensitive to SO₂ than male group. The effect of ozone on admission rate in male group was higher than that in female group (Fig 6).

Figs 7–11 demonstrated the effect of air pollution on AECOPD based on the stratification of age. Ambient air pollution had a weak influence on age≤50 group (Figs 7–11). Optimal delay date for PM_{2.5} to 60<age≤70 group and age>70 group both appeared on lag3 (Fig 7).

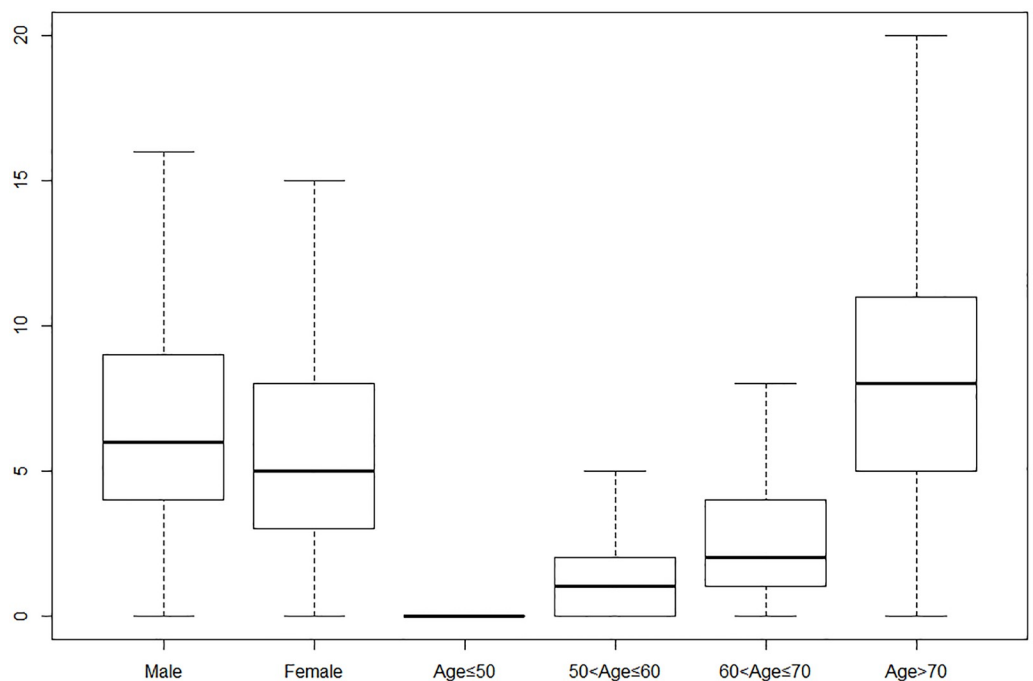


Fig 1. Boxplot of daily AECOPD hospitalization.

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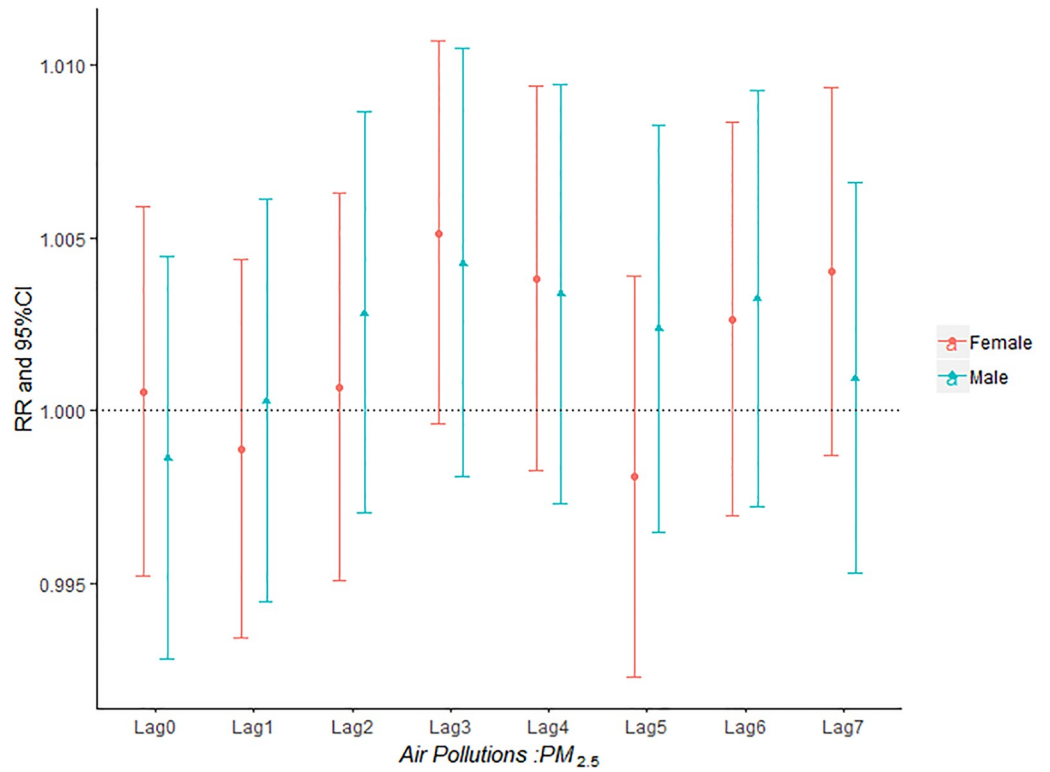


Fig 2. The effect of PM_{2.5} on the relative risk of AECOPD hospitalization based on the stratification of gender.

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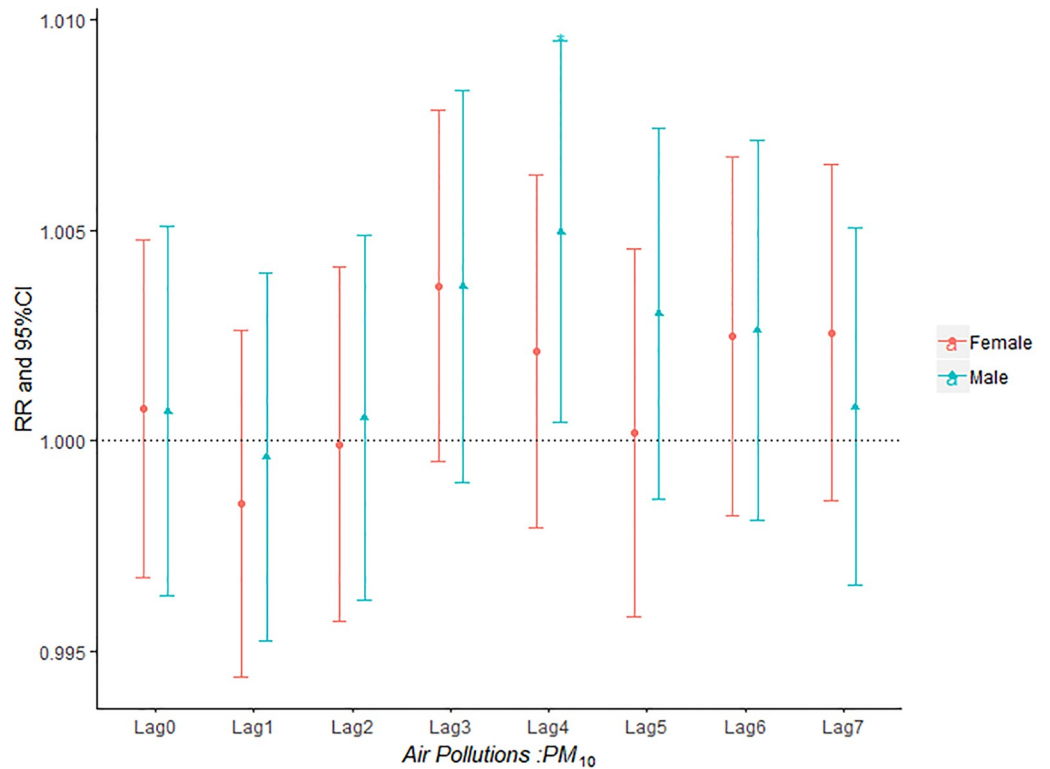


Fig 3. The effect of PM₁₀ on the relative risk of AECOPD based on the stratification of gender.

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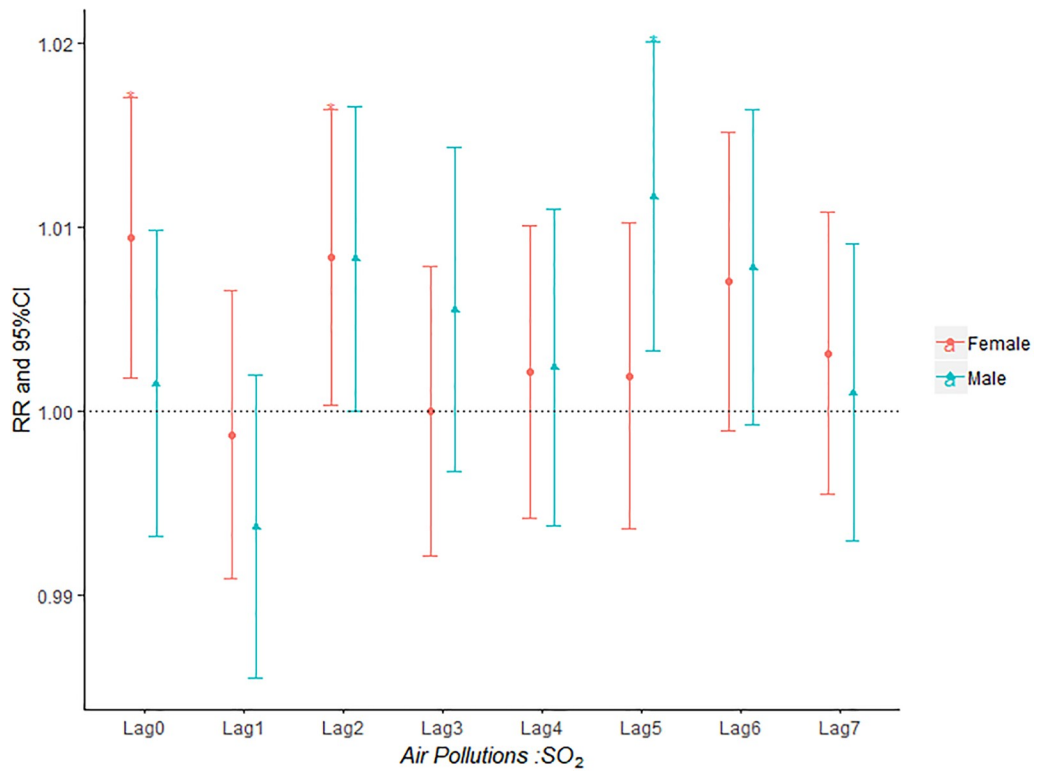


Fig 4. The effect of SO₂ on the relative risk of AECOPD based on the stratification of gender.

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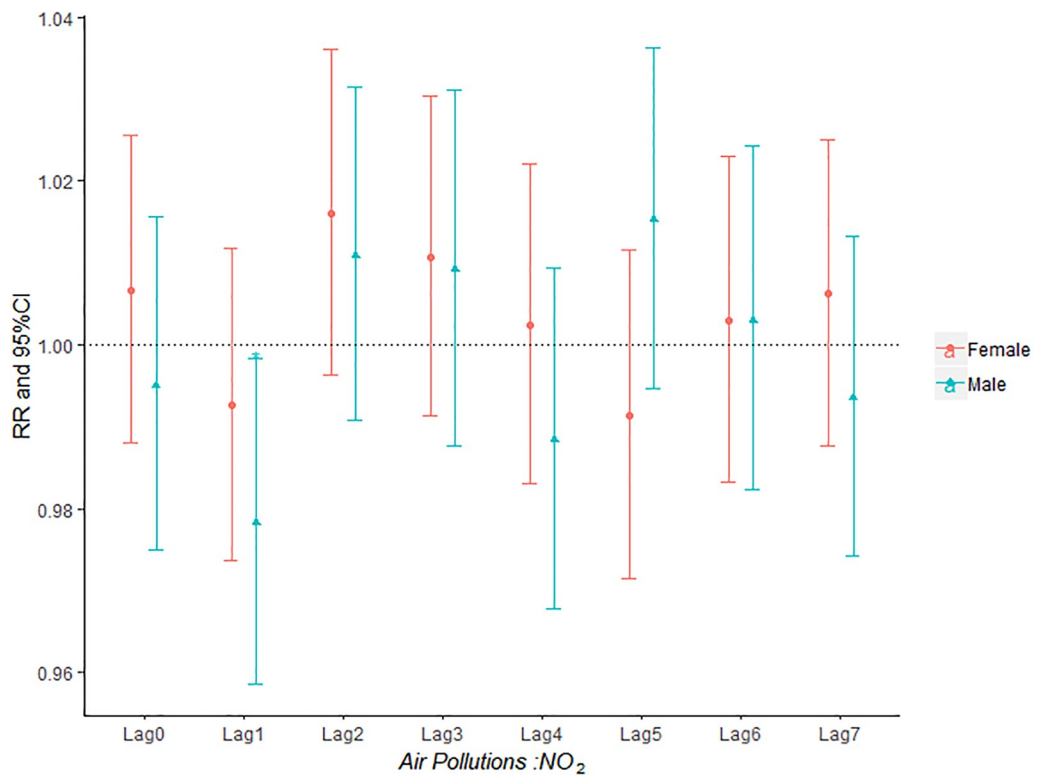


Fig 5. The effect of NO₂ on the relative risk of AECOPD based on the stratification of gender.

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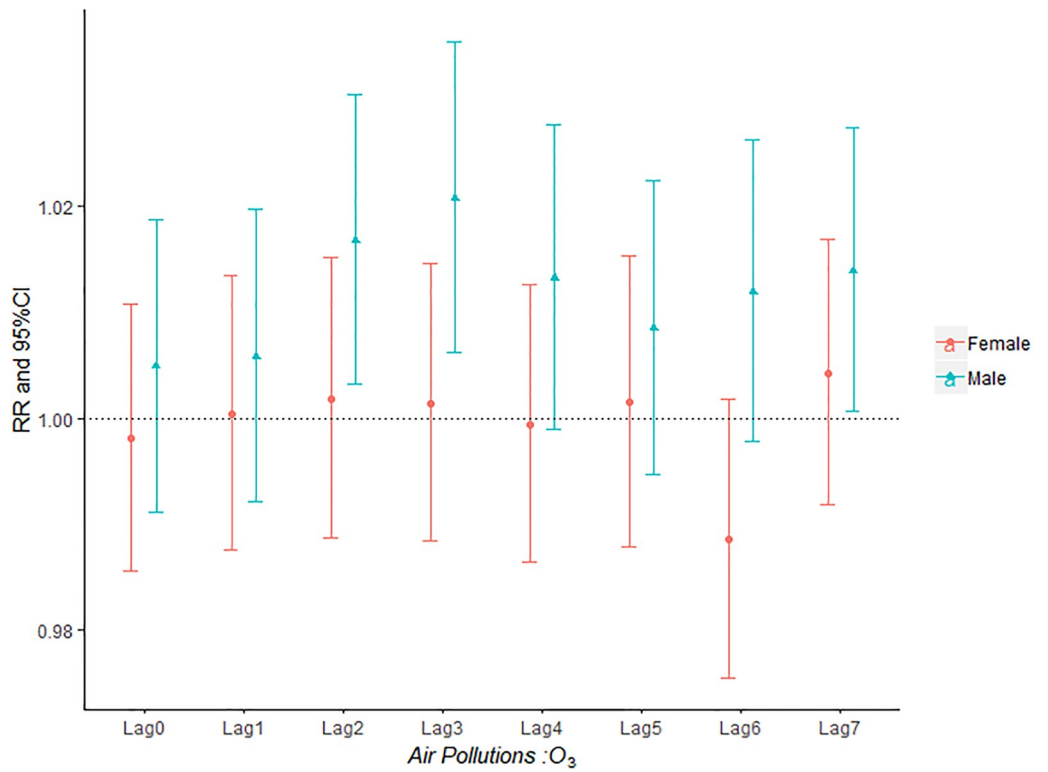


Fig 6. The effect of O₃ on the relative risk of AECOPD based on the stratification of gender.

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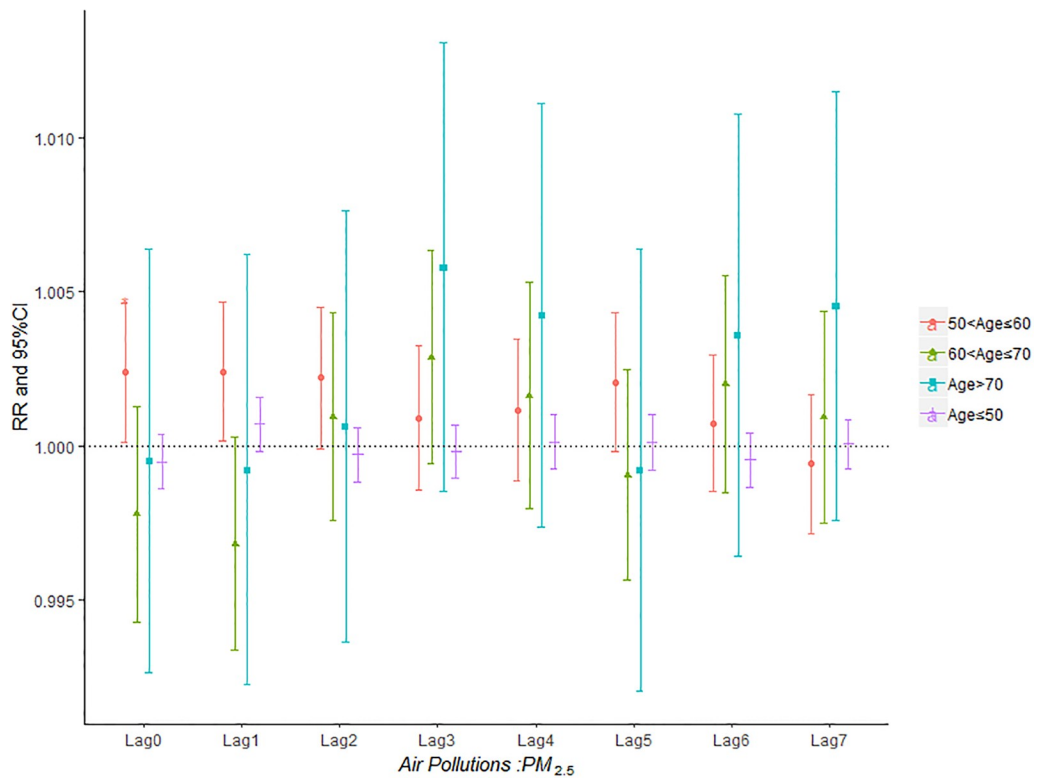


Fig 7. The effect of PM_{2.5} on the relative risk of AECOPD based on the stratification of age.

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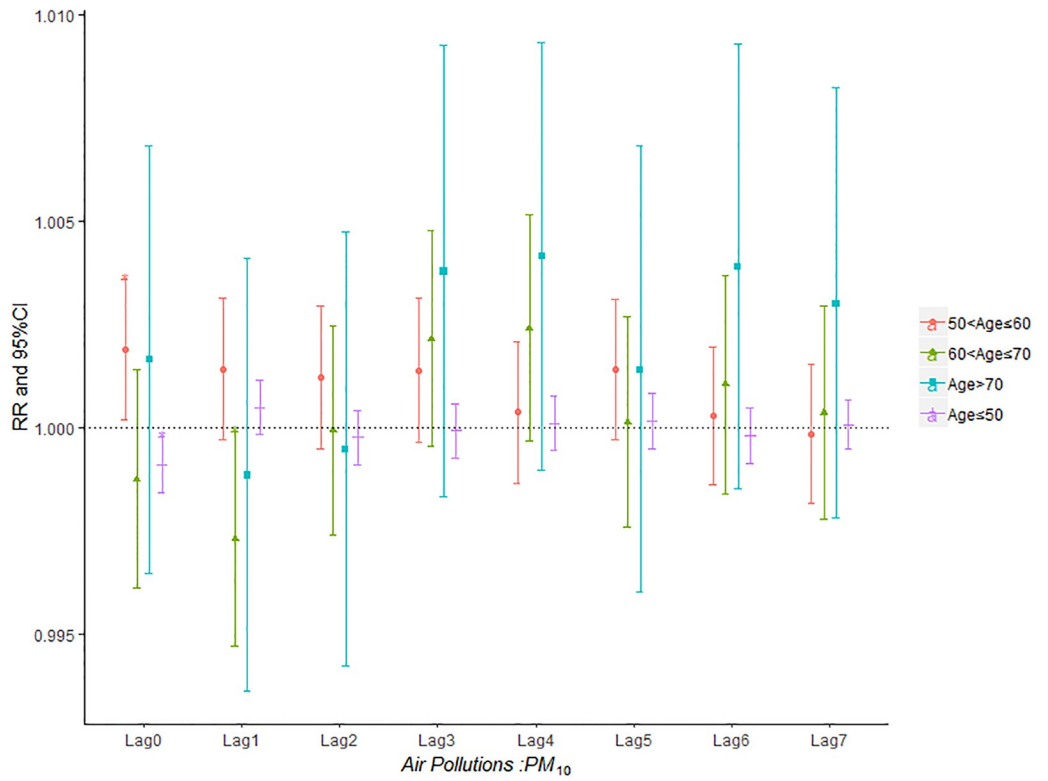


Fig 8. The effect of PM₁₀ on the relative risk of AECOPD based on the stratification of age.

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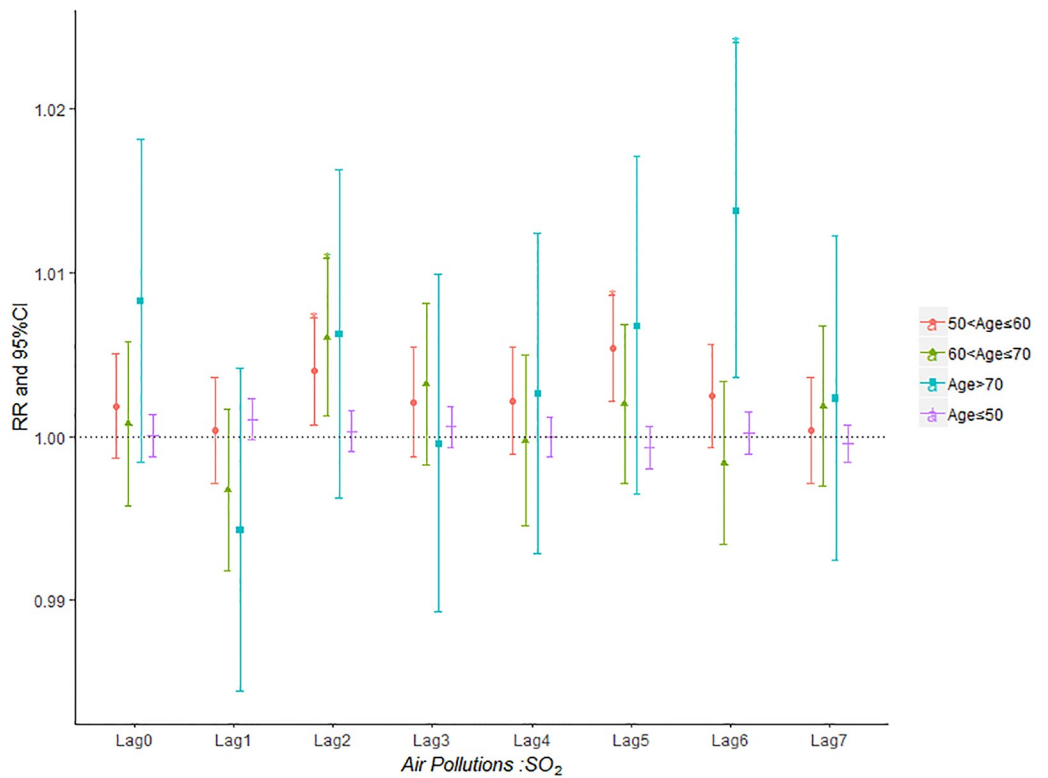


Fig 9. The effect of SO₂ on the relative risk of AECOPD based on the stratification of age.

<https://doi.org/10.1371/journal.pone.0225307.g009>

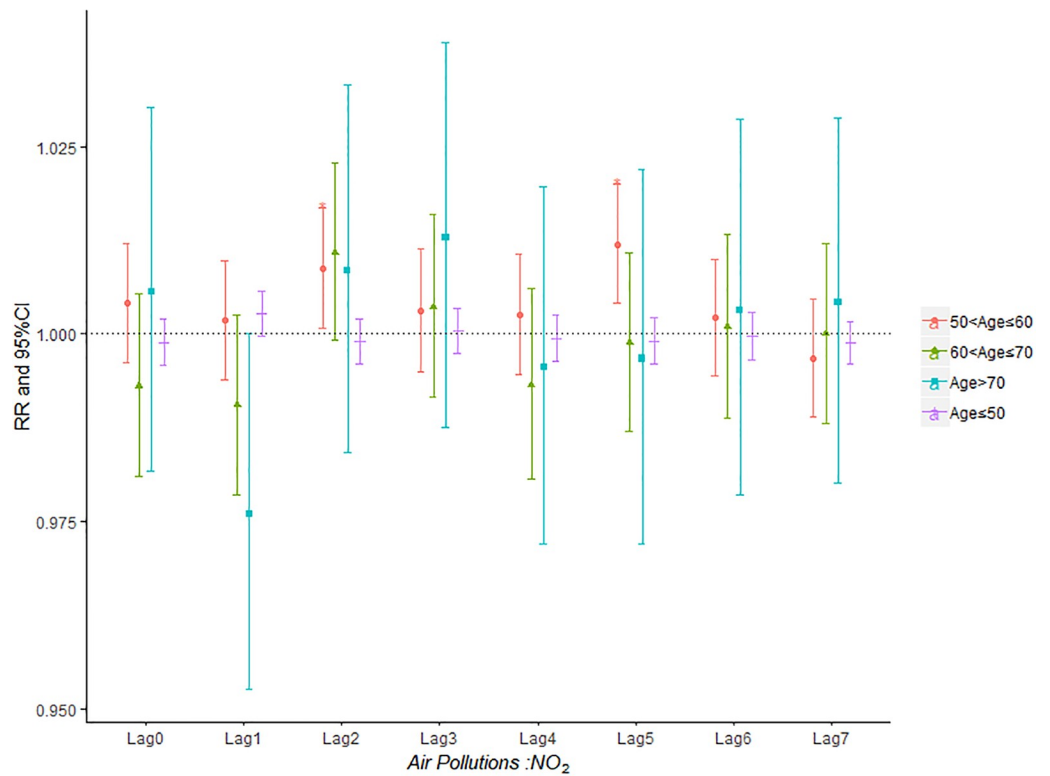


Fig 10. The effect of NO₂ on the relative risk of AECOPD based on the stratification of gender.

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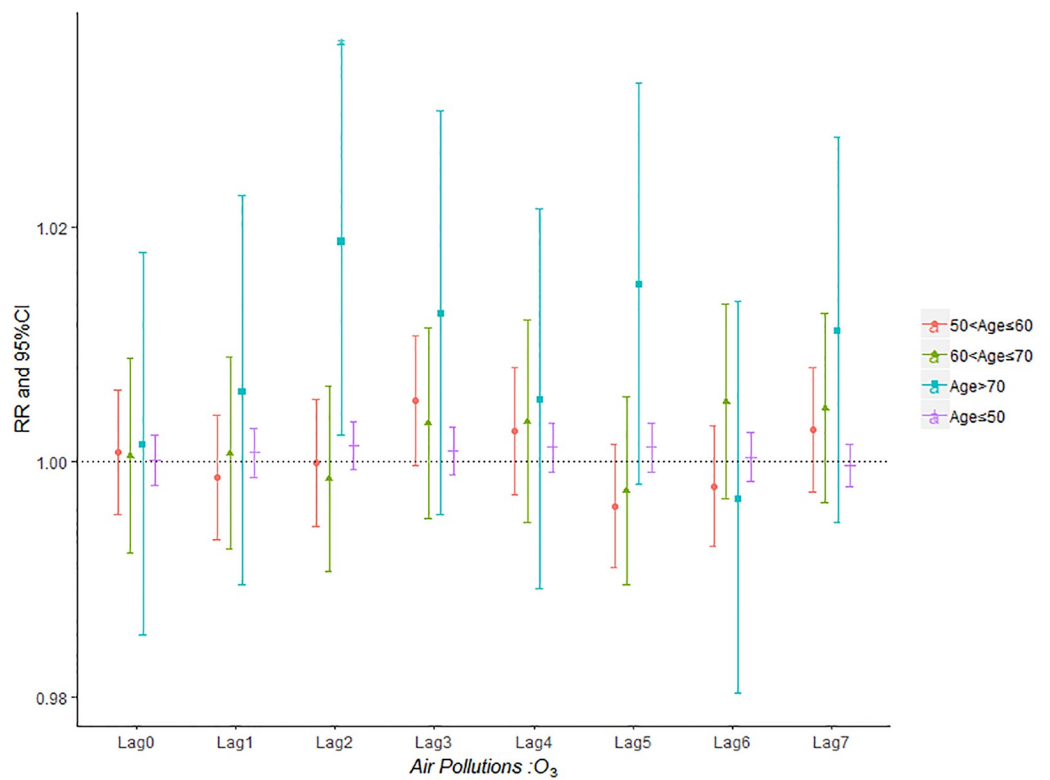


Fig 11. The effect of O₃ on the relative risk of AECOPD based on the stratification of gender.

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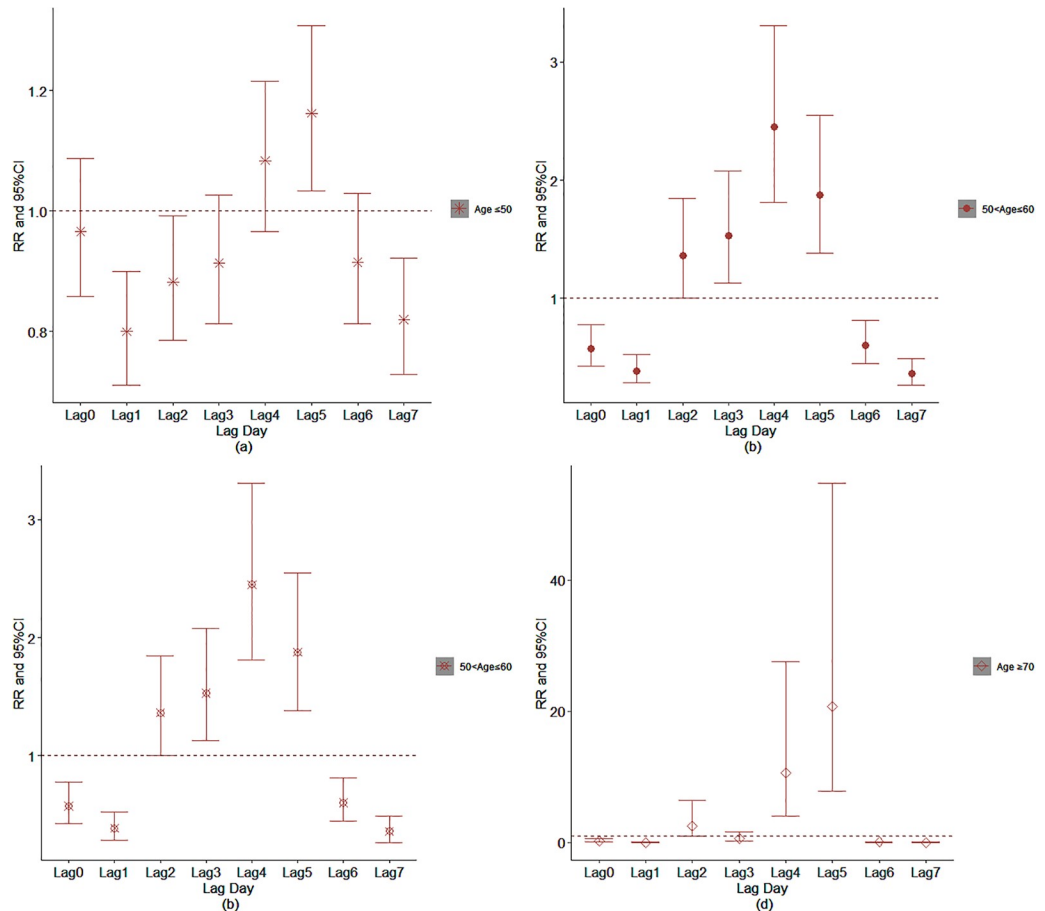


Fig 12. The effect of daily relative humidity on the AECOPD hospitalization based on the stratification of age; (a: Age ≤ 50; b: 50 < age ≤ 60; c: 60 < age ≤ 70; d: Age > 70).

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PM₁₀ could exacerbate 50 < age ≤ 60 group hospitalization risk on lag0-lag6 (Fig 8). The risk due to exposure to SO₂ on lag0, lag2, lag4-6 in the age > 70 group was greater than among the other age group (Fig 9). The change in risk by age group due to O₃ is displayed in Fig 11, revealing that the risk among the age > 70 group on lag2 was higher than that among the other three group.

The effect of daily relative humidity on the AECOPD hospitalization based on the stratification of age was displayed in Fig 12. It was found that the optimal lag day for daily relative humidity to age ≤ 50 group, 50 < age ≤ 60, 60 < age ≤ 70 group and age > 70 group was on lag5, lag4, lag4 and lag5, respectively. Similarly, the optimal lag day for age ≤ 50 group, 50 < age ≤ 60, 60 < age ≤ 70 group and age > 70 group under the influence of daily average temperature occurred on lag5, lag4, lag4 and lag5, respectively (Fig 13). Fig 14 demonstrated the effect of ambient air pollution on the total AECOPD hospitalization.

Discussions

Chronic obstructive pulmonary disease (COPD) has become one of the main contributors to the global burden of disease. It was reported that COPD was the third leading cause of death in China [16]. This paper purposed to investigate the relationship between hospitalization of

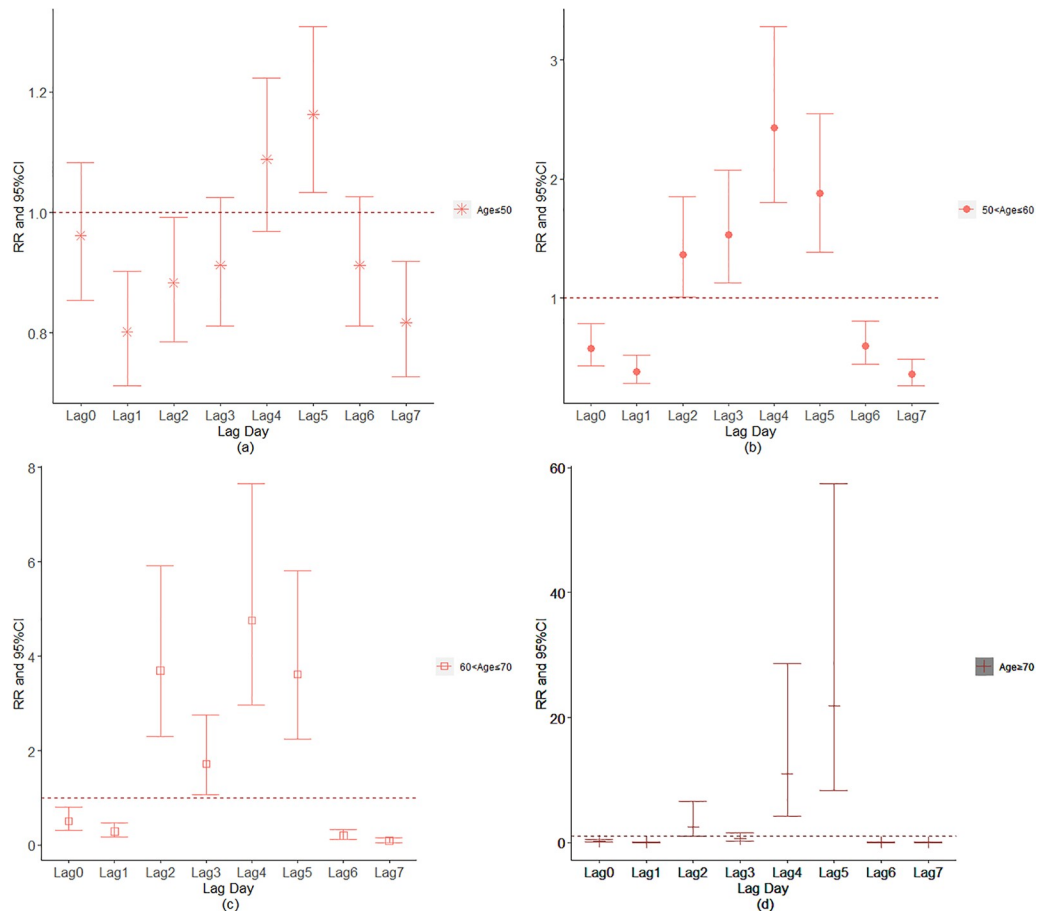


Fig 13. The effect of daily average temperature on the AECOPD hospitalization based on the stratification of age (a: Age ≤ 50; b: 50 < age ≤ 60; c: 60 < age ≤ 70; d: Age > 70).

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acute exacerbations of COPD and ambient air pollution, daily average temperature and daily average pressure.

It was found that there was a delayed effect between the hospitalization of AECOPD and ambient gaseous pollution (PM_{2.5} and PM₁₀). Our results are consistent with previous studies. One research conducted in China, found that the largest effect of PM_{2.5} and PM₁₀ on the AECOPD admission was observed on lag12 (RR, 1.068; 95%CI, 1.017–1.121) and lag10 (RR, 1.031; 95%CI, 1.002–1.060), respectively[3]. Additionally, there was a statistical significance between AECOPD hospitalization and the particulate matter levels of three days before hospitalization[17]. One possible reason, which could be account for this phenomenon, was that particulate matter was attached to the respiratory mucosa or deposited in the bottom of lung after it entering human body, thus which induced pneumonia response and oxidative stress response. This process leads to a delayed effect [13]. When PM entered human’s respiratory tract, its metal component such Zn²⁺, Cu²⁺ and etc. can increase the production of reactive oxygen species (ROS), which damages the dynamic balance of ROS and leads to the imbalance of oxidation-antioxidant mechanism, which could aggravate the symptom of COPD[18]. Exposure to fine particulate matter could cause infiltration of inflammatory cell and increase the release of inflammatory factors such as interleukin, which damage people’s respiratory tract and lung. Suspension of PM_{2.5} was intranasally instilled to rats, it generated higher level

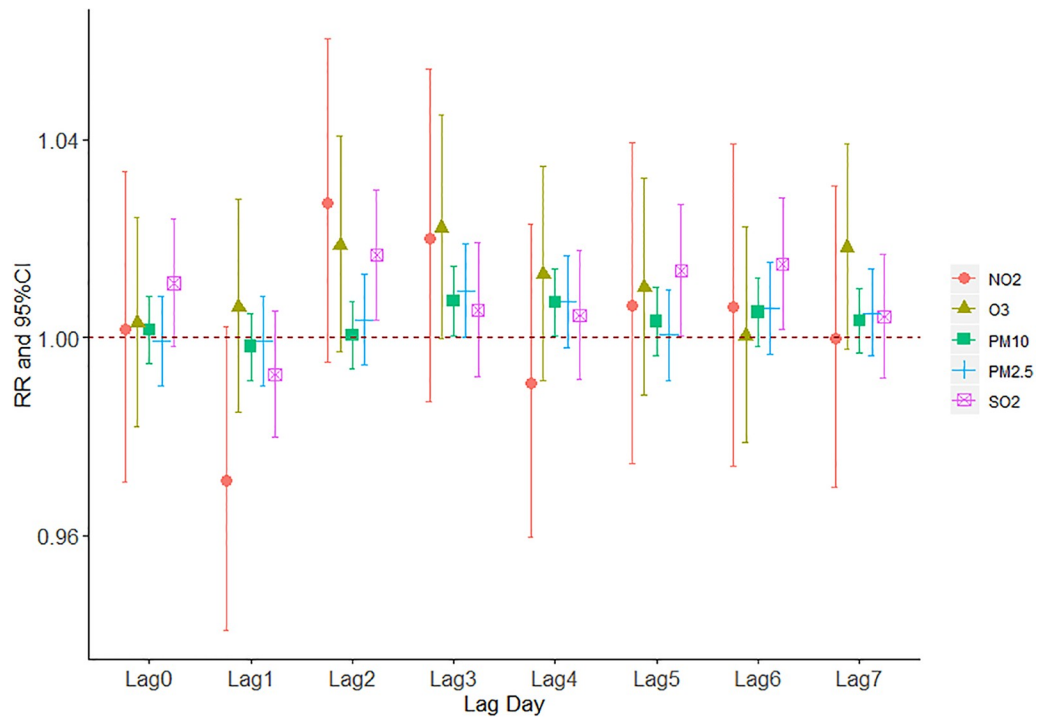


Fig 14. The effect of ambient air pollution on the total AECOPD hospitalization.

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of interleukin-6 and tumor necrosis factor- α and activated the body's immune response. When the human body is exposed to ambient SO_2 , due to its good water-solubility, part of SO_2 dissolved directly in the mucous membrane of the respiratory tract to form SO_3^{2-} , resulting in toxic effects on the respiratory system of the human body. The other part entered the bloodstream and dissolved directly in the body to form SO_3^{2-} , which acted as a toxic agent[19]. The elderly (≥ 70 years) showed that the most susceptible group to the effect of ambient air pollution, which could be explained that the elderly's respiratory fiber villi clearance ability and immunity decreased[20].

In this paper, we investigated the effect of daily average temperature and humidity on the hospitalization of AECOPD. We found that daily average temperature had an adverse effect on acute admission of COPD, which seems to be in accord with recent studies indicating that the aged was more susceptible with RR values of 1.048 (95%CI: 1.029–1.066) in cold season[21]. A published report demonstrated that low temperature could enhance exacerbate COPD symptom, indoor temperature was supposed to keep at least on average at 18.2°C , while for people in Shenyang, located in northeast China (123.38E , 41.8N), more attention should paid to low temperature[22]. Another research showed that a 1°C decrease in temperature was linked with a 0.8% increase for AECOPD admission on event-days (95% CI: 1.015–1.138). Moreover, with a 5°C decrease in average temperature, the low temperature (28-day average temperature) was a long-term effect on AECOPD [23]. Our results confirm the association between humidity and AECOPD admission. A population-based study in a metropolitan area found that hospital admissions increased by 5.04%, for per degree Celsius decrease in average weekly temperature [24].

Conclusions

The present study was designed to determine the effect of air pollution (PM_{2.5}, PM₁₀, SO₂, NO₂ and O₃), relative humidity and temperature on the hospitalization of acute exacerbation of COPD. The findings of this research provide insights for that air pollution, relative humidity and temperature can increase the risk of admission for acute exacerbation of COPD. The findings of this investigation complement those of earlier studies, especially in Shenyang.

The limitations of this paper are as followings. We didn't consider that the time of hospitalization visits was on daytime or nighttime for that these data were not available. Seasonal factor was not considered in this paper. Our future work is to investigate the long-term effect of seasonal factor on the AECOPD admission.

Supporting information

S1 File. This is air pollution data in this study.
(XLSX)

S2 File. This is meteorology data in this study.
(XLSX)

S3 File. This is the visual code in R language.
(TXT)

Author Contributions

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Funding acquisition: Wei Li, Wenxiu Qu.

Methodology: Cai Chen, Wenxiu Qu.

Software: Xueqing Yang.

Visualization: Xueqing Yang.

Writing – original draft: Cai Chen.

Writing – review & editing: Wenxiu Qu.

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