



# Air pollution and hospital outpatient visits for conjunctivitis: a time-series analysis in Tai'an, China

Renchao Chen<sup>1</sup> · Jun Yang<sup>1,2</sup> · Di Chen<sup>3,4,5,6</sup> · Wen-jing Liu<sup>7</sup> · Chunlin Zhang<sup>1,2</sup> · Hao Wang<sup>1,2</sup> · Bixia Li<sup>1,2</sup> · Peng Xiong<sup>8</sup> · Boguang Wang<sup>1,2</sup> · Yi Wang<sup>4,5,6,7</sup> · Shanshan Li<sup>9</sup> · Yuming Guo<sup>9</sup>

Received: 20 August 2020 / Accepted: 18 November 2020 / Published online: 25 November 2020  
© Springer-Verlag GmbH Germany, part of Springer Nature 2020

## Abstract

Conjunctivitis is one of the most common eye-related health problems and significantly influences patients' quality of life. Whether air pollution increased the risks of conjunctivitis is still unclear. Daily counts of outpatient visits for conjunctivitis, air pollution, and meteorological data during January 1, 2015–December 31, 2019 were collected from Tai'an, China. Generalized additive model with Poisson distribution was used to estimate the relationship between air pollution and visits for conjunctivitis, after controlling for the long-term and seasonal trends, weather variables, and day of the week. The effect of air pollution on visits for conjunctivitis was generally acute and significant at the current day and disappeared after 2 days. The relative risk of conjunctivitis visits associated with per 10  $\mu\text{g}/\text{m}^3$  increases in  $\text{PM}_{2.5}$ ,  $\text{PM}_{10}$ ,  $\text{SO}_2$ , and  $\text{NO}_2$  at lag 0–2 days was 1.006 (95% CI: 1.001–1.011), 1.003 (95% CI: 1.000–1.0107), 1.023 (95% CI: 1.009–1.037), and 1.025 (95% CI: 1.010–1.040), respectively. The impact of air pollution on visits for conjunctivitis varied greatly by individual characteristics. The impact of  $\text{NO}_2$  was higher in males than in females, with the opposite trend for  $\text{SO}_2$  and  $\text{PM}_{2.5}$ . Effect estimates of air pollutants were higher among return visits for conjunctivitis, the elderly, and white-collar workers. Our study highlights that the vulnerable subpopulations should pay more attention to protect themselves from air pollution.

**Keywords** Air pollution · Conjunctivitis · Vulnerable populations · Generalized additive model · Time-series analysis

Renchao Chen, Jun Yang, and Di Chen are co-first authors.

Responsible Editor: Lotfi Aleya

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s11356-020-11762-4>.

✉ Boguang Wang  
tbongue@jnu.edu.cn

✉ Yi Wang  
sanyuanwangyi@163.com

✉ Shanshan Li  
shanshan.li@monash.edu

<sup>1</sup> Institute for Environmental and Climate Research, Jinan University, Guangzhou 511443, China

<sup>2</sup> Guangdong-Hongkong-Macau Joint Laboratory of Collaborative Innovation for Environmental Quality, Guangzhou 511443, China

<sup>3</sup> Department of Management Of Hospital Infection, The Second Affiliated Hospital of Shandong First Medical University, Tai'an 271000, China

<sup>4</sup> Department of Ophthalmology, The Second Affiliated Hospital of Shandong First Medical University, Tai'an 271000, China

<sup>5</sup> Department of Optometry, Shandong First Medical University, Tai'an 271016, China

<sup>6</sup> Institute of Optometry, Shandong First Medical University, Tai'an 271016, China

<sup>7</sup> Department of Ophthalmology, Tai'an City Central Hospital, Tai'an 271000, China

<sup>8</sup> Division of Medical Psychology and Behavioral Sciences, Department of Public Health and Preventive Medicine, School of Medicine, Jinan University, Guangzhou 510632, China

<sup>9</sup> School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia

## Introduction

Conjunctivitis, known as the “red eye” or “pink eye,” often presents with hyperemia or injection of the conjunctiva. The symptoms include a diffuse redness of the eye, a gritty-eye sensation, itching or watery eyes, and eye discharge (Richards and Guzman-Cottrill 2010). Population at all ages and socioeconomic status are vulnerable to conjunctivitis, which reduces the patients’ learning and working efficiency, and significantly affects the quality of their lives (Pitt et al. 2004; Smith et al. 2005; Szyszkowicz et al. 2016). Conjunctivitis is the most common eye disease diagnosed in emergency departments, which has caused increasing health and economic burden around the world. For example, in the USA, conjunctivitis accounted for almost one-third of all eye-related diseases, with annual 4–6 million outpatient visits for conjunctivitis and the treatment cost of 377–857 million dollar (Alfonso et al. 2015; Ali and Pantanelli 2016; Ramirez et al. 2017). According to the data from the Chinese Center for Disease Control and Prevention, the number of acute hemorrhagic conjunctivitis cases in China was 34,576 in 2015, 34,253 in 2016, and 34,652 in 2017, with corresponding incidence of 2.54, 2.50, and 2.51 per 100,000 population respectively ([http://www.moh.gov.cn/jkj/new\\_index.shtml](http://www.moh.gov.cn/jkj/new_index.shtml)). Therefore, it is urgent to identify the conjunctivitis-associated risk factors and provide public health implication for the government and communities on reducing its disease burden.

As directly exposure to ambient environmental condition, the eyes could be easily affected by various airborne risk factors, including pollen (Calderon-Ezquerro et al. 2018), dust storms (Chien et al. 2014), and air pollutants (Chang et al. 2012; Nucci et al. 2017; Szyszkowicz et al. 2016). Recently, increasing number of investigations has been conducted to assess the risk of air pollutants on outpatient visits for conjunctivitis. However, current evidence on the association between air pollution and visits for conjunctivitis is hardly conclusive (Chen et al. 2019). For instance, Lu et al. (2019) found that NO<sub>2</sub> has a greater harmful effect on conjunctivitis visits, while Chang et al. (2012) reported that O<sub>3</sub> has a more pronounced effect. In addition, the lag structures of air pollution on conjunctivitis visits are not well elucidated in previous studies, and the vulnerable subpopulations are also unclear.

Tai’an City, located in Shandong Province, has attracted over millions of tourists each year, where the large flow of people could promote the spread of conjunctivitis. Therefore, we aimed to systematically explore the lag pattern of various air pollutants on outpatient visits for conjunctivitis, and also test the effect modification of air pollution by individual characteristic, which could provide significant public health implications on protecting the vulnerable subpopulations.

## Materials and methods

### Study site

Tai’an is located in the central part of Shandong Province of China. The east, south, west, and north are the Shopping Mall Linyi, the Hometown of Confucius Qufu, the Yellow River, and the provincial capital of Shandong Province, respectively. The locations of Tai’an City and the exposure and health monitoring sites are provided in Supplementary Fig. S1.

### Health data

From January 1, 2015 to December 31, 2019, the daily counts of visits for conjunctivitis were obtained from two largest hospitals in Tai’an, namely Tai’an Central Hospital and the Affiliated Hospital of Taishan Medical College. A total of 99,276 conjunctivitis patients were collected, with about 54 patients per day. Daily number of visits for conjunctivitis was further categorized according to individual characteristics, including age, sex, occupational status, and primary/secondary examinations. And the information of the occupational status was only available for the period of January 1, 2015–December 31, 2016.

### Exposure data

Air pollution data were obtained from three national ambient air monitoring sites in Tai’an, including Taishan Air Pollution Monitoring Station, Population School Air Pollution Monitoring Station, and Shandong Electric Power School Air Pollution Monitoring Station. Daily concentrations of air pollutants were collected, including aerodynamic diameter of particulate matter less than or equal to 2.5  $\mu$  (PM<sub>2.5</sub>), aerodynamic diameter of particulate matter less than or equal to 10  $\mu$  (PM<sub>10</sub>), sulfur dioxide (SO<sub>2</sub>), and nitrogen dioxide (NO<sub>2</sub>). Daily average concentrations of these air pollutants across all these stations were computed to represent the exposure levels of residents.

The corresponding daily meteorological variables were collected from the Tai’an Meteorological Bureau, including daily average atmospheric pressure (hPa), average relative humidity (%), average temperature (°C), average wind speed (m/s), and duration of sunshine (h).

### Data analysis

Generalized additive model with quasi-Poisson distribution was used to examine the relationship between air pollutants and the number of outpatient visits with conjunctivitis, after adjusting for potential covariates. Since strong correlations among different air pollutants have been reported in previous studies (Dai and Zhou 2017; Wang et al. 2014; Yang et al.

2016), we mainly analyzed the effect of a single pollutant on the daily variation of visits for conjunctivitis to avoid the collinearity. The model is provided as follows:

$$\begin{aligned}\text{Log}[E(Y_t)] = & \alpha_i + \beta_i X_i + \text{NS}(\text{time}_t, 5*7) + \text{NS}(\text{hum}_t, 3) \\ & + \text{NS}(\text{temp}_t, 3) + \text{NS}(\text{press}_t, 3) \\ & + \text{NS}(\text{sun}_t, 3) + \text{NS}(\text{wind}_t, 4) + \eta \text{DTR}_t \\ & + \gamma \text{Dow}_t + \nu \text{Holiday}_t\end{aligned}$$

where  $Y_t$  is the number of visits for conjunctivitis at day  $t$  ( $t = 1, 2, \dots, 1826$ );  $\alpha_i$  is the intercept ( $i$  corresponds to different kinds of pollutants);  $X_i$  is the concentration of air pollutants ( $\text{PM}_{2.5}$ ,  $\text{PM}_{10}$ ,  $\text{SO}_2$ ,  $\text{NO}_2$ );  $\beta_i$  is the vector of coefficients for  $X_i$ ; NS(.) means a natural cubic spline; 7 degrees of freedom (df) per year for time and 3 df respectively for relative humidity ( $\text{hum}_t$ ), mean temperature ( $\text{temp}_t$ ), barometric pressure ( $\text{press}_t$ ), duration of sunshine ( $\text{sun}_t$ ), and mean wind speed ( $\text{wind}_t$ ) were selected;  $\text{DTR}_t$  denotes the diurnal temperature range that was calculated by the difference between daily maximum temperature and daily minimum temperature, and  $\eta$  was the coefficient;  $\text{Dow}_t$  and  $\text{Holiday}_t$  are the day of the week and public holidays represented as categorical variables, with corresponding coefficients of  $\gamma$  and  $\nu$ . The model specifications were consistent with previous studies (Fu et al. 2017; Guo et al. 2014; Yang et al. 2020a; Yang et al. 2020b).

Sensitivity analyses of the main results were performed by changing the degrees of freedom (df) (6–8 per year) for time variable and 3–5 df respectively for average temperature, relative humidity, sunshine, wind speed, and atmospheric pressure (Yang et al. 2020a, Yang et al. 2020b). Furthermore, we also adopted the double-pollutant models and triple-pollutant models to validate the influence of one air pollutant impact on visits for conjunctivitis by another.

All statistical analyses were performed through the R language software (version 3.4.3).

## Results

Table 1 shows descriptive statistics for air pollutants, meteorological variables, and visits for conjunctivitis in Tai'an between January 1, 2015 and December 31, 2019. The average concentrations of  $\text{PM}_{2.5}$ ,  $\text{PM}_{10}$ ,  $\text{SO}_2$ , and  $\text{NO}_2$  were  $60.5 \mu\text{g}/\text{m}^3$ ,  $109.9 \mu\text{g}/\text{m}^3$ ,  $26.9 \mu\text{g}/\text{m}^3$ , and  $37.8 \mu\text{g}/\text{m}^3$ , respectively. The average values of air pressure, wind speed, sunshine hours, relative humidity, diurnal temperature range, and mean temperature were 1002.0 hPa, 1.8 m/s, 6.1 h, 62.0%, 10.9 °C, and 14.6 °C, respectively. For subgroups of visits for conjunctivitis, the average number of women, outpatients for return visits, and those aged 19–60 years was higher than other groups.

Table 2 shows the Spearman's correlation between meteorological variables and air pollution in Tai'an, China. Air pollutants were generally negatively correlated with wind speed, relative humidity, duration of sunshine, and temperature, but positively correlated with air pressure.

Figure 1 presents the time-series patterns of the number of outpatient visits for conjunctivitis and air pollutants during the study period. The number of visits for conjunctivitis showed an obviously increasing trend, but with a weak seasonal trend. Differently, air pollutants generally present significant seasonal trends, with the lowest concentrations in the summer but the highest in the winter. Except for DTR and wind speed, we observed obvious seasonal trends for relative humidity, temperature, air pressure, and duration of sunshine (Supplementary Fig. S2). The wind rose diagrams in Supplementary Fig. S3 presented that the main frequency wind direction was from east, at which the highest number of visits for conjunctivitis and air pollution concentrations was also observed.

Figure 2 shows the dose-response curves of air pollutants and visits for conjunctivitis. Generally, monotonic and positive relationships were observed between air pollutants and visits for conjunctivitis.

Figure 3 depicts the lag distribution of air pollution on visits for conjunctivitis. Generally, the effect of air pollution was acute and significant at the current day, and then disappeared after 2 days. Therefore, we mainly reported the quantified estimates of air pollution at lag 0–2 days. An increase of  $10 \mu\text{g}/\text{m}^3$  of 3-day moving average concentrations of  $\text{PM}_{2.5}$ ,  $\text{PM}_{10}$ ,  $\text{SO}_2$ , and  $\text{NO}_2$  was associated with 0.6% (95% CI: 0.1–1.1), 0.3% (95% CI: 0.1–0.7), 2.3% (95% CI: 0.9–3.7), and 2.5% (95% CI: 1.0–4.0) increase of outpatient visits for conjunctivitis, respectively.

Table 3 presents the effect of air pollution on visits for conjunctivitis stratified by individual characteristics. The effect of  $\text{NO}_2$  was higher in males than in females, with the opposite for  $\text{SO}_2$  and  $\text{PM}_{2.5}$ . The effect estimates of air pollutants were generally higher among return visits for conjunctivitis, those aged over 60 years, and white-collar workers. Similar tendency of air pollution on visits for conjunctivitis among different subpopulations was also observed at lag 0 day and lag 0–1 day (Supplementary Table S1 and Table S2).

Table 4 shows estimates of air pollution on visits for conjunctivitis using double- and triple-pollutant models. The effects of  $\text{SO}_2$  and  $\text{NO}_2$  were stable when  $\text{PM}_{2.5}$  and  $\text{PM}_{10}$  were separately included in the model, while the significant effects of  $\text{PM}_{2.5}$  and  $\text{PM}_{10}$  disappeared, when  $\text{SO}_2$  and  $\text{NO}_2$  were included in the model.

Several sensitivity analyses were conducted to check the robustness of the results to the model specifications. The effect estimates of air pollutants at lag 0–2 days did not materially change, when changing the time of degrees of freedom (df) (6–

**Table 1** Descriptive statistics of daily air pollutants, meteorological variables, and visits for conjunctivitis during January 1, 2015–December 31, 2019 in Tai'an, China

| Variables                                   | Min    | P25   | P50    | P75    | Max    | Mean   | SD   |
|---|--------|-------|--------|--------|--------|--------|------|
| Air pollutants ( $\mu\text{g}/\text{m}^3$ ) |        |       |        |        |        |        |      |
| NO <sub>2</sub>                             | 4      | 25    | 36     | 48     | 107    | 37.8   | 15.9 |
| PM <sub>10</sub>                            | 5      | 68    | 98     | 135    | 486    | 109.9  | 59.8 |
| PM <sub>2.5</sub>                           | 2      | 32    | 49     | 76     | 346    | 60.5   | 41.6 |
| SO <sub>2</sub>                             | 3      | 14    | 21     | 35     | 150    | 26.9   | 19.1 |
| Meteorological factors                      |        |       |        |        |        |        |      |
| Mean temperature (°C)                       | − 11.5 | 5.0   | 16.0   | 23.8   | 32.6   | 14.6   | 10.4 |
| Diurnal temperature range (°C)              | 1.4    | 7.8   | 10.8   | 14.0   | 23.0   | 10.9   | 4.1  |
| Relative humidity (%)                       | 15.3   | 49.2  | 63.3   | 75.0   | 96.0   | 62.0   | 16.2 |
| Air pressure (hPa)                          | 977.8  | 993.9 | 1002.2 | 1009.3 | 1026.7 | 1002.0 | 9.4  |
| Sunshine hours (h)                          | 0.0    | 2.9   | 7.0    | 9.0    | 12.9   | 6.1    | 3.7  |
| Wind speed (m/s)                            | 0.0    | 1.2   | 1.6    | 2.1    | 6.2    | 1.8    | 0.8  |
| No. of visits for conjunctivitis            |        |       |        |        |        |        |      |
| Total                                       | 2      | 42    | 54     | 66     | 117    | 54     | 18   |
| Gender                                      |        |       |        |        |        |        |      |
| Male  | 1      | 18    | 24     | 31     | 58     | 25     | 9    |
| Female                                      | 1      | 22    | 29     | 36     | 72     | 30     | 11   |
| Age (years)                                 |        |       |        |        |        |        |      |
| 0–18  | 1      | 11    | 16     | 21     | 47     | 17     | 8    |
| 19–59                                       | 2      | 21    | 28     | 36     | 65     | 29     | 11   |
| 60+   | 1      | 5     | 8      | 12     | 37     | 9      | 5    |
| Visit status                                |        |       |        |        |        |        |      |
| Newly diagnosed                             | 1      | 19    | 24     | 30     | 62     | 25     | 8    |
| Return visit                                | 1      | 21    | 29     | 38     | 78     | 30     | 12   |
| Occupational classification                 |        |       |        |        |        |        |      |
| White collar                                | 0      | 1     | 2      | 4      | 23     | 3      | 4    |
| Blue collar                                 | 1      | 7     | 13     | 23     | 61     | 16     | 11   |
| Unemployment                                | 0      | 7     | 11     | 16     | 36     | 12     | 6    |
| Other                                       | 0      | 10    | 17     | 28     | 75     | 20     | 13   |

P25, P50, and P75 denote the 25th, 50th, and 75th percentiles. Other refers to those other than white collar, blue collar, and unemployment

**Table 2** Spearman's correlation between daily meteorological variables and air pollutants in Tai'an, China

| Variables         | Temperature | DTR        | Humidity   | Air pressure | Sunshine   | Wind speed | NO <sub>2</sub> | PM <sub>10</sub> | PM <sub>2.5</sub> |
|-------------------|-------------|------------|------------|--------------|------------|------------|-----------------|------------------|-------------------|
| Temperature       | 1           |            |            |              |            |            |                 |                  |                   |
| DTR               | − 0.061     | 1          |            |              |            |            |                 |                  |                   |
| Humidity          | 0.235***    | − 0.387*** | 1          |              |            |            |                 |                  |                   |
| Air pressure      | − 0.898***  | 0.046      | − 0.252*** | 1            |            |            |                 |                  |                   |
| Sunshine          | 0.209***    | 0.625***   | − 0.474*** | − 0.158***   | 1          |            |                 |                  |                   |
| Wind speed        | − 0.053***  | − 0.249*** | − 0.289*** | 0.025**      | 0.008*     | 1          |                 |                  |                   |
| NO <sub>2</sub>   | − 0.625***  | 0.359***   | − 0.085*   | 0.564***     | − 0.119*** | − 0.323*** | 1               |                  |                   |
| PM <sub>10</sub>  | − 0.383***  | 0.294***   | − 0.070    | 0.297***     | − 0.111*** | − 0.211*** | 0.722***        | 1                |                   |
| PM <sub>2.5</sub> | − 0.471***  | 0.193***   | 0.061      | 0.389***     | − 0.234*** | − 0.236*** | 0.748***        | 0.907***         | 1                 |
| SO <sub>2</sub>   | − 0.486***  | 0.242***   | − 0.284*** | 0.446***     | − 0.074*** | − 0.098*** | 0.668***        | 0.599***         | 0.628***          |

DTR denotes diurnal temperature range. Asterisk denotes statistical significance (\* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ )



**Fig. 1** Time-series plot of daily visits for conjunctivitis and daily air pollution concentrations during January 1, 2015–December 31, 2019 in Tai'an, China

8 per year) to control for the long-term trends and seasonality, and 3–5 df respectively for relative humidity, average temperature, atmospheric pressure, sunshine, and wind speed (Supplementary Fig. S4).

## Discussion

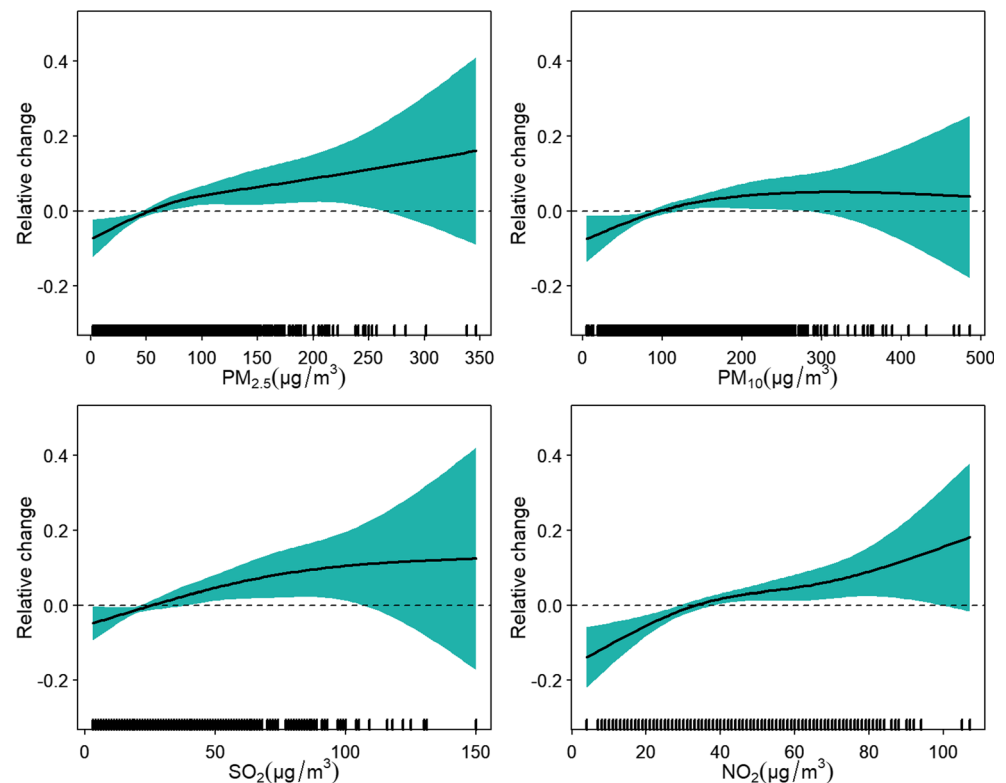
In the present study, we systematically examined the lag pattern of air pollutants on visits for conjunctivitis and assessed the effect modification by individual characteristics. Air pollutants were significantly and positively associated with visits for conjunctivitis, which were consistent with previous studies (Fu et al. 2017; Hong et al. 2016; Szyszkowicz et al. 2016). Blood vessels and lymphoid tissues of the conjunctiva are easily affected by the combination of physical, chemical, and biological factors by air pollution, which might increase the possibility of inflammation of the conjunctivitis (Gerard et al. 2015; Singh et al. 2013). Furthermore, some studies have

shown that air pollutants are closely related to the mechanism of ocular surface diseases. For instance, Yoon et al. (2018) found that the chemical and physical effects of PM components accumulated in the tear film lead to cell damage, inflammation, and oxidative stress in corneal epithelial cells. Torricelli et al. (2014) found that traffic-related air pollution affected the expression of 5AC gene in conjunctival goblet cells in the ocular surface. The secretion mainly comes from lacrimal gland, accessory lacrimal gland, goblet cells, exudative inflammatory cells, pathogenic microorganisms, and necrotic tissues. Air pollution affects the normal functioning of the lacrimal gland, accessory lacrimal gland, and goblet cells, and may therefore exacerbate the complications of conjunctivitis.

The evidence on lag pattern of environmental risk factors on health may be critical in developing early response measures for policymakers and local communities. Our results presented that the effects of air pollutants on visits for conjunctivitis were generally acute but limited within 3 days. This



**Fig. 2** Dose-response curves of air pollutants and visits for conjunctivitis. A natural spline with three degrees of freedom for air pollutant was used to plot this curve

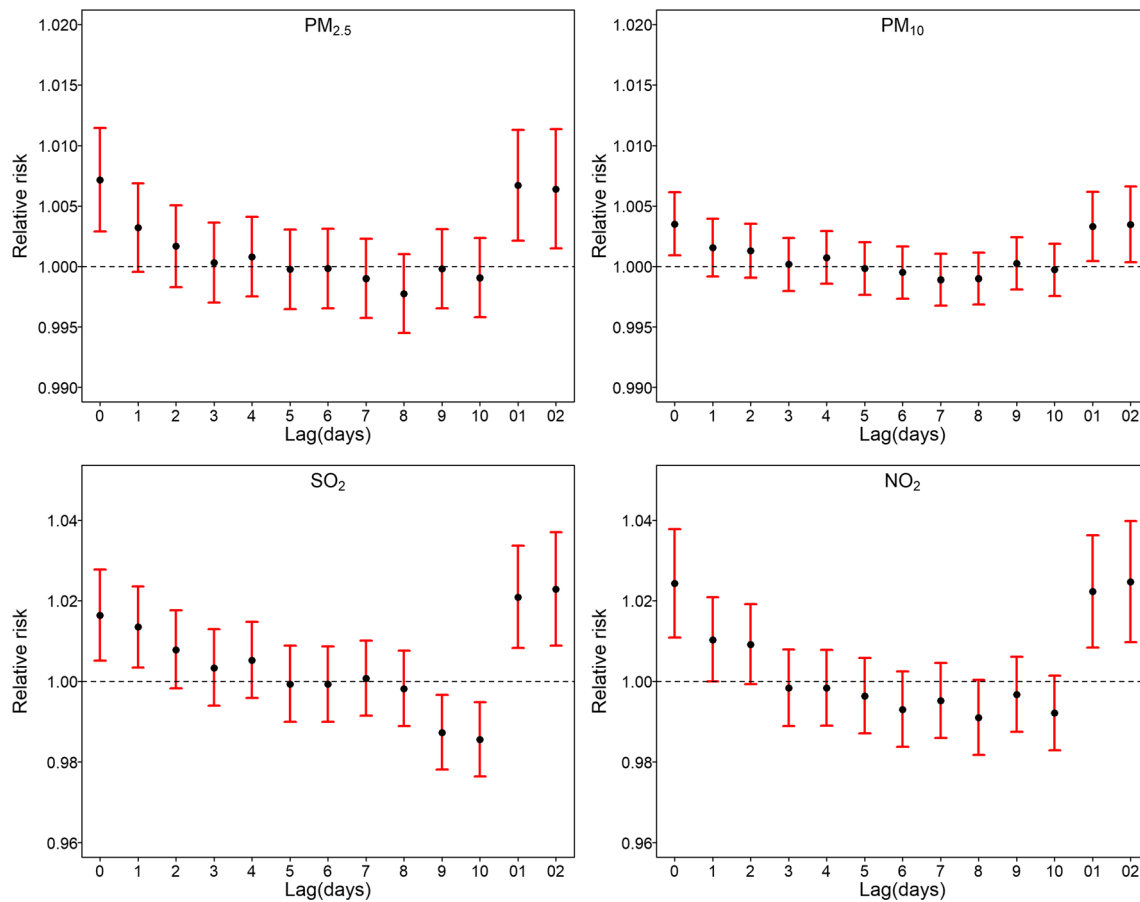


finding confirmed that timely preventive response should be applied impeding the high concentrations of air pollutants. Furthermore, we found that the magnitude of risk of visits for conjunctivitis differed from air pollutants. The strongest association was found for  $\text{NO}_2$ , with RR of 1.025 (95% CI: 1.010–1.040), while the lowest RR was 1.003 (95% CI: 1.000–1.007) for  $\text{PM}_{10}$ . The possible explanation may be due to that  $\text{NO}_2$  is irritating to the eye (Geravandi et al. 2015), and it may rapidly change the cells in the ocular structure through chemical reactions, and cause inflammation of the eye. Furthermore,  $\text{NO}_2$  is a toxic acid gas that may damage the appropriate environmental pH of the conjunctiva after invading the epidermal cells of the eye (Chiang et al. 2012). The chemical components of  $\text{PM}_{10}$  in Tai'an may be less toxic and this pollutant is relatively easier to be wiped out through washing the face comparing to other pollutants.

The impacts of air pollutants on outpatient visits for conjunctivitis varied greatly by gender, age, and occupational class. The risks of  $\text{NO}_2$  and  $\text{PM}_{10}$  on males with conjunctivitis were greater than that in females, with the opposite trend for  $\text{SO}_2$ . The possible reason may be that men are more likely to work outdoor, suffering from more accumulative concentrations of air pollutants (Yang et al. 2020a). For  $\text{SO}_2$ , females' vulnerability may be related to the makeup of the eyes, such as wearing a beautiful pupil, false eyelashes, and eyeliner (Chen et al. 2019). These cosmetic events may increase the likelihood of  $\text{SO}_2$  attachment, and lead to a higher risk of  $\text{SO}_2$  triggering conjunctivitis for females. The relative risk of air

pollution on return outpatient visits for conjunctivitis was significantly larger than those newly diagnosed patients. We speculated that outpatient visits for conjunctivitis second times or over are relatively easy to relapse with conjunctivitis because of its weak immunity capacity to protect their eyes from the harmful risk of air pollution. In terms of age, those aged over 60 years old suffered from greater adverse effects of air pollutants. The elderly's vulnerability may be explained by the declining age-related metabolic capacity and immunity. Furthermore, more outdoor activities for Chinese elderly after retirement happen in the morning and evening. These periods always coincide with relatively high concentrations of air pollutants. Therefore, during the period of high concentrations of air pollution, it is important to protect the public through reducing the time of outdoor activities and eating more foods rich in vitamin A (Chander et al. 2013) and vitamin D (Dadaci et al. 2014; Lee et al. 2017).

For the occupational aspect, we found that the effects of air pollutants were much higher among white-collar workers than others. The possible explanation may be that white-collar employees work with the computer for a longer time (Pransky et al. 1999), which may cause certain damage to the eyes and is easily affected by air pollutants in the confined space. For the unemployed people, the higher risk of conjunctivitis among this subpopulation may be associated with lower socioeconomic status (Yang et al. 2012), such as assessing to limited medical service and lacking of proper preventive knowledge.



**Fig. 3** The relative risk of visits for conjunctivitis associated with 10 µg/m<sup>3</sup> increase of air pollutants during single-day lags (lag 0, 1, 2, ..., 10 days) and cumulative lags (lag 0-1 and lag 0-2 days)

Our study has several important public health implications. Since the effect of air pollution on visits for conjunctivitis is

rapid, preventive action needs to be taken timely to protect the vulnerable population from air pollution. Personal measures,

**Table 3** The relative risks of per 10 µg/m<sup>3</sup> increase in air pollutants on visits for conjunctivitis at lag 0-2 days, stratified by individual characteristics

| Variables       | PM <sub>2.5</sub>    | PM <sub>10</sub>     | SO <sub>2</sub>      | NO <sub>2</sub>      |
|-----------------|----------------------|----------------------|----------------------|----------------------|
| Total           | 1.006 (1.001, 1.011) | 1.003 (1.000, 1.007) | 1.023 (1.009, 1.037) | 1.025 (1.010, 1.040) |
| Gender          |                      |                      |                      |                      |
| Male            | 1.005 (0.999, 1.011) | 1.004 (1.000, 1.007) | 1.019 (1.001, 1.036) | 1.027 (1.009, 1.045) |
| Female          | 1.007 (1.002, 1.013) | 1.003 (1.000, 1.007) | 1.026 (1.010, 1.043) | 1.023 (1.006, 1.040) |
| Visit status    |                      |                      |                      |                      |
| Newly diagnosed | 1.006 (1.000, 1.012) | 1.002 (0.999, 1.006) | 1.013 (0.997, 1.030) | 1.013 (0.995, 1.031) |
| Return visit    | 1.006 (1.001, 1.012) | 1.004 (1.000, 1.008) | 1.031 (1.014, 1.048) | 1.033 (1.015, 1.051) |
| Age (years)     |                      |                      |                      |                      |
| 0-18            | 1.003 (0.995, 1.011) | 1.002 (0.997, 1.007) | 1.004 (0.982, 1.027) | 1.027 (1.003, 1.052) |
| 19-60           | 1.007 (1.001, 1.012) | 1.004 (1.000, 1.008) | 1.026 (1.010, 1.042) | 1.015 (0.998, 1.033) |
| 61+             | 1.012 (1.004, 1.021) | 1.006 (1.001, 1.012) | 1.047 (1.022, 1.072) | 1.046 (1.018, 1.074) |
| Occupation      |                      |                      |                      |                      |
| White collar    | 1.039 (1.012, 1.067) | 1.024 (1.007, 1.042) | 1.083 (1.021, 1.150) | 1.125 (1.037, 1.222) |
| Blue collar     | 1.004 (0.993, 1.015) | 1.000 (0.993, 1.008) | 1.029 (1.002, 1.056) | 1.004 (0.969, 1.040) |
| Unemployment    | 1.008 (0.995, 1.022) | 1.006 (0.997, 1.014) | 1.024 (0.994, 1.055) | 1.072 (1.030, 1.115) |
| Other           | 1.013 (1.000, 1.026) | 1.013 (1.005, 1.022) | 1.000 (0.974, 1.028) | 1.019 (0.981, 1.059) |

**Table 4** The relative risk of per 10  $\mu\text{g}/\text{m}^3$  increase in air pollution on visits for conjunctivitis using single- and multi-contamination models

| Pollutant and model                                 | lag 0 day            | lag 0-1 day          | lag 0-2 days         |
|---|----------------------|----------------------|----------------------|
| PM <sub>2.5</sub>                                   | 1.007 (1.003, 1.011) | 1.007 (1.002, 1.011) | 1.006 (1.001, 1.011) |
| PM <sub>2.5</sub> +SO <sub>2</sub>                  | 1.006 (1.001, 1.010) | 1.005 (1.001, 1.010) | 1.005 (1.000, 1.010) |
| PM <sub>2.5</sub> +NO <sub>2</sub>                  | 1.004 (0.999, 1.009) | 1.004 (0.999, 1.009) | 1.004 (0.998, 1.009) |
| PM <sub>2.5</sub> +SO <sub>2</sub> +NO <sub>2</sub> | 1.003 (0.998, 1.009) | 1.003 (0.998, 1.009) | 1.004 (0.998, 1.009) |
| PM <sub>10</sub>                                    | 1.004 (1.001, 1.006) | 1.003 (1.000, 1.006) | 1.003 (1.000, 1.007) |
| PM <sub>10</sub> +SO <sub>2</sub>                   | 1.003 (1.000, 1.005) | 1.002 (0.999, 1.005) | 1.003 (1.000, 1.006) |
| PM <sub>10</sub> +NO <sub>2</sub>                   | 1.001 (0.998, 1.004) | 1.001 (0.998, 1.004) | 1.002 (0.998, 1.005) |
| PM <sub>10</sub> +SO <sub>2</sub> +NO <sub>2</sub>  | 1.001 (0.998, 1.004) | 1.001 (0.998, 1.004) | 1.002 (0.998, 1.005) |
| SO <sub>2</sub>                                     | 1.016 (1.005, 1.028) | 1.021 (1.008, 1.034) | 1.023 (1.009, 1.037) |
| SO <sub>2</sub> +PM <sub>2.5</sub>                  | 1.011 (0.998, 1.023) | 1.014 (1.001, 1.028) | 1.016 (1.002, 1.031) |
| SO <sub>2</sub> +PM <sub>10</sub>                   | 1.013 (1.001, 1.025) | 1.017 (1.004, 1.031) | 1.019 (1.005, 1.034) |
| SO <sub>2</sub> +NO <sub>2</sub>                    | 1.009 (0.997, 1.022) | 1.014 (1.000, 1.028) | 1.016 (1.001, 1.031) |
| SO <sub>2</sub> +PM <sub>2.5</sub> +NO <sub>2</sub> | 1.007 (0.995, 1.020) | 1.012 (0.998, 1.026) | 1.014 (0.999, 1.029) |
| SO <sub>2</sub> +PM <sub>10</sub> +NO <sub>2</sub>  | 1.008 (0.996, 1.021) | 1.013 (1.000, 1.027) | 1.015 (1.001, 1.030) |
| NO <sub>2</sub>                                     | 1.024 (1.011, 1.038) | 1.022 (1.008, 1.036) | 1.025 (1.010, 1.040) |
| NO <sub>2</sub> +PM <sub>2.5</sub>                  | 1.017 (1.001, 1.033) | 1.013 (0.997, 1.030) | 1.017 (1.000, 1.033) |
| NO <sub>2</sub> +PM <sub>10</sub>                   | 1.021 (1.005, 1.036) | 1.017 (1.002, 1.033) | 1.020 (1.004, 1.036) |
| NO <sub>2</sub> +SO <sub>2</sub>                    | 1.019 (1.005, 1.035) | 1.017 (1.002, 1.032) | 1.020 (1.005, 1.036) |
| NO <sub>2</sub> +PM <sub>2.5</sub> +SO <sub>2</sub> | 1.014 (0.998, 1.031) | 1.011 (0.994, 1.028) | 1.015 (0.998, 1.032) |
| NO <sub>2</sub> +PM <sub>10</sub> +SO <sub>2</sub>  | 1.017 (1.000, 1.034) | 1.014 (0.998, 1.030) | 1.017 (1.001, 1.034) |

such as reducing outdoor activities and the frequency of contact lenses and beauty, using clear water to wash the hands and face, and eating more foods rich in lutein, are recommended for the public during the period of air pollution. As NO<sub>2</sub> and SO<sub>2</sub> presented the largest effects on visits for conjunctivitis, it is important to control and manage the main sources of these air pollutants, such as motor vehicle emissions, fossil fuels, and biomass burning. Furthermore, more attentions from the government and local communities should be paid to protect the vulnerable groups (such as the elderly, children, and white-collar workers), publicize relevant knowledge of eye health, and implement policies to reduce the outdoor activities in heavy polluted weather.

Some limitations should be noted in this study. Similar with previous studies (Fu et al. 2017; Guo et al. 2014; Yang et al. 2019; Yang et al. 2020a), we used ambient air pollutants and weather variables from fixed sites instead of individual exposure, which may result in measurement bias. And the data were only collected from one city. The potential spatial heterogeneity of health effects of air pollutants is warranted to be further examined in future multi-city studies.

## Conclusions

Our study implies that short-term exposure to air pollutants was significantly associated with increased risk of visits for conjunctivitis. Much stronger associations were

observed for NO<sub>2</sub> and SO<sub>2</sub> relative to other pollutants. The elderly, the return outpatient visits for conjunctivitis, and the white-collar workers suffered from greater harmful effects of air pollutants. Considering the substantial risk of air pollutants, more stringent control and mitigation measures are still needed to protect the public health from the adverse impacts of air pollution. And promoting the health education of proper preventive actions is recommended to help those vulnerable populations to cope with upcoming air pollution episode.

**Author contributions** Y.G., J.Y., S.L., and B.W. initiated the study. Y.G., Y.W., and S.L. collected the data. R.C. and J.Y. performed statistical analysis. J.Y. and R.C. drafted the manuscript. Y.G., B.W., D.C., W.L., C.Z., H.W., B.L., B.W., Y.W., P.X., and S.L. revised the manuscript. All authors read and approved the final manuscript.

**Funding** The study was supported by the National Natural Science Foundation of China (No. 82003552), the Guangdong Basic and Applied Basic Research Foundation (No. 2020A1515011161), the Fundamental Research Funds for the Central Universities (No. 11618323), and the Department of Science and Technology of Guangdong Province (2019B121202002, 2019B121205004, 2019B110206002). YG was supported by the Career Development Fellowship of Australian National Health and Medical Research Council (#APP1107107). SL was supported by the Early Career Fellowship of Australian National Health and Medical Research Council (#APP1109193).

**Data availability** The datasets used and/or analyzed under the current study are available from the corresponding author on reasonable request.



## Compliance with ethical standards

**Competing interests** The authors declare that they have no competing interests.

**Ethical approval** Ethical approval was not required for secondary analysis of anonymous data in this study.

**Consent to participate** Not applicable (This study does not contain any individual person's data in any form).

**Consent to publish** Not applicable (This study does not contain any individual person's data in any form).

## References

- Alfonso SA, Fawley JD, Alexa Lu X (2015) Conjunctivitis. *Prim Care* 42:325–345
- Ali TK, Pantanelli SM (2016) *Conjunctivitis*. Springer, Berlin
- Calderon-Ezquerro MC, Guerrero-Guerra C, Galán C, Serrano-Silva N, Guidos-Fogelbach G, Jiménez-Martínez MC, Larenas-Linnemann D, López Espinosa ED, Ayala-Balboa J (2018) Pollen in the atmosphere of Mexico City and its impact on the health of the pediatric population. *Atmos Environ* 186:198–208
- Chander A, Chopra R, Batra N (2013) Vitamin A deficiency: an eye sore. *J Med Nutr Nutraceuticals* 2:41
- Chang C-J, Yang H-H, Chang C-A, Tsai H-Y (2012) Relationship between air pollution and outpatient visits for nonspecific conjunctivitis. *Invest Ophthalmol Vis Sci* 53:429–433
- Chen R, Yang J, Zhang C, Li B, Bergmann S, Zeng F, Wang H, Wang B (2019) Global associations of air pollution and conjunctivitis diseases: a systematic review and meta-analysis. *Int J Environ Res Public Health* 16:3652
- Chiang CC, Liao CC, Chen PC, Tsai YY, Wang YC (2012) Population study on chronic and acute conjunctivitis associated with ambient environment in urban and rural areas. *J Expo Sci Environ Epidemiol* 22:533–538
- Chien LC, Lien YJ, Yang CH, Yu HL (2014) Acute increase of children's conjunctivitis clinic visits by Asian dust storms exposure—a spatio-temporal study in Taipei, Taiwan. *PLoS One* 9:e109175
- Dadaci Z, Borazan M, Kiyici A, Oncel Acir N (2014) Plasma vitamin D and serum total immunoglobulin E levels in patients with seasonal allergic conjunctivitis. *Acta Ophthalmol* 92:e443–e446
- Dai Y-H, Zhou W-X (2017) Temporal and spatial correlation patterns of air pollutants in Chinese cities. *PLoS One* 12:e0182724–e0182724
- Fu Q, Mo Z, Lyu D, Zhang L, Qin Z, Tang Q, Yin H, Xu P, Wu L, Lou X, Chen Z, Yao K (2017) Air pollution and outpatient visits for conjunctivitis: a case-crossover study in Hangzhou, China. *Environ Pollut* 231:1344–1350
- Gerard C, Aida C, Marta C, Arcadi G, Carolina L (2015) Acid-sensing ion channels detect moderate acidifications to induce ocular pain. *Pain* 156:483–495
- Geravandi S, Goudarzi G, Mohammadi MJ, Taghavi-rad SS, Salmanzadeh S (2015) Sulfur and nitrogen dioxide exposure and the incidence of health endpoints in Ahvaz, Iran. *Health Scope* 4:e24318
- Guo Y, Li S, Tian Z, Pan X, Zhang J, Williams G (2014) The burden of air pollution on years of life lost in Beijing, China, 2004–08: retrospective regression analysis of daily deaths. *BMJ* 347:f7139
- Hong J, Zhong T, Li H, Xu J, Ye X, Mu Z, Lu Y, Mashaghi A, Zhou Y, Tan M, Li Q, Sun X, Liu Z, Xu J (2016) Ambient air pollution, weather changes, and outpatient visits for allergic conjunctivitis: a retrospective registry study. *Sci Rep* 6:23858
- Lee HS, Kwon JY, Joo C-K (2017) Vitamin D supplementation modulates Th2 immune response by inducing T regulatory cells in allergic conjunctivitis. *J Immunol* 198:194–211
- Lu P, Zhang Y, Xia G, Zhang W, Li S, Guo Y (2019) Short-term exposure to air pollution and conjunctivitis outpatient visits: a multi-city study in China. *Environ Pollut* 254:113030
- Nucci P, Sacchi M, Pichi F, Allegri P, Serafino M, Dello Strologo M, De Cilla S, Villani E (2017) Pediatric conjunctivitis and air pollution exposure: a prospective observational study. *Semin Ophthalmol* 32:407–411
- Pitt AD, Smith AF, Lindsell L, Voon LW, Rose PW, Bron AJ (2004) Economic and quality-of-life impact of seasonal allergic conjunctivitis in Oxfordshire. *Ophthalmic Epidemiol* 11:17–33
- Pransky G, Snyder T, Dembe A, Himmelman J (1999) Under-reporting of work-related disorders in the workplace: a case study and review of the literature. *Ergonomics* 42:171–182
- Ramirez DA, Porco TC, Lietman TM, Keenan JD (2017) Epidemiology of conjunctivitis in US emergency departments. *JAMA Ophthalmol* 135:1119–1121
- Richards A, Guzman-Cottrill JA (2010) Conjunctivitis. *Pediatr Rev* 31:196–208
- Singh P, Tyagi M, Kumar Y, Gupta KK, Sharma PD (2013) Ocular chemical injuries and their management. *Oman J Ophthalmol* 6:83–86
- Smith AF, Pitt AD, Rodriguez AE, Alio JL, Marti N, Teus M, Guillen S, Bataille L, Barnes JR (2005) The economic and quality of life impact of seasonal allergic conjunctivitis in a Spanish setting. *Ophthalmic Epidemiol* 12:233–242
- Szyszkowicz M, Kousha T, Castner J (2016) Air pollution and emergency department visits for conjunctivitis: a case-crossover study. *Int J Occup Med Environ Health* 29:381–393
- Torricelli AA, Matsuda M, Novaes P, Braga AL, Saldiva PH, Alves MR, Monteiro ML (2014) Effects of ambient levels of traffic-derived air pollution on the ocular surface: analysis of symptoms, conjunctival goblet cell count and mucin 5AC gene expression. *Environ Res* 131:59–63
- Wang Y, Ying Q, Hu J, Zhang H (2014) Spatial and temporal variations of six criteria air pollutants in 31 provincial capital cities in China during 2013–2014. *Environ Int* 73:413–422
- Yang J, Ou CQ, Ding Y, Zhou YX, Chen PY (2012) Daily temperature and mortality: a study of distributed lag non-linear effect and effect modification in Guangzhou. *Environ Health* 11:63
- Yang J, Ou CQ, Song YF, Li L, Chen PY, Liu QY (2016) Estimating years of life lost from cardiovascular mortality related to air pollution in Guangzhou, China. *Sci Total Environ* 573:1566–1572
- Yang J, Yin P, Sun J, Wang B, Zhou M, Li M, Tong S, Meng B, Guo Y, Liu Q (2019) Heatwave and mortality in 31 major Chinese cities: definition, vulnerability and implications. *Sci Total Environ* 649:695–702
- Yang J, Zhou M, Li M, Yin P, Hu J, Zhang C, Wang H, Liu Q, Wang B (2020a) Fine particulate matter constituents and cause-specific mortality in China: a nationwide modelling study. *Environ Int* 143:105927
- Yang J, Zhou M, Zhang F, Yin P, Liu Q (2020b) Diabetes mortality burden attributable to short-term effect of PM10 in China. *Environ Sci Pollut Res* 27:18784–18792
- Yoon S, Han S, Jeon KJ, Kwon S (2018) Effects of collected road dusts on cell viability, inflammatory response, and oxidative stress in cultured human corneal epithelial cells. *Toxicol Lett* 284:152–160

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.