The burden of air pollution and weather condition on daily respiratory deaths among older adults in China, Jinan from 2011 to 2017

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Abstract
The health effects of short-term exposure to air pollutants on respiratory deaths and its modifiers such as meteorological indexes have been widely investigated. However, most of the previous studies are limited to single pollutants or total respiratory deaths, and their findings are inconsistent. To comprehensively examine the short-term effects of air pollutants on daily respiratory mortality, we included 16,931 nonaccidental respiratory deaths (except lung cancer and tuberculosis) among older adults (>65 years) from 2011 to 2017 in Jinan, China. We used a generalized additive Poisson model adjusted for meteorology and population dynamics to examine the associations between air pollutants (particulate matter with an aerodynamic diameter of b2.5 μm [PM2.5], particulate matter with an aerodynamic diameter of b10 μm [PM10], SO2, NO2, O3, and daily mortality for the total patients, males, females, chronic airway diseases, pneumonia patients, and rest patients in Jinan. Outdoor air pollution was significantly related to mortality from all respiratory diseases especially from chronic airway disease in Jinan. The effects of air pollutants had lag effects and harvesting effects, and the effects estimates usually reached a peak at lag 1 or 2 day. An increase of 10 μg/m3 or 10 ppb of PM2.5, PM10, SO2, NO2, and O3 corresponds to increments in mortality caused by chronic airway disease of 0.243% (95% confidence interval [CI]: –0.172–0.659) at lag 1 day, 0.127% (95% CI: –0.161–0.415) at lag 1 day, 0.605% (95% CI: 0.060–1.139) at lag 3 day, 0.649% (95% CI: –0.808–2.128) at lag 0 day and 0.944% (95% CI: 0.156–0.1598) at lag 1 day, respectively. The effects of air pollutants were usually greater in females and varied by respiratory subgroups. Spearman correlation analysis suggested that there was a significant association between meteorological indexes and air pollutants. Sex, age, temperature, humidity, pressure, and wind speed may modify the short-term effects of outdoor air pollution on mortality in Jinan. Compared with the other pollutants, O3 had a stronger effect on respiratory deaths among the elderly. Moreover, chronic airway diseases were more susceptible to air pollution. Our findings provided new evidence for new local environmental and health policies making.

Abbreviations: CI = confidence interval, NO2 = nitrogen dioxide, O3 = ozone, PM = particulate matter, PM10 = particulate matter with an aerodynamic diameter of b10 μm, PM2.5 = particulate matter with an aerodynamic diameter of b2.5 μm, RR = relative risk, SO2 = sulfur dioxide.

Keywords: air pollution, daily deaths, meteorological index, relative risk, respiratory disease

1. Introduction
It is known to all that air pollutants have obvious adverse effects on human health, especially on the respiratory system, and they are mainly composed of solid particles and gaseous pollutants such as SO2, NO, NOx. Over recent decades, China has become one of the most polluted countries around the world because of rapid economic development, accelerated urbanization, and industrialization. So far, most of the previous studies were focused on the short-term or long-term relationship between air pollution and increased total respiratory or cardiovascular disease mortality, as well as increased rates of hospital admissions and emergency department visits. For instance, a nationwide time-series analysis in 272 major Chinese cities from 2013 to 2015 found that a 10 μg/m3 increase in SO2 at lag 01 was associated with increments of 0.59%, 0.70%, and 0.53% in mortality from total non-accidental diseases, cardiovascular diseases, total respiratory diseases, respectively. While the pollutants involved in each research were usually no more than 2. In studies by Wang, Dominici, and Chen et al, health impacts of air pollutants on daily cause-specific mortality were limited to 1 pollutant such as SO2, fine particulate, and NO2, respectively. Moreover, the disease mortality was roughly divided into respiratory or cardiovascular disease mortality, and no further classification was made. So we conducted...
relatively comprehensive research on the association of the 5 main air pollutants and specific respiratory diseases mortality (J00-J99) in Jinan, Shandong province, Eastern China, modified by various meteorological indexes. Jinan is one of the most polluted cities in China due to its heavy industry-led economic model and coal burning in winter. To a certain extent, the conclusions of our study may have a reference value for other heavily polluted cities in China. We found that about 89.33% of deaths caused by respiratory diseases were observed among older adults (>65 years), suggesting that the elderly exposed to air pollutants were at higher risk of death than the young, consistently to other documented evidence. Therefore it is urgently for us to explore the exact effects of air pollution on mortality especially among older adults with the aim of promoting public health policy-making. The objective of our study is to explore the lag impact and the cumulative impact of air pollutants on various respiratory diseases daily mortality in eastern China. We also examined the modifying effects of gender, age, and meteorological indexes.

2. Materials and methods

2.1. Ethics

Ethics approval was obtained from the Ethics Committee of Shandong Provincial Hospital, Affiliated to Shandong University, Jinan, Shandong, China. Patient records were anonymized and deidentified before our analysis.

2.2. Data

Causes of death were classified according to the International Classification of Diseases, Tenth Revision (ICD-10; WHO 1993). We examined total daily mortality caused by respiratory disease (J00–J99) and cause-specific daily mortality attributed to chronic airway diseases (J40–47, including chronic obstructive pulmonary diseases [COPD], asthma, chronic respiratory failure, bronchietasis), pneumonia (J12–J18), the rest (J30–39, J60–J99). To gain a more accurate result, this research has ruled out acute respiratory infections (J00–J11, J20–J22) due to its negligible mortality, tuberculosis and lung cancer were excluded as well. Daily non-accidental mortality data from 2011 to 2017 were obtained from Jinan Municipal Center for Disease Control and Prevention. The data of daily air pollutants concentration during the same period, including particulate matter with an aerodynamic diameter of 2.5 μm (PM2.5), particulate matter with an aerodynamic diameter of 10 μm (PM10), SO2, NO2, and O3, were collected from the Environmental Monitoring Center of Jinan. The pollutant monitoring network was composed of 12 urban monitoring stations and 2 suburban monitoring stations. We abstracted the daily 24-hours average concentrations of air pollutants (PM2.5, PM10, SO2, and NO2) collected from these 14 monitoring stations as well as maximal 8-hours mean concentrations for O3. Meteorological data of Jinan from 2011 to 2017 were collected from the National Meteorological Information Center in China (http://www.nmic.gov.cn/web/channel-46-4.htm) to explore their impacts to the association of air pollution and daily mortality. Meteorological indexes were daily mean temperature, air pressure, humidity, and wind speed, respectively.

2.3. Method of analysis

We applied generalized additive Poisson models to examine the associations between air pollution (PM2.5, PM10, SO2, NO2, and O3) and day-to-day variations in the respiratory mortality for the total patients, males, females, chronic airway diseases, pneumonia patients, and rest patients in Jinan. The Quasi-Poisson distribution was adopted if there was an overdispersion in mortality data. Generalized additive models allow for highly flexible fitting as the outcome is assumed to be dependent on a sum of the smoothed and linear functions of the predictor variables. A smoothed function captures the nonlinear relationship between daily deaths and the time-varying covariates such as the temperature and the calendar time. The nonlinear term in generalized additive models can be estimated by using smoothing splines, which transform a possible nonlinear relationship into a linear form by separating the data into subintervals based on the basis functions. Degrees of freedom (df) of smoothed functions were determined by the Akaike information criterion (Akaike, 1987). The daily ambient air pollutant (PM10, PM2.5, SO2, and NO2) concentrations for the 0 to 6 day lags were analyzed separately in association with daily deaths. Then the cumulative effects of air pollution on daily mortality were conducted by using a moving average. We also applied 2-pollutant and all pollutant models, by including pollutants at the same lag. Briefly, we fitted the data into the following model:

$$\log(E(Y_i)) = \alpha + \beta X_i + s(\text{time}) + \sum_i s(Z_{ij}) + DOW$$ (1)

where $E(Y_i)$ is the expected number of daily COPD deaths at day $i$, $\alpha$ is the intercept term, $\beta$ is the regression coefficient, and $X_i$ is the pollutant measurements on day $i$ $s(\text{time})$ denotes the smoothing splines of calendar time and $s(Z_{ij})$ denotes the smoothing splines of the meteorological variables $Z_i$ such as the temperature, relative humidity, pressure, and wind speed, respectively. The dummy variable DOW is the indicator for the day of the week. All statistical analyses were performed with R V.3.4.3 (URL http://www.R-project.org) using the package mgcv (V.1.8–17). Then all results were presented as the percentage change in the relative risk (RR) of mortality and its 95% confidence interval (CI) in association with a 10 μg/m3 or a 10 ppb increase in daily air pollutants.

3. Results

3.1. Mortality and air pollution data

There were 18,952 deaths due to respiratory disease including chronic airway diseases (10,983), pneumonia (4942), acute respiratory infections (228), and others (2799) in Jinan, China from 2011 to 2017, of which 10,090 males, 8862 females, and 16,931 patients over 65 years old, 2020 records for those under 65. Table 1 provides data on daily mortality, air pollutants, temperature (ºC), humidity (%), pressure (kPa), wind speed (m/s). The mean concentration of PM2.5, PM10, SO2, NO2, CO, O3 were 96 μg/m3, 164 μg/m3, 71 μg/m3, 53 μg/m3, 1401 μg/m3, respectively. Annual average value of temperature (ºC), humidity (%), pressure (kPa), wind speed (m/s) were 15 (ºC), 96 (%), 997 (kPa), 2 (m/s), respectively. Total daily death counts caused by respiratory disease (except lung cancer and lung tuberculosis) were 8.6, of which the males and the females are 4.6 cases and 4 cases, respectively. When the causes of death were further classified by disease entities, we found that daily death counts caused by chronic respiratory disease, pneumonia and the rest were 5 cases, 2.3 cases, 1.3 cases, respectively.
Table 1

Descriptive statistics of air pollutants, daily mortality and weather condition in Jinan, China from 2011 to 2017.

| Pollutants, μg/m³ | X ± S | Min | P25 | P50 | P75 | Max |
|-------------------|-------|-----|-----|-----|-----|-----|
| PM₁₀              | 96 ± 58 | 15  | 56  | 83  | 117 | 443 |
| PM₁₀              | 164 ± 80 | 29  | 112 | 149 | 200 | 693 |
| SO₂               | 71 ± 54 | 12  | 36  | 53  | 89  | 429 |
| NO₂               | 53 ± 21 | 13  | 38  | 49  | 64  | 165 |
| CO                | 1401 ± 682 | 445 | 955 | 1210 | 1589 | 6555 |
| O₃                | 93 ± 56 | 10  | 48  | 82  | 134 | 270 |
| **Meteorology**   |       |     |     |     |     |     |
| Temperature, °C   | 15 ± 11 | 12  | 5   | 17  | 24  | 34  |
| Humidity (%)      | 56 ± 20 | 13  | 40  | 55  | 70  | 100 |
| Pressure, kPa      | 997 ± 9 | 976 | 989 | 997 | 1004 | 1022 |
| Wind speed, m/s    | 2 ± 1 | 0  | 2  | 2  | 3  | 8  |
| **Mortality (cases/per d)** | 8.6 ± 4.3 | 0  | 6  | 8  | 11  | 37  |
| Total             | 4.6 ± 2.7 | 0  | 3  | 4  | 6  | 17  |
| Male              | 4 ± 2.6 | 0  | 2  | 4  | 6  | 19  |
| Female            | 5 ± 3.2 | 0  | 3  | 4  | 7  | 23  |
| Chronic airway diseases* | 2.3 ± 1.7 | 0  | 1  | 2  | 3  | 11  |
| **Rest**          | 1.3 ± 1.2 | 0  | 0  | 1  | 2  | 8  |

Diseases are classified according to the International Classification of Diseases, Tenth Revision (ICD-10; WHO 1993).

* Particulate matter with an aerodynamic diameter of <2.5 μm.

3.2. Spearman correlation analysis

Table 2 illustrates the correlation between air pollutants and weather conditions in Jinan, China from 2011 to 2017. At the mean level, there were positive and moderate-to-strong correlations among PM₂.₅, PM₁₀, SO₂, NO₂, CO other than inverse and weak correlations for O₃. The correlation coefficient of PM₂.₅ with PM₁₀ and CO with NO₂ was 0.862 (P < .01) and 0.797 (P < .01), respectively. Air pollutants (except for O₃) had an inverse and weak-to-moderate correlation with temperature and wind. The correlation coefficient of temperature and O₃ was as high as 0.798 (P < .01). In addition, as shown in Table 2, there was an inverse and weak correlation between humidity and air pollutants (except for CO and PM₂.₅). Pressure was weak-to-moderate correlated with air pollutants (except for O₃), but negative with other weather conditions. The correlation coefficients of pressure with O₃ and pressure with temperature were −0.686 (P < .01) and −0.888 (P < .01), respectively. The correlation coefficients were negative between weather conditions except for temperature with humidity and wind. It suggests that the research about estimates of air pollutants on daily specific-caused deaths should control the effects of other pollutants and meteorological factors.

### 3.3. Single pollutant models

It is shown in Table 3 and Figure 1 that the association of air pollutants with respiratory diseases caused mortality varied by gender and respiratory disease categories in single-pollutant
| Lag0  | Lag1  | Lag2  | Lag3  | Lag4  | Lag5  | Lag6  | Lag7  | Lag8  | Lag9  | Lag10 | Lag11 | Lag12 | Lag13 | Lag14 | Lag15 | Lag16 |
|------|------|------|------|------|------|------|------|------|------|-------|-------|-------|-------|-------|-------|-------|
| Total| 0.206| 0.383| 0.008| 0.309| 0.198| 0.438| 0.205| 0.431| 0.208| 0.527| 0.202| 0.527| 0.201| 0.527| 0.201| 0.527|
| Male | 0.192| 0.378| 0.007| 0.300| 0.197| 0.437| 0.204| 0.430| 0.208| 0.527| 0.202| 0.527| 0.201| 0.527| 0.201| 0.527|
| Female| 0.219| 0.396| 0.011| 0.312| 0.202| 0.444| 0.211| 0.433| 0.210| 0.527| 0.205| 0.527| 0.208| 0.527| 0.208| 0.527|

Table 3: Percent increases in relative risk (RR) of daily non-accidental and cause-specific mortality associated with a 10 μg/m^3 increase in air pollutants using single pollutant models at lag 0 to 7 day and lag 01 to 06 day in Jinan, China from 2011 to 2017. Results were controlled for seasonality, day of the week, temperature, relative humidity, air pressure, and wind speed.
### Table 3 (continued)

|        | Lag0     | Lag1     | Lag2     | Lag3     | Lag4     | Lag5     | Lag6     | Lag01    | Lag02    | Lag03    | Lag04    | Lag05    | Lag06    |
|--------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|        | 0.645 (<0.076, 0.571 (<0.751, 0.082 (<1.818, 0.577 (<1.812, 0.500 (<1.726, 0.31 (<1.536, 0.206 (<1.455, 0.870 (<0.826, 0.74 (<0.973, 0.27 (<0.702, 0.043 (<2.754, 0.214 (<2.454, 0.031 (<2.680, 2.181, 0.191) 1.362, 0.672, 0.742, 0.933, 1.038, 2.599, 2.617, 2.297, 2.113, 2.077, 2.111 |
| Chronic airway diseases<sup>†</sup> | 0.649 (<0.808, 0.404 (<0.859, 0.303 (<1.508, 0.650 (<1.827, 0.532 (<1.806, 0.933 (<0.975, 0.272 (<1.793, 0.236 (<2.419, 0.494 (<2.805, 0.756 (<3.207, 2.128, 1.683, 0.91, 0.054, 0.033, 0.61, 0.689, 2.383, 2.143, 1.819, 1.386, 1.230, 1.124) |
| Pneumonia<sup>‡</sup> | 0.649 (<0.808, 0.404 (<0.859, 0.303 (<1.508, 0.650 (<1.827, 0.532 (<1.806, 0.933 (<0.975, 0.272 (<1.793, 0.236 (<2.419, 0.494 (<2.805, 0.756 (<3.207, 2.128, 1.683, 0.91, 0.054, 0.033, 0.61, 0.689, 2.383, 2.143, 1.819, 1.386, 1.230, 1.124) |
| Rest<sup>§</sup> | 0.130 (<2.012, 1.041 (<0.839, 1.130 (<0.665, 0.667 (<2.423, 0.045 (<1.703, 0.830 (<0.97, 0.359 (<1.319, 0.938 (<1.468, 1.596 (<1.079, 0.935 (<1.906, 0.845 (<2.154, 1.315 (<1.938, 1.464 (<1.974, 2.319, 2.963, 2.979, 1.120, 1.828, 2.620, 2.138, 3.404, 4.261, 3.859, 4.018, 4.666, 5.023) |
| The rest | 2.427 (<0.306, 1.675 (<0.783, 0.947 (<3.395, 1.015 (<3.299, 0.658 (<2.93, 1.067 (<3.337, 0.518 (<2.800, 2.864 (<0.283, 1.592 (<1.800, 0.749 (<2.888, 0.305 (<3.57, 0.306 (<4.413, 0.571 (<4.917, 5.330, 4.199, 1.443, 1.324, 1.666, 1.259, 1.817, 6.110, 5.100, 4.523, 4.354, 3.977, 3.916) |

Diseases are classified according to the International Classification of Diseases, Tenth Revision (ICD-10; WHO 1993).

CI = confidence interval, NO<sub>2</sub> = nitrogen dioxide, O<sub>3</sub> = ozone, PM<sub>2.5</sub> = particulate matter, PM<sub>10</sub> = particulate matter with an aerodynamic diameter of b10 μm, PM<sub>2.5-10</sub> = particulate matter with an aerodynamic diameter of b2.5 μm, SO<sub>2</sub> = sulfur dioxide.

<sup>†</sup>Chronic airway diseases refer to J40–47 including chronic obstructive pulmonary diseases (COPD), asthma, chronic respiratory failure, bronchiectasis.

<sup>‡</sup>Pneumonia refers to J12–18.

<sup>§</sup>Rest refers to J30–39 and J60–69 including interstitial pneumonia and other respiratory diseases.

Statistically significant.

<sup>∗</sup><br><sup>∗∗</sup><br><sup>∗∗∗</sup><br><sup>∗∗∗</sup><br><sup>∗∗∗</sup><br><sup>∗∗∗</sup><br>
models. What’s more, Table 3 also illustrated the single-day effects and the cumulative effects of a 10 μg/m³ or a 10 ppb increase in pollutants to the RR of mortality from respiratory diseases. However, all presented a trend of earlier increase and later decrease from lag 0 to 6 days. PM2.5 (lag 1), SO2 (lag 1), O3 (lag 3), PM10 (lag 1), NO2 (lag 0) had a highest positive association with the RR of mortality caused by total daily respiratory diseases, and the RR estimates of daily cause-specific mortality was associated with a 10 μg/m³ increase in pollutants is 0.383% (95% CI: 0.068, 0.699), 0.514% (95% CI: 0.095, 0.936), 0.975% (95% CI: 0.463, 1.489), 0.194% (95% CI: −0.023, 0.412), 0.822% (95% CI: −0.284, 1.941), respectively, of which the former 3 is statistically significant (P < 0.05). While considering a modifier of death estimates such as gender, we found that nothing but the increased RR of death estimates associated with a 10 μg/m³ increase in O3 (lag 1–3) was statistically significant (P < 0.05) among males and they were 1.139% (95% CI: 0.347, 1.937), 0.737% (95% CI: 0.028, 1.451), 1.034% (95% CI: 0.336, 1.738) in turn. In females, increments in SO2 exposure at lag 0 to 1 day and O3 exposure at lag 0, 3, 6 day had a statistically significant association with increases in RR of respiratory diseases caused deaths (P < 0.05), with an odds ratio of 0.841% (95% CI: 0.222, 1.463), 0.653% (95% CI: 0.059, 1.251), −1.180% (95% CI: −2.164, −0.187), 0.902% (95% CI: 0.161, 1.649), −0.623% (95% CI: −1.128, −0.115), respectively. However, when the causes of death were further divided into chronic airway diseases (including COPD, asthma, chronic respiratory failure, bronchiectasis), various pneumonia and the rest (including interstitial pneumonia and the rest respiratory diseases), the degree of correlation between exposure concentrations of pollutants and death and the optimal lag day were also changed. At the same time, the lag days corresponding to the maximum effect also varied. As shown in Table 3, for death counts attributed to chronic airway diseases, a 10 μg/m³ increase in 6, 7 day mean PM10, 3 day mean lag SO2, and 2, 4, 7 day mean O3 concentrations had a statistically significant association with a −0.285% (95% CI: −0.556, −0.013), −0.295% (95% CI: −0.565, −0.024), 0.603% (95% CI: 0.069, 1.139), 0.944% (95% CI: 0.156, 1.739), 0.897% (95% CI:0.200, 1.598), −0.772% (95% CI: −1.459, −0.081) increased OR of death, respectively. In addition, various pneumonia (except Interstitial pneumonia) mortality were associated with PM2.5 (lag 1) and O3 (lag 3) with 0.672% (95% CI: 0.049, 1.298) and 1.114% (95% CI: 0.159, 2.078) for an increase of 10 μg/m³ (P < 0.05). Moreover, a 10 μg/m³ increase in same day PM2.5 concentration contributed to an increased RR estimates of deaths caused by the rest respiratory diseases of 1.032% (95% CI: 0.110, 1.962) (P < 0.05). As for cumulative effects, we found that its RR estimates of different groups were usually larger than that of single-day effects, but the trends were consistent when the lag days were going on.

### 3.4. Copollutant models

Table 4 summarizes the relationship between PM2.5, PM10, SO2, NO2, O3 at lag 0 to 1 with excess daily total, gender-stratified and respiratory disease-stratified mortality count (%) of Jinan, China from 2011 to 2017 in single and copollutant models. In the single-pollutant models for PM2.5 and SO2, an increase of 10 μg/m³ were statistically related to the increased daily respiratory mortality of 0.383% (95% CI: 0.068, 0.699) and 0.514% (95% CI: 0.095, 0.936), respectively. We found that the excess mortality estimates increased to 0.387% (95% CI: 0.073, 0.703), 0.596 (95% CI: 0.173, 1.022), respectively when PM10 and SO2 were separately adjusted by O3. As shown in Table 4, the mortality estimates varied by gender and disease.

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**Figure 1.** The excess risk and 95% CI per 10 μg/m³ increase of air pollutants on cause-specific daily deaths using single pollutant models at lag 0 to 7 day and lag 01 to 06 day in Jinan, China from 2011 to 2017. Results were controlled for seasonality, day of the week, temperature, relative humidity, air pressure, and wind speed. A. lag effects; B. cumulative effects. Chronic refers to chronic airway diseases (J40–47) including COPD, asthma, chronic respiratory failure, bronchiectasis. Pneumonia refers to J12–J18. Rest refers to J30–39 and J60–J99 including interstitial pneumonia and other respiratory diseases. Diseases are classified according to the International Classification of Diseases, Tenth Revision (ICD-10; WHO 1993). Statistically significant (P < 1, P < 0.5, P < 0.1). CI = confidence interval, COPD = chronic obstructive pulmonary diseases, NO2 = nitrogen dioxide, O3 = ozone, PM = particulate matter, PM10 = particulate matter with an aerodynamic diameter of b10 μm, PM2.5 = particulate matter with an aerodynamic diameter of b2.5 μm, SO2 = sulfur dioxide.
### Table 4

Percent changes (95% posterior intervals) in the relative risk (RR) of daily total respiratory mortality, male/female respiratory mortality, chronic airway diseases/pneumonia /the rest mortality per 10 μg/m³ or per 10 ppb increase in 2-day moving average (lag 0) concentrations of PM$_{2.5}$, PM$_{10}$, SO$_2$, NO$_2$, O$_3$ in Jinan, China from 2011–2017, with adjustment of copollutants.

|                      | Total | Male | Female | Chronic$^1$ | Pneumonia$^1$ | Rest$^1$ |
|----------------------|-------|------|--------|-------------|---------------|---------|
| PM$_{2.5}$           |       |      |        |             |               |         |
| Single-pollutant      | 0.383 | 0.068| 0.699  |             |               |         |
| +PM$_{10}$           | 0.64  | −0.056| 1.341 | 0.385       | −0.569, 1.349 | 0.929   |
| +SO$_2$              | 0.254 | −0.110| 0.618 | 0.268       | −0.232, 0.770 | 0.236   |
| +NO$_2$              | 0.393 | −0.025| 0.813 | 0.392       | −0.183, 0.970 | 0.393   |
| +O$_3$               | 0.387 | 0.073 | 0.703  | 0.35        | −0.084, 0.787 | 0.247   |
| +All                 | 0.638 | −0.063| 1.343 | 0.407       | −0.556, 1.379 | 0.897   |
| PM$_{10}$            |       |      |        |             |               |         |
| Single-pollutant      | 0.194 | −0.023| 0.412 | 0.206       | −0.093, 0.506 | 0.238   |
| +PM$_{2.5}$          | 0.199 | −0.678| 0.283 | −0.03       | −0.688, 0.631 | 0.156   |
| +SO$_2$              | 0.073 | −0.185| 0.331 | 0.139       | −0.214, 0.493 | −0.012  |
| +NO$_2$              | 0.151 | −0.154| 0.647 | 0.154       | −0.333, 0.644 | 0.123   |
| +O$_3$               | 0.193 | −0.024| 0.411 | 0.202       | −0.097, 0.502 | 0.213   |
| +All                 | −0.312| −0.826| 0.205 | −0.135      | −0.841, 0.576 | 0.723   |
| NO$_2$               |       |      |        |             |               |         |
| Single-pollutant      | 0.514 | 0.095| 0.936  | 0.468       | −0.100, 1.040 | 0.841   |
| +PM$_{2.5}$          | 0.345 | −0.139| 0.832 | 0.755       | 0.001, 1.424 | 0.853   |
| +SO$_2$              | 0.439 | −0.057| 0.938 | 0.775       | 0.096, 1.458 | 0.852   |
| +NO$_2$              | 0.587 | −0.020| 1.197 | 0.947       | 0.114, 1.787 | 1.109   |
| +O$_3$               | 0.596 | 0.173| 1.022 | 0.546       | −0.026, 1.122 | 0.723   |
| +All                 | 0.591 | −0.016| 1.202 | 0.982       | 0.146, 1.824 | 1.003   |
| O$_3$                |       |      |        |             |               |         |
| Single-pollutant      | 0.975 | 0.463| 1.489  | 0.902       | 0.161, 1.649 | 0.994   |
| +PM$_{2.5}$          | 0.970 | 0.458| 1.485  | 1.141       | 0.351, 1.938 | 0.899   |
| +SO$_2$              | 0.991 | 0.479| 1.507  | 1.132       | 0.342, 1.929 | 0.912   |
| +NO$_2$              | 0.950 | 0.435| 1.469  | 1.229       | 0.43, 2.033 | 0.861   |
| +O$_3$               | 0.934 | 0.415| 1.456  | 1.229       | 0.426, 2.077 | 0.845   |
| +All                 | 1.021 | 0.486| 1.559  | 1.203       | 0.387, 2.026 | 0.874   |

**Consistent with previous researches,[11,16,17] our study suggested subgroups, which was higher in females than males, as well as among deaths caused by pneumonia than deaths caused by chronic airway disease. We also found that when O$_3$ was adjusted by PM$_{2.5}$, PM$_{10}$, SO$_2$, or NO$_2$ in copollutant models, the mortality estimates still remained to be statistically significant.**

### 4. Discussion

This time-series analysis of all deaths caused by respiratory diseases from 2011 to 2017 in Eastern China, Jinan found that 10 μg/m³ daily increments of PM$_{2.5}$, SO$_2$, and 10 ppb daily increments of O$_3$ were statistically associated with percent changes on the RR of cause-specific daily mortality. In addition, We found that short-term exposure to PM$_{10}$ had limited impacts on daily mortality, similar to the results of a study involved 0.235 million people in China in 2015.[11,12] However, some previous studies conducted in China showed an opposite conclusion that PM$_{10}$ was significantly associated with respiratory disease.[13,14] especially among population suffered from chronic diseases rather than health groups.[15] Therefore, whether PM10 has an influence on respiratory mortality remains to be explored. Consistent with previous researches,[11,16,17] our study suggested...
that the estimates of health effects had a lag effect and harvesting effect, besides which they also differed between single pollutant models and multiple pollutants model as well as females and males. Previous studies have shown that exposure to air pollution has an impact on additional deaths and hospitalization rates among the public, especially among older adults and people who are sick. A decrease in mortality during the subsequent weeks has been observed because those whose health is already so compromised would be more likely to have died in the short term during early stages of ecological studies, and this would result in an overestimation of health effects attributed to air pollution in the early stages but an underestimation in the later stages. Therefore harvesting effect also refers to mortality displacement, which denotes a temporary increase in the mortality rate in a given population during the early period of ecological researches, indicating the important role of harvesting effect on ecological researches[18,19]. As the data shown in all Figure 1, single day effects of PM_{2.5}, PM_{10}, SO_{2}, NO_{2}, O_{3} on mortality risk of total respiratory disease usually reached a peak at lag 1 or lag 2 (Fig. 1B), consistently with which the moving average over the same day and the previous day (lag 01) of PM_{2.5}, PM_{10}, NO_{2} had a maximal effects, and the cumulative effects of SO_{2} and O_{3} reached a peak at lag 02 and lag 04, respectively (Fig. 1A). In single pollutant models, we observed an increased RR in mortality of 0.283% (95% CI: 0.068, 0.699), 0.194% (95% CI: -0.023, 0.412), 0.514% (95% CI: -0.095, 0.936), 0.822% (95% CI: -0.284, 1.941), 0.975% (95% CI: -0.463, 1.489) per 10 μg/m^{3} daily increments of PM_{2.5}, PM_{10}, SO_{2}, NO_{2}, and per 10 ppb daily increments of O_{3}, respectively. As the results shown, gaseous pollutants, especially O_{3}, had a greater impact on daily respiratory deaths than fine particulate matter, and the effects of ozone on mortality from chronic lower respiratory diseases observed in our research was identical with the results from a study of 265,223 deaths (aged ≥45 years) in the contiguous United States during 2007 to 2008.[20] A potential explanation was that O_{3} could induce or accelerate excess pulmonary inflammation through some pathophysiological pathways, resulting in damage on the airway epithelium cells which could make people especially COPD patients become more susceptible to environmental aggressions, meanwhile contributed to a reduced lung function.[20-22] We observed that there was a greater impact on total respiratory mortality among females than males. The opinions of previous studies on the gender-specific effects of air pollutants on mortality were inconsistent, a majority of studies[11,23,24] held the opinion that females were more susceptible than males due to the narrower respiratory tract and slightly greater airway reactivity.[23,25] Another possible explanation was the different socioeconomic status and stress experiences between females and males, females were more likely to be unemployed thus spend more time outdoors.[26-28] In contrast, some studies supported that males were more sensitive because a larger proportion of women preferred to use a mask when outdoors.[11,29,30] Thus, further studies that assess the gender-stratified pattern of pollutant-health relationship are necessary. A number of previous studies[17,31-33] had revealed that the estimated effects of multiple pollutants models on total mortality were smaller than that of single pollutant models because of the colinearity among air pollutants as well as photochemical interactions and commonality of sources, which was also found in our study except for O_{3}. We found a novel phenomenon that air pollutants especially SO_{2} exhibited greater health effects on chronic airway diseases (including COPD, asthma, chronic respiratory failure, and bronchiectasis) than pneumonia and the rest respiratory diseases. Actually, few previous studies had applied respiratory diseases subgroups-stratified pattern on the analysis of the association between air pollution and daily mortality. Our findings to some extent are consistent with earlier observation results that exposure to air pollution has been significantly related to non-infectious respiratory diseases, but few evidence has suggested the association of air pollutants with infectious respiratory diseases.[34-36]

This study has several strengths. First, unlike previous air pollution studies, most of which only analyzed the impact of 1 or 2 pollutants on daily mortality, 2 particulate matter (PM_{2.5}, PM_{10}) and 3 gas pollutants (SO_{2}, NO_{2}, O_{3}) were considered in this study to make a comprehensive analysis. Second, the health effects of these 5 pollutants were estimated both in single-pollutant models and multiple pollutants models considering the highly colinear components of ambient air pollutants. Third, our study was distinguished from the former ecologic analysis in that we divided respiratory disease into 3 subgroups including chronic airway diseases, various pneumonia, and the rest, resulted in a novel finding that the estimates effects also varied by respiratory disease subgroups. Fourth, our study was conducted in a classical metropolitan area of heavy industries which was one of the most heavily polluted cities in China,[39] and the time span of this study was up to 7 years, which was contributed to make a more accurate estimation of air pollution effects.

There are also some limitations. The primary limitation of this research was that we used average ambient pollutant concentration as a surrogate of individual level rather than exact exposure, so it was inevitable to some unknown measurement errors. As a result, it may lead to a bias of pollution effects. However, this problem also exists in other investigations. Second, this study was limited to be performed in only 1 city, thus the generalizability of our finding is constrained. Moreover, personal behaviors such as smoking, time spent outdoors, and other factors such as occupational exposures also have an influence on the relationship of daily mortality and air pollution. For instance, the elderly were more likely to stay at home, so there may be an underestimation of the health effects on the elderly. However, relevant data is difficult to assess and obtain.

5. Conclusion

This study highlights the significant association of PM_{2.5}, PM_{10}, SO_{2}, NO_{2}, O_{3} with daily respiratory deaths in a heavily polluted city in Eastern China, and the association between daily respiratory deaths and air pollutants varied by disease subgroups. O_{3} had a stronger effect on respiratory deaths among the elderly than other pollutants. We found that the impacts of SO_{2} on chronic airway diseases among the elderly were greater than other respiratory diseases. Moreover, air pollution had a greater impact on total respiratory mortality among females than males. Our findings could make a contribution to develop public policy for individualized protection and protect human health. Our results suggested that in order to intensively explore the individual mechanism of pollutants on specific disease, the future study on the association of air pollution exposure and daily mortality may be conducted among cause-specific deaths, for instance, deaths caused by COPD, pneumonia, tuberculosis, lung cancer, asthma, and so on. There are still some limitations of mortality risk as an indicator to evaluate the health effects of air pollution, so new complementary indicators remains to be found such as years of life lost. Furthermore, it remains a great problem
on how to control and evaluate individual risk factors during such ecological studies.

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