We aimed to assess the acute effects of ambient air pollution and weather conditions on mortality in the context of Chinese smog episodes. A total of 209,321 deaths were recorded in Jinan, a large city in eastern China, during 2011–15. The mean concentrations of daily particulate matter ≤10 μm (PM$_{10}$), fine particulate matter (PM$_{2.5}$), sulfur dioxide (SO$_2$) and nitrogen dioxide (NO$_2$) were 169 μg/m$^3$, 100 μg/m$^3$, 77 μg/m$^3$, and 54 μg/m$^3$, respectively. Increases of 10 μg/m$^3$ in PM$_{10}$, PM$_{2.5}$, SO$_2$ and NO$_2$ were associated with 1.11% (95% CI 0.96–1.26%), 0.71% (95% CI 0.60–0.82%), 1.69% (95% CI 1.56–1.83%), and 3.12% (95% CI 2.72–3.53%) increases in daily non-accidental mortality rates, respectively. Moreover, the risk estimates for these 4 pollutants were higher in association with respiratory and cardiovascular mortality. The effects of all the evaluated pollutants on mortality were greater in winter than in summer. Smog episodes were associated with a 5.87% (95% CI 0.16–11.58%) increase in the rate of overall mortality. This study highlights the effect of exposure to air pollution on the rate of mortality in China.

At present, air pollution is undoubtedly one of China's most pressing public health issues. Northern China has experienced frequent and severe smog episodes since 2011, particularly in winter. High concentrations of fine particulate matter (PM$_{2.5}$) may not only cause substantially reduced visibility by scattering and absorbing sunlight but may also have detrimental effects on human health. These severe smog episodes have been cause for unprecedented public concern regarding the health impacts of air pollution. To address this issue, the Chinese State Council released the “Atmospheric Pollution Prevention and Control Action Plan” on September 10, 2013 with the aim of reducing PM levels. Although many other industrialized countries have experienced severe air pollution problems in the past, including Belgium (Meuse Valley) in 1930, the United States (Pennsylvania) in 1948, and the United Kingdom (London) in 1952, the intensity and geographic extent of and number of people affected by the recent serious air pollution events in China are unprecedented.

The smog that has been observed in China is a complex mixture of air pollutants that are present at high concentrations in a city or a region. This mixture includes such major components as particulate matter (PM; e.g., PM$_{10}$ and PM$_{2.5}$) and gaseous pollutants (e.g., nitrogen dioxide (NO$_2$), carbon monoxide (CO), and sulfur dioxide (SO$_2$)). Many studies conducted worldwide have shown that short-term exposure to air pollution is associated with increased mortality and morbidity, especially due to cardiovascular and respiratory diseases; exacerbation of chronic respiratory conditions; and decreased lung function. Although there existed a strong and useful body of evidence derived from research conducted in other countries, the exposure–response functions of other countries cannot simply be applied to the Chinese context because of differences in particulate composition and population characteristics. For example, in addition to the substantially higher PM$_{2.5}$ concentrations in Chinese smog, the concentrations of SO$_2$ and NO$_2$ are now quite high as well. Moreover, most Chinese studies on air pollution and mortality were conducted before 2010 and lacked PM$_{2.5}$ data. Indeed, the consequences of China’s recent severe air pollution and smog episodes remain largely unknown.

The objective of this paper was to examine the acute effect of PM and gaseous pollutants on daily mortality rates in Jinan, a large urban city in eastern China. Daily ambient air pollutant, weather condition, and mortality data were systematically collected from 2011 to 2015. Obtaining such a large and up-to-date dataset allowed us to assess the effects of ambient air pollutants and weather conditions on mortality in the context of Chinese smog episodes.
Results

Table 1 presents a summary of the daily air pollution concentrations and meteorological conditions in Jinan. The mean concentrations of PM\textsubscript{10}, PM\textsubscript{2.5}, SO\textsubscript{2}, and NO\textsubscript{2} were 169 μg/m\textsuperscript{3}, 100 μg/m\textsuperscript{3}, 77 μg/m\textsuperscript{3}, and 54 μg/m\textsuperscript{3}, respectively.

The daily average counts of non-accidental, cardiovascular, and respiratory deaths are shown in Table 2. Data were obtained for the total of 209,321 deaths that were reported during the 5-year period between January 2011 and December 2015. During the study period, an average of 115 non-accidental deaths occurred each day, of which 65, 40 and 18 deaths were due to cardiovascular diseases, cerebrovascular and respiratory diseases, respectively. The daily mortality rate was higher for men than women and higher for people less than 65 years old than for those who were older than 65 years. The daily mortality rate exhibited a seasonal trend and was higher in the winter months than the summer months. The highest daily mortality rates were observed during smog episodes.

Correlations were identified between different air pollutants and meteorological parameters, and the 5 pollutants were significantly correlated with each other (Table 3). Table 3 shows the mean values of the Spearman coefficients for the correlations between air pollutants and weather conditions in Jinan. Positive correlations were identified between PM\textsubscript{10}, PM\textsubscript{2.5}, SO\textsubscript{2}, and NO\textsubscript{2}. Temperature was negatively correlated with SO\textsubscript{2} and PM\textsubscript{10}.

Table 4 shows the mean percent increases in daily mortality identified in association with air pollutants in Jinan during 2011–2015 using single- and multi-pollutant models. In the single-pollutant models for PM (PM\textsubscript{10} and PM\textsubscript{2.5}), an increase of 10 μg/m\textsuperscript{3} of PM\textsubscript{10} was associated with an increase of 1.11% (95% CI 0.96–1.26%) in the rate of non-accidental mortality, 1.40% (95% CI 1.18–1.61%) in the rate of cardiovascular mortality, 1.58% (95% CI 1.32–1.85%) in the rate of respiratory mortality, and 0.61% (95% CI 0.32–0.90%) in the rate of cerebrovascular mortality; additionally, an increase of 10 μg/m\textsuperscript{3} in PM\textsubscript{2.5} was associated with an increase of 0.71% (95% CI 0.60–0.82%) in the rate of non-accidental mortality, 1.14% (95% CI 0.98–1.30%) in the rate of cardiovascular mortality, 1.02% (95% CI 0.82–1.21%) in the rate of respiratory mortality, and 0.43% (95% CI 0.30–0.55%) in the rate of cerebrovascular mortality. In the two/three-pollutant models, the associations between air pollutants and...
mortality were attenuated but remained statistically significant. The estimates for the effects of PM$_{2.5}$ and PM$_{10}$ on the rates of cardiovascular and respiratory mortality were higher than the estimates for the effects of these pollutants on the rate of non-accidental mortality. The gaseous pollutants (SO$_2$ and NO$_2$) were also significantly associated with non-accidental, cardiovascular, and respiratory mortality rates. The air pollutant and daily mortality associations tended to be linear (Fig. 1).

PM$_{2.5}$, PM$_{10}$ and NO$_2$ demonstrated similar lag patterns in association with total non-accidental, cardiovascular and respiratory mortality (Fig. 2). For single-day lags, the rates of overall and cardiopulmonary mortality decreased from lag day 0 to 5 but remained statistically significant at lag day 5. The estimates for the effects of PM$_{2.5}$, PM$_{10}$ and NO$_2$ on cardiovascular mortality were higher than those identified than the estimates for the effects of these pollutants on respiratory and overall non-accidental mortality. The effect of SO$_2$ on respiratory mortality was higher than the effects of this pollutant on overall and cardiovascular mortality.

Figure 3 presents the pooled effect estimates (mean and 95% CI) for the increases in overall non-accidental, cardiovascular and respiratory mortality associated with air pollutants in winter, summer and smog episodes using moving average lag models (lag 0–1). The associations between air pollutants and mortality differed by season. We observed that the associations between air pollutants and mortality were stronger during winter than during summer. Furthermore, we observed the greater estimates for the effects of the evaluated pollutants on overall, cardiovascular, and respiratory mortality during smog episodes.

In Table 5, we present the results of our investigation of the heterogeneous effects of smog episodes across different age and gender groups. A smog episode is associated with 5.87%, 6.31% and 7.10% increase in total non-accidental, cardiovascular, and respiratory mortality rates in winter.

| Pollutant | SO$_2$ | NO$_2$ | PM$_{10}$ | PM$_{2.5}$ | Temperature | Humidity | Pressure | Wind speed |
|-----------|--------|--------|-----------|-----------|-------------|----------|----------|------------|
| SO$_2$    | 0.728** | 0.533** | 0.428**   | -0.289**  | 0.064       | -0.260   | 0.110**  | -0.038     |
| NO$_2$    | 0.728** | 0.533** | 0.428**   | -0.289**  | 0.064       | -0.260   | 0.110**  | -0.038     |
| PM$_{10}$ | 0.563** | 0.738** | 0.800**   | 0.091     | 0.010       | 0.033    | 0.184    | -0.018     |
| PM$_{2.5}$| 0.649** | 0.732** | 0.854**   | 0.91      | 0.000       | -0.190   | -0.185   | -0.711**   |
| Humidity  | 0.073** | 0.222** | 0.416**   | -0.096*   | 0.010       | 0.033    | 0.184    | -0.395**   |
| Pressure  | 0.314** | 0.246** | 0.072*    | -0.734*   | 0.010       | 0.033    | 0.184    | -0.395**   |
| Wind speed| 0.291** | 0.509** | 0.267**   | -0.329**  | 0.276**     | -0.336** | 0.184    | 0.033      |

**Table 3.** Spearman’s correlation between air pollutants and weather conditions in Jinan, China, 2011–2015. *P < 0.05. **P < 0.01. The summer months (May–September) are shown above the diagonal; the winter months (October–April) are shown below the diagonal.

Discussion

We conducted an exploratory study of the short-term health effects of air pollution using data for the 209,321 non-accidental deaths that occurred during 2011–2015 in a highly polluted large urban city in eastern China. To our knowledge, this is the latest large study to systematically assess the acute effects of air pollution and smog episodes on mortality in China. We found that all the evaluated pollutants (PM$_{2.5}$, PM$_{10}$, SO$_2$, and NO$_2$) significantly impacted non-accidental mortality after adjustment for meteorological factors. Moreover, the risk estimates were greater in magnitude in association with respiratory and cardiovascular mortality than overall non-accidental mortality, and the effects of air pollutants on mortality rates were higher in winter than in summer. We also observed that smog episodes were typically positively and significantly associated with higher rates of mortality, and females and older persons were more vulnerable to smog exposure.

In the present analysis, an increase of a 10 $\mu$g/m$^3$ in the 2-day moving average concentrations of PM$_{10}$ corresponds to 1.11%, 1.40%, and 1.58% increases in the rates of total, cardiovascular, and respiratory mortality, respectively. Generally, the magnitudes of our effect estimates for PM$_{10}$ were slightly higher than those reported in previous studies conducted in China and worldwide. For example, a study assessing data from 75 individual cities worldwide estimated that a 10 $\mu$g/m$^3$ increase in PM$_{10}$ corresponded to a 0.6% increase in the rate of overall mortality$^{10}$. A USA study including data from 90 cities generated an estimate of 0.2% for PM$_{10}$, while a multicity study in four Asian cities (Bangkok, Seoul, Inchon, and Hong Kong) provided a pooled estimate of 0.55%$^{12}$. The CAPES study, which included data registered in 17 Chinese cities (but not Jinan) between 1996 and 2008, showed that a 10 $\mu$g/m$^3$ increase in PM$_{10}$ was associated with a 0.35% increase in daily mortality rates$^{13}$. An explanation for this difference might be that previous studies conducted in China and other developing counties used relatively old data. However, beginning in early 2011, China experienced unprecedented serious air pollution and severe smog events that were characterized by extremely high concentrations of ambient PM. In our study, we collected PM data from the most recent five years in Jinan, and the daily mean PM$_{10}$ level identified in this study was much higher than those reported in previous studies in China. The stronger association observed between the level of particulate matter and the rate of mortality suggests that particulate air pollution may represent a major and growing public health problem in Chinese cities.

PM$_{2.5}$ is a pollutant that is a major component of Chinese haze. However, real-time PM$_{2.5}$ data have been only available since 2012 in most districts in China, after public outcry regarding the thick smog in China resulted in
analyses were adjusted for seasonality, day of the week, temperature, relative humidity, air pressure and wind including increased heart rate, decreased heart rate variability, and increased cardiac arrhythmias. These findings suggest that people with heart or lung diseases may be more sensitive to PM. Particulate matter has been reported to be associated with increased plasma viscosity, changes in blood characteristics, and indicators of anomalies in the autonomic function of the heart, including increased heart rate, decreased heart rate variability, and increased cardiac arrhythmias. These findings provide possible pathways through which particulate matter may affect the cardiopulmonary system.

For SO2 and NO2 in the single-pollutant model, an increase of 10 μg/m3 was associated with increases of 1.69%, 2.29%, and 2.52% and 3.12%, 4.80%, and 4.48% in the rates of total, respiratory and cardiovascular mortality, respectively. Inclusion PM or NO2 in the model did not significantly influence the estimates for association between SO2 and mortality, while the estimates for association between NO2 and mortality decreased when SO2 was added. The associations between PM and the evaluated outcomes also became weaker after gaseous pollutants, particularly SO2, were included in the model. The estimates for the effect of SO2 on mortality in Jinan were slightly higher than those reported in most previous studies but were generally comparable with recent data from Chinese cities. A meta-analysis reported that the excess rate of non-accidental mortality associated with a 10 μg/m3 increase in SO2 was 1.00% (95% CI, 0.75 to 1.24%) in four Asian cities (Bangkok, Hong Kong, Shanghai and Wuhan). A recent time series analysis conducted in Ningbo (2009–2013) reported a 10 μg/m3 increase in SO2 to be associated with a 2.89% (95% CI 2.04–3.76%) increase in the rate of daily mortality. However, some North American studies did not report a significant association between SO2 and mortality, which may be because of the very low levels of SO2 air pollution in these cities. Our results suggested SO2 to have a greater impact on

Table 4. Percent increase in the rate of overall non-accidental mortality and cause-specific mortality associated with a 10 μg/m3 increase in air pollutants at lag 0–1 day using single- and multi-pollutant models. *P < 0.05. The analyses were adjusted for seasonality, day of the week, temperature, relative humidity, air pressure and wind speed.
mortality in Jinan, and previous studies have suggested that the risk of mortality associated with exposure to SO2 may be greater in China than in Western countries.

We also investigated the effects of weather conditions on the association between air pollution and mortality, and we found that the adverse effects of air pollution were much stronger during the cool season in Jinan. One possible explanation may be that the composition of air pollution varies across seasons. From 2011 to 2015, the median levels of PM were all higher in the winter months than in the summer months. In general, atmospheric inversions are more likely to occur during the cold seasons, limiting the dispersion and dilution of pollutants emitted at the ground level. In addition, the combustion of fuel for space heating may results in increased PM2.5 emissions during the winter months. One could postulate that the ambient pollutant concentrations identified in this setting may reflect the mixed pollutants present in a smog episode, which may potentially have adverse health effects. Moreover, we also found that the smog episodes had a more substantial impact on mortality in older persons and females.

In conclusion, we identified significant associations between ambient air pollutant (PM2.5, PM10, SO2, and NO2) concentrations, smog episodes and daily mortality rates in Jinan, China. These estimates were robust due to the inclusion of meteorological factors and model specifications, and the pollutants exerted greater effects on the rates of respiratory and cardiovascular mortality than the rate of overall non-accidental mortality. In addition, the smog episodes had effects that were more detrimental on females and older persons. These findings highlight the importance and urgency of air pollution control; additionally, they call for the implementation of effective and evidence-based policies to improve air quality in China.

Methods

Mortality data. Jinan is a metropolitan area with a population of approximately 7 million located in the eastern part of China. Daily mortality data for Jinan during the 5-year period from January 2011 to December 2015 were obtained from the Jinan Municipal Center for Disease Control and Prevention, and the collected data included date of death, sex, and underlying cause of death according to the International Classification of Diseases, 10th Revision (ICD-10). A total of 209,321 deaths (117,857 male, 91,464 female) occurred during the five-year study period. The mortality data were categorized into deaths due to total non-accidental causes (ICD-10: A00-R99), cardiovascular disease (ICD-10: I00-I99), respiratory disease (ICD-10: J00-J99), and cerebrovascular disease (ICD-10: I60-I69). For overall mortality, the data were stratified by gender (female and male), and age (≤60y, 60–70y, and >70y).

Pollution data. Mean hourly PM10, PM2.5, SO2, and NO2 concentration data were obtained from the Environmental Monitoring Center of Jinan for the same 5-year period for which mortality data were available. The data were obtained from 14 monitoring stations. The pollutant monitoring network spanned the entire region, including 12 sites located in the city and 2 sites located in a suburban county. We abstracted the daily 24-hr mean concentrations of PM2.5, PM10, SO2, and NO2. The daily air pollutant concentrations were calculated as the average of the concentrations recorded at the 14 stations.

Figure 1. Associations between air pollutants (lag 0–1 day) and daily mortality in Jinan, China, 2011–2015. A natural cubic spline with 3 degrees of freedom for air pollutants was included in the single pollutant models, while controlling for day of the week, temperature, relative humidity, wind speed, and air pressure.
Meteorological data. We collected daily weather information for the period from January 1, 2011 to December 31, 2015 from the China Meteorological Science Data Sharing Service Network (http://cdc.cma.gov.cn/home.do). We downloaded the following data: daily mean temperature, air pressure, humidity, and wind speed.

Statistical analysis. Generalized linear models (GLM) with quasi-Poisson regression were constructed using the MGCV package in R software to analyze the associations between daily concentrations of air pollutants and the number of all cause and cause-specific deaths. Considering the confounding effects of long-term trends, seasonal patterns and meteorological parameters, the smoothing spline functions involved in calendar time, daily

Figure 2. Percent increases in daily mortality associated with a 10 μg/m³ increase in PM$_{2.5}$, PM$_{10}$, SO$_2$ and NO$_2$ concentrations using different lag structures in Jinan, China, 2011–2015.

Figure 3. Estimated increases (and 95% confidence intervals) in daily mortality rates (overall non-accidental, respiratory, and cardiovascular) corresponding to a 10 μg/m³ increase in each pollutant during summer (May–September), winter (October–April) and smog periods (a total of 269 days) based on multi-pollutant models (lag 0–1 day).
mean temperature, relative humidity, wind speed and air pressure were applied. We used a natural cubic spline with 7 degrees of freedom per year for time. Based on Akaike’s information criterion (AIC), we specified the appropriate degrees of freedom in the smoothing spline functions for the evaluated weather conditions. The day of week was controlled for as a categorical variable. After establishing the basic model, we introduced the air pollutant concentrations into the models. The regression model can be written as follows:

$$\log E(Y_t) = \text{intercept} + \beta Z_t + \text{ns}(\text{time, df}) + \text{DOW} + \text{ns}(\text{temperature, df})$$

$$+ \text{ns}(\text{humidity, df}) + \text{ns}(\text{wind speed, df}) + \text{ns}(\text{air pressure, df})$$

where $E(Y_t)$ represents the expected number of daily deaths on day $t$; $\beta$ represents the regression coefficient; $Z_t$ is indicative of the pollutant concentrations on day $t$; $\text{ns}(\text{time, df})$ denotes a smooth function of calendar time with 7 df per year to control seasonality and longer-term trends; “DOW” is the dummy variable for day of the week; and $\text{ns}(\text{temperature/humidity/wind speed/air pressure, df})$ is a smoothed function of temperature, humidity, wind speed or air pressure with 3 df.

We examined these associations using different lag structures, including a single-day lag (from lag 0 to lag 5) and moving average lag (lag 0–1). For the single-day lag models, a lag of 0 days (lag 0) corresponded to the current-day air pollution concentration, and a lag of 1 day (lag 1) referred to the previous day’s pollutant concentrations. For the moving average lag models, lag 0–1 corresponded to a 2-day moving average of the air pollution concentrations recorded on the current and previous day. For each pollutant, we fitted both single-pollutant and multi-pollutant models to assess the stability of the associations. Stratified analyses were conducted according to sex, age and cause of death to identify populations who were potentially more sensitive to air pollution. To examine whether the effects of air pollutants on mortality differed by season in Jinan, we also evaluated the following time periods: summer months (June, July, August), winter months (January, February, and December) and smog episodes. The percentages increase in death associated with a 10 μg/m³ increase in each pollutant as well as their 95% confidence intervals (CI) were computed.

Any period during which daily PM$_{2.5}$ concentrations exceed 100 μg/m³ for three or more consecutive days was defined as a smog episode. We used the following models to compare the mortality differences between the smog episodes and the regular days.

$$\log E(Y_t) = \alpha + \beta \text{smog t} + \sum_{i=1}^{P} S_i(Z_{it}, df z_i)$$

where $yt$ is the number of deaths on day $t$; smog is a dummy indicator for the smog episodes; $\beta$ represents the log-relative rate of mortality associated with a smoggy day. Zit are meteorological factors that are correlated with air pollution levels, and Si are their natural spline smooth functions.

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| Pollutant and model | Overall mortality | Cardiovascular mortality | Respiratory mortality |
|-------------------|-------------------|-------------------------|----------------------|
|                   | % (95% CI)        | % (95% CI)              | % (95% CI)           |
| Overall           | 5.87 (0.16–11.58) | 6.31 (0.22–12.4)        | 7.10 (0.11–14.09)    |
| Age               | % (95% CI)*       | % (95% CI)              | % (95% CI)*          |
| <60y              | 3.64 (0.07–7.35)  | 4.02 (0.03–8.01)        | 4.41 (0.17–8.65)     |
| 60–70y            | 5.35 (0.44–11.14) | 4.91 (0.11–9.70)        | 5.71 (0.76–10.66)    |
| >70y              | 8.32 (0.23–16.41) | 8.86 (0.55–17.17)       | 9.47 (0.23–18.71)    |
| Gender            | % (95% CI)        | % (95% CI)              | % (95% CI)           |
| Male              | 4.97 (0.23–9.71)  | 6.02 (0.13–11.91)       | 6.88 (0.32–14.09)    |
| Female            | 6.46 (0.47–13.39) | 6.70 (0.05–13.35)       | 7.33 (0.89–15.56)    |

Table 5. Age- and gender-stratified effects of smog on mortality rates. *P < 0.05.
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Author Contributions
Y.L. and Z.J. conceived and designed the study, and H.C.L. directed its implementation, including the data analysis and writing of the paper. L.L.C. and Z.J. analyzed the data; S.-Q.L. and X.X.Y. contributed materials/analytic tools; Y.L. and Z.J. wrote and revised the manuscript. All authors reviewed and approved the manuscript prior to submission.

Additional Information
Competing Interests: The authors declare that they have no competing interests.

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