Identification of Health Effects of Complex Air Pollution in China

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Abstract

With the progress of air pollution control in China, the concentration of particulate matter has decreased, but the concentration of ozone has increased, the problem of complex air pollution has become more severe, posing a serious threat to public health. However, there is less study on the health effects of complex air pollution in China. Instead of introducing pollutant concentrations directly, we converted them into a set of predictors to prevent collinearity and other problems will occur when the concentrations of multiple correlated pollutants are introduced in general multi-pollution models. Based on different combinations of $PM_{2.5}$, $NO_{2,}$ and O_3 concentration levels, air pollutant constituent condition is divided into eight types, including three single-pollutant types and four multi-pollutant types. The health effects of different pollution types on mortality in eight typical Chinese cities from 2013 to 2016 were evaluated using a generalized additive model. The results from eight cities collectively indicate that multi-pollutant type leads to a higher impact on mortality risk than single-pollutant type. Type 7 with higher $PM_{2.5}$, O_3, and NO_2 and type 4 with higher $PM_{2.5}$ and NO_2 have a greater relative risk among them. In most northern cities, the multi-pollutant type has a higher mortality effect in the warm season, but the single-pollutant type with high $PM_{2.5}$ has a higher effect in the cold season. In southeastern cities, the multi-pollutant type had a higher mortality effect in both seasons. The results also showed that the excess risk of multi-pollutants was less than the simple sum of individual air pollutants effects, partially false conclusions would have been reached by ignoring the presence of interactions between air pollutants. The result further highlights the urgency and necessity of moving towards a multi-pollutant approach in air pollution health research under the background of atmospheric emission reduction and global warming.

1. Introduction

Nowadays, air pollution is one of the major health issues facing the world's metropolitans, especially in developing countries (Chan and Yao, 2008; Tao et al., 2012; Khaefi et al., 2016; Dastoorpoor et al., 2018; Javanmardi et al., 2018). With the rapid development of China's economy, urban construction is expanding, the number of motor vehicles is increasing rapidly, and the emission of primary particulate matter, carbon monoxide (CO), nitrogen oxides (NOx) and volatile organic compounds (VOCs) in some economically developed areas has raised significantly. Some primary pollutants can generate secondary pollutants, such as fine particulate matter ($PM_{2.5}$) and ozone (O_3), through complex chemical reactions under certain conditions. This makes the problem of complex air pollution, such as haze and photochemical smog more prominent, posing a serious threat to public health. Therefore, complex air pollution and its health effects have become a major concern of the whole society (Chen, 2013; Li et al., 2017; Schwartz et al., 2018; Duan et al., 2019; Strassmann et al., 2021).

To improve the overall air quality, the Chinese government has issued a series of policies (Action Plan for The Prevention and Control of Air Pollution and Three-year Action Plan (2013) to Win the Blue Sky Defense War (2018)) to step up the fight against air pollution, focusing on fine particulate matter (PM2.5) to prevent and control air pollution (Xin et al., 2021). Although significant progress has been made in

improving air quality in China, the situation remains grim. On the one hand, the Action Plan for The Prevention and Control of Air Pollution mainly aims at the emission reduction policy of inhalable particulate matter, but it does not effectively limit the emission of ozone and other pollutants, leading to the prominent problem of ozone pollution in key areas. Since the release of O_3 data in 2013, the concentration levels of O_3 in China have been rising, especially in key cities and regions. On the other hand, the World Health Organization (WHO) (2021) issued the latest revised Global Air Quality Guidelines (2021) (AQG, 2021), tightened the annual average target value of $PM_{2.5}$, PM_{10}, NO_2 and other long-term exposure indicators based on new evidence of the health effects of low concentration levels and long-term exposure to pollutants. The target annual $PM_{2.5}$ value was lowered from 10 μg/m^3 to 5 μg/m^3. The annual NO_2 target value changed from 40 μg/m^3 to 10 μg/m^3. By 2020, although the overall annual average concentration of $PM_{2.5}$ was reduced to 33 μg/m^3 for the first time, 34% lower than the annual average concentration of 50μg/m^3 in 2015 (China Environmental Status Bulletin 2015), there was still a big gap between the new AQG target value. Therefore, the problem of complex air pollution is not only prominent now but also continues to exist at least for a while. Under the background of atmospheric emission reduction and global climate change, it is an important challenge to strengthen the coordinated control and treatment of multiple pollutants and effectively solve the regional and complex pollution problems represented by $PM_{2.5}$ and ozone, so as to protect public health. At the same time, it also puts forward higher requirements for research in the field of air pollution and health.

Many studies (Bell et al., 2006; Rojas et al., 2007; Dominici et al., 2010) have been conducted to ascertain the effects of air pollution on mortality by single-pollutant models, which assess the health effect of one pollutant, primarily the effect of particulate matter (PM) (Cao et al., 2012; Chen et al., 2017) (e.g. particulate matter < 10 μm in aerodynamic diameter (PM_{10}) and particulate matter < 2.5 μm ($PM_{2.5}$)) and gaseous pollutants (Atkinson et al., 2012; Yin et al., 2017; Duan et al., 2019) (e.g. nitrogen dioxide (NO_2), sulfur dioxide (SO_2) and ozone (O_3)) on health, especially mortality outcomes. Nowadays, as far as China is concerned, however, air pollution exists as a complex mixture whose nature and consequences are without doubt multi-dimensional. The results of both epidemiologic and laboratory research indicate that even if single pollutants can dominate certain effects when multiple air pollutions co-exist, their overall toxicity may differ from that found in investigations specific to individual pollutants (Mauderly et al., 2009). The World Health Organization also focused on “Multi-pollutant effect estimates as a basis for joint health impact assessment” in the discussions for updating the global air quality guidelines (WHO, 2018). Now is the time to shift the emphasis of air pollution health research toward a more comprehensive, forward-looking, multipollutant perspective in view of the increasing trend toward multipollutant regulatory strategies.

In fact, to make up for the lack of studying health risks from the perspective of single pollutants, some scholars have studied the health effects of multiple pollutants. Since current statistical methods are insufficient to address the health risks and estimate higher-order interactions of multiple pollutants. Some form of dimensionality reduction is required to reduce the data to a set of key predictors (Dominici et al.,

2010). Therefore, Health Canada and Environment Canada developed the Air Quality Health Index (AQHI) to capture the combined health effects of multiple air pollution based on the association between death and multi-pollutants (Stieb et al., 2008). Since then, AQHI is used in some countries and regions as a tool developed to reflect the health risks linked with simultaneous exposure to several different air pollutants. Similar approaches were used in South Africa (Cairncross et al., 2007) and Europe (Sicard et al., 2011; Olstrup et al., 2019). In China, some research and forecasting work has been carried out, with local AQHI established in Hong Kong (Wong et al., 2013), Guangdong province (Li et al., 2017) and Lishui City in Zhejiang Province (Lishui Ecological environment Bureau, 2020). However, it is not very clear that whether AQHI is an ideal indicator for predicting health risk (Li et al., 2017). The general idea of these methods is to estimate each single pollutant effect while controlling for the presence of the others, and then define the multi-pollutant effect as the sum of the effects of each air pollutant, regardless of interactions or nonlinear effects. Since interactions among ambient air pollutants are plausible, partially false conclusions would have been reached by ignoring the presence of interrelations between air pollutants (Mauderly et al., 2009). In addition, even if there is research can define similar statistical models to account for higher-order interaction, so as to capture the health burden associated with the simultaneous exposure to more than two pollutants (Dominici et al., 2010; Bobb et al., 2015), when some highly correlated pollutants are simultaneously included in the regression model, the results can become highly unstable and often inaccurate (Godzinski et al., 2021). Ozone, for example, is negatively correlated with $PM_{2.5}$ and NO_2 due to its formation and characteristics (Evangelopoulos et al., 2021); PM_{10} is highly correlated with nitrogen dioxide in characterizing urban pollution (Dominici et al., 2010). In these cases, the main effects of these pollutants or their interactions cannot be reliably estimated by regression models (Godzinski et al., 2021). Therefore, disentangling the health effect of multi-pollutants has been a long-discussed challenge.

For another, the broad consistency exists between the effect estimates of ambient pollution to health across the world (Speizer et al., 2008). That means differences in pollutant concentrations and source, population susceptibility, and time-activity types of the population can not substantially change the relationship between mortality risk and absolute pollutant concentrations. However, that broad consistency does not mean complete agreement (Wong et al., 2001). As the largest developing country in the world, China has a large population, higher energy consumption and more serious combined pollution problems. The fifth assessment report of IPCC also indicates that climate change in the 21st century is expected to exacerbate health threats in many regions, particularly in developing countries (IPCC, 2014). In addition, due to China's vast territory, there are regional differences in climate and emissions structure. Therefore, it is of great practical significance to carry out a multi-city study in developing countries and quantitatively analyze the relationship between acute multi-pollutant exposure and mortality more accurately for promoting atmospheric environmental protection and improving the health level of Chinese residents.

Considering these problems, instead of introducing pollutant concentrations directly, we converted them into a set of predictors that divided the air pollution levels into different types according to the

composition of the air pollution, thereby estimating the death risks of multi-pollutants. At the same time, multi-city research in developing countries will be carried out to strengthen the capacity of health-driven coordinated air pollution control following local conditions, so as to provide a basis for the formulation of multi-pollution air quality standards that meet local needs.

2. Methods

2.1 Study area

A multicity time-series study was conducted to assess the adverse effects of short-term exposure to a single or multi-pollutant type on daily mortality in eight metropolises in China. The cities, which were not chosen randomly but because there were relatively complete data in each and these are large cities in different climate regions of China, were Changchun (short for CC, temperate continental monsoon climate, Northeast China), Urumqi (short for WLMQ, temperate continental arid and semi-arid climate, west of Northwest China), Beijing (short for BJ, warm temperate semi-humid climate, North China), Xian (short for XA, temperate semi-arid monsoon climate, east of Northwest China), Nanjing (short for NJ, the transition zone between warm temperate zone and subtropical zone, East China), Wuhan (short for WH, subtropical humid monsoon climate, Central China), Kunming (short for KM, subtropical, tropical plateau monsoon climate, Southwest China), and Guangzhou (short for GZ, subtropical – tropical humid monsoon climate, South China).

2.2 Data Collection

For the period 2013–2016, daily mortality counts for all nonaccidental causes [International Classification of Diseases, Revision 10 (ICD-10, A00-R99] in each district of the eight cities were obtained from the Chinese Center for Disease Control and Prevention. Based on the district code, the total number of non-accidental deaths per day for each city was calculated.

Air pollutant concentration observations including ozone, nitrogen dioxide, and particulate matter with an aerodynamic diameter of < 2.5 μm ($PM_{2.5}$) were acquired from the Ministry of Ecology and Environment of the People's Republic of China. After hourly values greater than 500 μg/m^3 were converted into lacking values to protect against outliers (Bell et al., 2004), the daily mean values of $PM_{2.5}$ and NO_2 and the 1-hour maximum ozone at each monitor were calculated. For assessing the population exposure level in a city, a single monitoring station is unlikely to be sufficient (Romieu et al., 2012). To reduce random errors, multiple-site averages for a city were applied to reflect the population's exposure risk (Thurston et al., 2001; Ito et al., 2001). These daily, within-city average concentrations were used as the average exposure of the population at risk in each city.

Daily average meteorologic data regarding mean temperature, relative humidity, air pressure, wind speed and precipitation were obtained from the China Integrated Meteorological Information Service System of National Meteorological Information Center, China Meteorological Administration. Because the variability

of mean temperature and relative humidity within the city limits is small (Wong et al., 2008), the weather conditions for each city were derived entirely from one monitoring station there.

2.3 Classification of pollution types

Firstly, we selected the pollutants in this study. According to WHO (2018), PM, O_3, NO_2 and SO_2 are pollutants in its “Group 1”, which “should be considered of greatest importance in the process of updating the WHO Air Quality Guidelines”. However, high-level collinearity could be introduced when incorporating $PM_{2.5}$ and PM_{10} in the regression model simultaneously, leading to the instability of the model (Godzinski et al., 2021). Therefore, $PM_{2.5}$, which with smaller particle size and is more harmful to human health (Lin et al., 2016), is chosen to represent PM in the current study. Considering that the emissions of SO_2 have been drastically cut in recent years (CAA, 2020), in this paper, $PM_{2.5}$, O_3 and NO_2 were selected to evaluate the health effects of complex air pollution.

To define air pollution constituent condition as different types, first, each of the three pollutants is categorized into two levels (low and high), using the median of $PM_{2.5}$ and NO_2 and the 70-quartile of O_3 for each city (Table 1) as the cut-off. This is due to the asymmetrical distribution of ozone concentration, which is more distributed in the low concentration range, making it difficult to distinguish between high and low concentrations using the median. The cut-offs are different for each city. The cities with the highest cut-off value of $PM_{2.5}$ is Beijing (62.2μg/m^3), NO_2 is Urumqi (51.0μg/m^3), and ozone is Guangzhou (140.6μg/m^3), while the lowest city of $PM_{2.5}$ and NO_2 is Kunming (28.0μg/m^3 and 29.0μg/m^3, respectively), almost only half of the highest value, and O_3 is Urumqi (89.5μg/m^3).

Then a set of permutations of these three pollutants at different levels were grouped as eight different types (Table 2), including one reference type, three single-pollutant types and four multi-pollutant types. They are Type 0 (reference type): the concentrations of the three pollutants are all below the cut-off; Type 1 (single-pollutant): $PM_{2.5}$ concentration is above the cut-off, while the concentration of the other two pollutants is below the cut-off; Type 2 (single-pollutant): NO_2 concentration is above the cut-off, while the concentration of the other two pollutants is below the cut-off; Type 3 (single-pollutant): O_3 concentration is above the cut-off, while the concentration of the other two pollutants is below the cut-off; Type 4 (multi-pollutant): $PM_{2.5}$ and NO_2 concentration is above the cut-off, while the concentration of O_3 is below the cut-off; Type 5 (multi-pollutant): $PM_{2.5}$ and O_3 concentration is above the cut-off, while the concentration of NO_2 is below the cut-off; Type 6 (multi-pollutant): O_3 and NO_2 concentration is above the cut-off, while the concentration of $PM_{2.5}$ is below the cut-off; Type 7 (multi-pollutant): the concentrations of the three pollutants are all above the cut-off.

Because the types containing the condition that ozone concentration is above the cut-off (types 3, 5, 6, and 7) occurred very infrequently (less than 20 times) in some cities (eg. Type 3, 5, 6, and 7 in BJ) during the cold season (Fig. 1), they were excluded from the seasonal analysis of these cities.

Table 1
The cut-off of $PM_{2.5}$, NO_2 and O_3 in each city (μg/m^3)

City	Median of $PM_{2.5}$	Median of NO_2	70-quartile of O_3(1h-Max)
Changchun	43.667	39.925	113.000
Urumqi	49.146	50.967	89.514
Beijing	62.208	46.903	138.450
Xian	58.075	44.782	119.400
Nanjing	54.501	45.483	137.450
Wuhan	61.625	45.789	142.660
Kunming	27.954	29.043	105.667
Guangzhou	38.051	44.233	140.600

Table 2
The 8 types of pollution defined and the predominant pollutants for each type (the pollutant whose concentration is higher than the cut-off).

Pollutant type	Predominant pollutants
0	None
1	$PM_{2.5}$ only
2	NO_2 only
3	O_3 only
4	$PM_{2.5}$+NO_2
5	$PM_{2.5}$+O_3
6	NO_2 + O_3
7	$PM_{2.5}$+NO_2 + O_3

2.4 Data Analysis

Because daily mortality counts typically follow a Poisson distribution, we used a generalized additive model (GAM) with Poisson link to evaluate the association between mortality and air pollution types controlling for average temperature, relative humanity, seasonality and long-term trends using cubic smoothing spline (Ostro et al., 2006; Samet and Katsouyanni 2006). We created a variable with 8 levels

representing every combination of three pollutant concentration categories (high or low concentrations of NO_2, $PM_{2.5}$ and O_3), and used this variable as the main exposure in the model:

$$\log\left[E\left(Y_k\right)\right] = \alpha + DOW + \beta \times X_k + s(time, df) + s(temperature, df) + s(RH, df)$$

1

where $E\left(Y_k\right)$ is the expected number of deaths on day t. α is the model intercept. X_k is a dummy variable, representing different combinations of pollutant concentrations. β is the regression coefficient for X_k. Day of the week was also included as a dummy variable: DOW. time represents time to adjust for long-term trends and seasonality. s(time, df), s(temp, df) and s(RH, df) were spline smoothers for date, daily average temperature, and daily average relative humidity, respectively, which captures the nonlinear relationships of the covariates of daily mortality with time trend and the weather parameters. df is the degree of freedom determined by minimizing the Akaike's Information Criterion (AIC). Considering that similar studies have all used a degree of freedom below 10. In this study, tests are conducted in the range of 4 or 8 (1–2 per year) for each time term, and the degrees of freedom of the model with the lowest AIC is selected. The degrees of freedom of average temperature and average relative humidity was 4.

Lag structures are included as air pollution may affect health outcomes happening on the same day or on subsequent days. We analyzed the one-day lag mode from Lag0 to Lag5, where Lag0 represented the pollutant type on day 0, Lag1 was the pollutant type on the previous day, and so on. In addition to the overall analyses, all models were also stratified by season (cooler vs warmer months). The cold season was defined as November through May and the warm season as April through October.

All results were presented as relative risks (RRs) or excess risk (ER) of mortality and their 95% Confidence Interval (95%CI), calculated from the relative risk (RR) and excess risk (ER) as follows:

$$\mathrm{RR} = e^{\beta}$$

2

ER=(RR-1) × 100 (3)

All statistical tests were 2-sided, and p-values < 0.05 were considered statistically significant. The analysis was performed in R-software, version 4.1.0, using time-series analysis with the mgcv package.

2.5 Sensitivity analyses

Finally, sensitivity analysis is performed to ensure the stability of the model. Within a range of 4 to 10 df, a change in the number of degrees of freedom at intervals of 2 for time trend did not substantially affect the estimated effects of each pollutant type (Figure A1). We also compared the effects of each pollutant type with alternative values for degrees of freedom for meteorological conditions. Within a range of 4 to 10 df, a change in the number of degrees of freedom at intervals of 2 for temperature and relative

humidity resulted in almost identical estimated effects of air pollution on all-cause mortality (Figure A1). In this respect, our findings were relatively robust.

3. Results

We made statistics on the frequency and ratio of single-pollutant type and multi-pollutant type, as well as the frequency of each pollution type in each city. In general, multi-pollutant types (type 4, type 5, type 6, and type 7) occur more frequently than single-pollutant types (type 1, type 2, and type 3). The frequency ratio of multi-pollutant types to single-pollutant types was the largest in Beijing, the frequency of multi-pollutant type was 2.22 times that of single-pollutant type there. While the ratio was the smallest in Urumqi, it is 1.48 times of frequency of single-pollutant types (Table 3). The frequency of each pollutant type was different during the study period (Fig. 1). In the whole year, the results in all 8 cities showed that type 4, the multi-pollutant type with a higher concentration of $PM_{2.5}$ and NO_2, was the most frequent pollution type. It appears more frequently than the reference type or any other pollution type in six central-northern cities, and was second only to the reference type in the two southern cities (Guangzhou and Kunming). During the study period, the frequency of type 4 in 8 cities ranged from 33.3% (486 days, Urumqi) to 24.4% (327 days, Kunming), and the frequency of the reference type was from 31.0% (453 days, Kunming) to 21.6% (315 days, Urumqi). The next type with high frequency was mainly type 7 ($PM_{2.5}$, NO_2 and O_3 are all above the cut-off) in southern cities, ranging from 15.1% (220 days, Guangzhou) to 10.3% (151 days, Nanjing), while type 3 (only O_3 higher than cut-off) in northern cities, ranged from 17.2% (251 days, Urumqi) to 8.9% (130 days, Beijing).

Table 3
Percentage and ratio of the frequency of multi-pollutant and single-pollutant types

City	Single-Pollutant(%)	Multi-Pollutant(%)	Multi-Pollutant/ Single-Pollutant
Changchun	25.5	47.2	1.851
Urumqi	30.7	45.4	1.479
Beijing	21.5	47.8	2.223
Xian	28.7	46.6	1.624
Nanjing	28.2	44.9	1.592
Wuhan	26.6	45.2	1.699
Kunming	22	45	2.045
Guangzhou	22.5	45.1	2.004

We found the frequency distribution of different pollutant types varied strongly across seasons (Fig. 1). In the warm season, the most frequent occurrence is the reference type (type 0). Apart from that, type 3 (only O_3 higher than cut-off) was the most frequent in central and northern cities. In southern cities (Kunming

and Guangzhou), the highest frequency was type 7 (O_3, $PM_{2.5}$ and NO_2 are all above the cut-off). In the cold season, the frequency of type 4 ($PM_{2.5}$ and NO_2 are both above the cut-off) almost accounted for half of the whole cold season, which was the type with the highest frequency in all eight cities. In the central and northern cities, the type containing high ozone concentration rarely appeared (less than 6%) in the cold season, while in southern cities, type 7, which means that the three pollutants including ozone are all above the cut-off, also appears relatively frequently (about 10% of the cold season).

As shown in Table A1, among the eight pollution types, there was an average of mortality from 49.5 ± 34.0 (type 6) to 65.0 ± 40.2 (type 7) person/day in all eight cities from 2013 to 2016. During the period, the highest daily average concentration of $PM_{2.5}$ and NO_2 were type 4 (113.8 ± 71.3 and 67.4 ± 20.9 μg/m^3 respectively). The highest daily 1-hr maximum O_3 was type 5 (175.1 ± 47.5 μg/m^3). In total, the highest average daily temperature and relative humidity were type 3 (24.8 ± 4.6℃) and type 1 (71.7 ± 17.2%), and the lowest was type 4 (5.9 ± 10.3℃) and type 6 (57.3 ± 17.4%), respectively. Statistics by city showed that the types of the highest concentration of the three pollutants for most cities were similar to the average for all of them.

By comparing the greatest RR along lag0-lag5 of each pollution type (Fig. 2), we studied the pollution type with the highest RR in each city throughout the year and in different seasons. In all-year analyses, we found that except Kunming, which had the lowest pollutant concentration among them, the largest types of RR of the other seven cities all belong to the multi-pollutant type. Among them, the pollution type with the highest RR values in most northern cities (Changchun, Beijing, Xi’an, and Nanjing) is type 7 ($PM_{2.5}$, NO_2, and O_3) while the type with the highest RR values in two southern cities (Wuhan and Guangzhou) is type 4 ($PM_{2.5}$ and NO_2). Different from cities in the central and eastern regions, Urumqi in the remote northwest has the highest RR (1.228 (1.129, 1.336)) of type 5 ($PM_{2.5}$ and O_3), while Kunming, which is located in the southwest, has the highest RR (1.069 (1.042, 1.096)) of type 1($PM_{2.5}$). The highest RR in all cities included the condition that $PM_{2.5}$ was above the cut-off. Results from lag models indicated that exposure to multi-pollutant air on more recent days, such as from the same day to 2 days ago was associated with a larger risk of mortality than exposure on less recent days (such as three days ago or earlier). In the warm season, the types with the highest RR of most cities also belong to multi-pollutant types, only Changchun (type 1) and Xi 'an (type 2) belong to single-pollutant types, while in Xi 'an, the risk of multi-pollutant type 4 (1.071 (1.043, 1.101)) ($PM_{2.5}$ and NO_2) is only slightly lower than that of type 2 (NO_2) (1.073 (1.040, 1.108)). In the cold season, most of the pollution types with high ozone concentrations were not calculated due to their low occurrence frequency. Half of the remaining pollution types (including most northern cities and Kunming in the southwest) had the highest RR of type 1($PM_{2.5}$). By comparing the maximum RRs value of each city in different seasons, we found that the relative risks of southeastern cities (Wuhan and Guangzhou) are higher in the cold season while that of northern and western cities is higher in the warm season.

Table 5
The pollutant type with the highest lag of 0–5 days and their corresponding risk values and lag days in 8 cities. Pollutants above the cut-off are listed in parentheses (Annual). **P < 0.01

City	The pollution type with the highest RR(Annual)	The highest RR (with 95% CIs)	lag
Changchun	Type 7(O_3 + $PM_{2.5}$+NO_2)	1.080 (1.032, 1.131)	lag2**
Urumqi	Type 5(O_3 + $PM_{2.5}$)	1.228 (1.129, 1.336)	lag0**
Beijing	Type 7(O_3 + $PM_{2.5}$+NO_2)	1.077 (1.042, 1.113)	lag0**
Xian	Type 7(O_3 + $PM_{2.5}$+NO_2)	1.077 (1.048, 1.107)	lag0**
Nanjing	Type 7(O_3 + $PM_{2.5}$+NO_2)	1.129 (1.080, 1.181)	lag1**
Wuhan	Type 4($PM_{2.5}$+NO_2)	1.089 (1.066, 1.113)	lag1**
Kunming	Type 1($PM_{2.5}$)	1.069 (1.042, 1.096)	lag1**
Guangzhou	Type 4($PM_{2.5}$+NO_2)	1.049 (1.034, 1.063)	lag1**

Table 6
The pollutant type with the highest lag of 0–5 days and their corresponding risk values and lag days in 8 cities. Pollutants above the cut-off are listed in parentheses (Warm Season). **P < 0.01

City	The pollution type with the highest RR(Warm Season)	The highest RR (with 95% CIs)	lag
Changchun	Type 1($PM_{2.5}$)	1.113 (1.028, 1.206)	lag4**
Urumqi	Type 5(O_3 + $PM_{2.5}$)	1.214 (1.112, 1.324)	lag1**
Beijing	Type 4($PM_{2.5}$+NO_2)	1.099 (1.059, 1.141)	lag0**
Xian	Type 2(NO_2)	1.073 (1.040, 1.108)	lag3**
Nanjing	Type 7(O_3 + $PM_{2.5}$+NO_2)	1.127 (1.071, 1.186)	lag1**
Wuhan	Type 4($PM_{2.5}$+NO_2)	1.077 (1.031, 1.124)	lag0**
Kunming	Type 6(O_3 + NO_2)	1.060 (1.009, 1.112)	lag4**
Guangzhou	Type 4($PM_{2.5}$+NO_2)	1.049 (1.023, 1.076)	lag5**

Table 7
The pollutant type with the highest lag of 0–5 days and their corresponding risk values and lag days in 8 cities. Pollutants above the cut-off are listed in parentheses (Cold Season). *P < 0.05, **P < 0.01

City	The pollution type with the highest RR(Cold Season)	The highest RR (with 95% CIs)	lag
Changchun	Type 1($PM_{2.5}$)	1.077 (1.015, 1.142)	lag3*
Urumqi	Type 2(NO_2)	1.127 (1.019, 1.248)	lag2*
Beijing	Type 1($PM_{2.5}$)	1.062 (0.998, 1.130)	lag0
Xian	Type 1($PM_{2.5}$)	1.032 (1.005, 1.061)	Lag1*
Nanjing	Type 7(O_3 + $PM_{2.5}$+NO_2)	1.070 (0.971, 1.178)	lag0
Wuhan	Type 4($PM_{2.5}$+NO_2)	1.092 (1.059, 1.125)	lag1**
Kunming	Type 1($PM_{2.5}$)	1.041 (1.005, 1.078)	lag5*
Guangzhou	Type 2(NO_2)	1.076 (1.045, 1.107)	lag2**

Furthermore, we compared the simple sum of the excess risks of individual pollutants above the cut-off with the excess risks of the multiple pollution type with all three pollutants is simultaneously higher than the cut-off. The concentration levels of other pollutants are not taken into account when calculating the exposure risk above the cut-off for each pollutant alone. While calculating the impact of combined exposure, the concentration level of three pollutants is all considered, and the risk is calculated when the three pollutants are higher than the cut-off simultaneously. The results for each type of excess risk higher than 0 were listed in Fig. 3. The results showed that combined effects that were less than simple additive.

4. Discussion

In this study, we examined associations between the mortality risk and the 8 pollution types based on the combination of different concentration levels of three major pollutants ($PM_{2.5}$, NO_2, and O_3). In our analysis, we found evidence that exposure to multi-pollutant types which several pollutants with high concentrations simultaneously was linked to a higher relative risk than exposure to single-pollutant types. The results from eight different areas collectively indicate that type 7 with higher of all three pollutants ($PM_{2.5}$, O_3, and NO_2) and type 4 with higher $PM_{2.5}$ and NO_2 have a greater relative risk than other types. We also found regional differences: in most northern cities, the highest risk of death in the warm season is the multi-pollutant type, while the risk of single-pollutant type with high $PM_{2.5}$ is highest in the cold season. In southeastern cities, the multi-pollutant type had a higher mortality effect in both seasons. In addition, the results also showed that the excess risk from simultaneous exposure to multiple pollutants was less than the sum of individual air pollutants effects, partially false conclusions would have been reached by ignoring the presence of interactions between air pollutants.

The difference in the mortality risk between each pollutant type modified by city and season is also observed. The results of the present study indicate that in most areas, the multi-pollutant type 7 and type 4 have a greater relative risk than other types. And the RR of type 1 is the highest in most northern cities in the cold season. These differences may be related to pollution conditions, pollutant composition, and indoor-outdoor activity patterns. In this study, the concentrations of O_3 and NO_2 in cities in economically developed areas such as Beijing and Guangzhou are higher, and the complex air pollution is more serious in these areas, which will lead to a higher health impact of multi-pollutant types in these areas than Kunming. At the same time, $PM_{2.5}$ has greater seasonal and regional differences. Specifically, $PM_{2.5}$ concentration in northern cities is much higher than that in southern cities in the cold season. Yan et al. (2019) found that evidence of the association between $PM_{2.5}$ and the risk of cardiovascular death was higher during periods with high $PM_{2.5}$ concentration than during periods with low $PM_{2.5}$ concentration. This may partly explain the reason for the type with the highest RR is type 1 in the cold season in northern cities.

In our analysis, type 4 ($PM_{2.5}$ and NO_2 are both above the cut-off) appeared most frequently, and the concentration of $PM_{2.5}$ and NO_2 has a good consistency in this pollution type. On the other hand, the occurrence frequency of multi-pollutant types with opposite levels of $PM_{2.5}$ and NO_2 concentration (type 5 and type 6) is very low. In these 8 cities, the highest is less than 10% (Beijing type 5), and the lowest is only 1.5% (Guangdong type 6). This result is consistent with a robust positive correlation between $PM_{2.5}$ and NO_2. Types 4 and 7, which carry a greater risk of death, are among those with high concentrations of both $PM_{2.5}$ and NO_2. In fact, vehicle emissions are a major source of NO_2, which is an important precursor of $PM_{2.5}$ and has complex links to it. This suggests that in highly urbanized areas, the structure of emissions has an important impact on health.

On the other hand, studies show that the chemical composition of $PM_{2.5}$ varies greatly by season and across China, and it may be different during periods of high and low pollution levels, which may affect toxicity (Bell et al., 2007; Dominici et al., 2006, 2010; Peng et al., 2009; Franklin et al., 2008; Cao et al., 2012). Generally, the period between mid-November and mid-March is the heating season in northern China, thus the use of coal-based heating adds a source of PM pollution. At this time, the contribution of fossil fuel burning to PM2.5 increases sharply in northern China (Zheng et al., 2005). Further, Cao et al. (2012) suggest that $PM_{2.5}$ constituents from the combustion of fossil fuel may have a distinct impact on the health effects attributable to $PM_{2.5}$. It has been proved that secondary inorganic species in $PM_{2.5}$ (composed of secondary inorganic substances such as sulfate, nitrate, and ammonia) have a greater impact on cardiovascular mortality than other PM components (Huang et al., 2012; Son et al., 2012; Yan et al., 2019). These secondary inorganic substances are the main components of $PM_{2.5}$ when $PM_{2.5}$ concentration is higher than 150μg/m³ in Beijing (Ma et al., 2017), and this situation is more likely to occur in the heating season in northern China. These could be partly responsible for our result that type 1 (only $PM_{2.5}$ higher than cut-off) usually is associated with the highest relative risk in most northern cities during the cold season.

In addition, different cities have different outdoor activities patterns and ventilation habits in different seasons due to each climate feature, which will affect indoor and outdoor exposure rates and thus affect health. The results of the present study indicate that the relative risk was higher during the warm season in northern and western cities, but higher during the cold season in southeastern cities, which may be related to the different exposure types of people living in cities with different climate features. The Severe cold in the cold season in the north and heatwave and heavy rain in the warm season in the south will reduce local people's exposure to pollutants outdoors. Also, the seasonal variation of ozone is obvious, and its concentration is much higher in the warm season than in the cold season. In the Pearl River Delta region, however, the cold season is cool and dry, with little temperature change, and people are more likely to go outside and open their windows for ventilation, thus exposing themselves to higher levels of air pollution. While the warm season is hot and humid, thus people often use air conditioning, which reduces the risk of exposure to ambient air pollution (Wong et al., 2001). This lifestyle will reduce the outdoor ozone exposure of people there. This may partly explain the reason why the difference between pollutant types with the highest relative risk between southern and north-central cities is only that the northern cities include ozone concentrations above the cut-off and the southern cities are below it.

We also found strong evidence for the health burden from simultaneous exposure to multiple pollutants was less than the sum of individual effects. This means that defining the health effects of multiple pollutants as the sum of the effects of each air pollutant can skew estimates. Some previous studies (Romieu et al., 2012; Li et al., 2017; Amini et al., 2019; Tang et al., 2021) of two-pollutant analyses have shown that the previously estimated effects were weaker and became no longer significant when adjusted for one pollution in two-pollutant models. This may arise from problems of interaction and multi-collinearity between $PM_{2.5}$, $NO_{2,}$ and O_3 (Romieu et al., 2012). Previous field and laboratory studies (He et al., 2014, Chen et al., 2016, Chu et al., 2019) confirmed that a high Correlation between $PM_{2.5}$ and NO_2 is caused by its chemical mechanism: NOx contributes to the formation of secondary $PM_{2.5}$ by directly forming nitrate and by indirectly enhancing aerosol-phase oxidation (Russell et al., 1988). These chemical mechanisms issued in the key roles of NOx in the formation of secondary $PM_{2.5}$, which explained why $PM_{2.5}$ is highly related to NO_2. In addition, the formation mechanism of ozone determines its complex correlation with the other two pollutants. First, the formation of ozone depends on a series of complicated photochemical reactions involving volatile organic compounds (VOCs) and nitrogen oxides (NOx) under light conditions.11.22. In other words, VOCs and NOx are the pathways of ozone formation and the precursors of ozone, but they are also the precursors of $PM_{2.5}$ (Zhang et al., 2019; Godzinski et al., 2021; Dominici et al., 2010). These common precursors are the possible reason for the positive correlation between $PM_{2.5}$ and O_3 (Chu et al., 2020). On the other hand, as $PM_{2.5}$ is produced by primary emission sources, however, will react with heterogeneous free radicals (e.g., HO2) needed to form ozone, consuming free radicals and thus reducing ozone formation (Shang et al., 2013; Chu et al., 2020). Also, the reduction of $PM_{2.5}$ concentration always coincided with a rise in atmospheric visibility, thus increasing sunshine intensity, which is a favor to the formation of ozone (Zhang et al., 2019). This mechanism partly explains the inverse correlation between ozone concentration and $PM_{2.5}$ concentration

in some Chinese areas during the past few years (Chu et al., 2020). The difference between cities and seasons in terms of the occurrence frequency of different multi-pollutant types is also observed. In the northern and central cities with significantly higher $PM_{2.5}$, the occurrence frequency of the multi-pollutant type (type 1,2,4,6) with opposite levels of $PM_{2.5}$ and O_3 concentration is much higher than that of the two cities with lower $PM_{2.5}$ concentration in the south, which may be caused by the complex correlation between $PM_{2.5}$ and O_3 mentioned above. Chu et al. (2020) found that $PM_{2.5}$ is negatively correlated with O_3 in areas where $PM_{2.5}$ concentration is greater than 50 μg M-3, but this negative correlation will weaken with the decrease of $PM_{2.5}$ concentration. Specifically, $PM_{2.5}$ and O_3 are negatively correlated in North China but positively correlated in South China. This is consistent with our findings. These complex chemical mechanisms lead to complex interactions among pollutants with regional differences. The presence of these interactions partly explicates the inequality between the health effects estimated from simultaneous exposure to multiple pollutants and from the simple sum of individual exposure to single pollutant.

Current results suggest that policymakers should shift to a multi-pollutant approach to air quality and achieve greater public health protection through the regulation of multiple sources of air pollution and the overall mixture air pollution. Additionally, multi-pollution control should also conform to the features of local ambient air pollution, climate, and population activities. Specifically, for most cities in northern China, more strict measures should be taken to control the multi-pollutant of $PM_{2.5}$, $O_{3,}$ and NO_2 in the warm season, while more attention should be paid to the control of $PM_{2.5}$ in the cold season. For southern cities, we should pay attention to multi-pollutant throughout the year and focus more on the coordinated control of $PM_{2.5}$ and NO_2 in the cold season.

Rather than following the type of previous air pollution health studies that looked at individual pollutants, this study is the first to consider air pollution as a mixture in China and calculate the impact of different pollutant types on mortality. This makes it outside of the very small set of the traditional two-pollutant model, in which the introduction of correlated pollutants can cause unstable. Furthermore, the research covers a wide range of 8 major cities in China, and these 8 cities are located in different regions with different climate, pollution levels, and economic development level features, which has strong regional representativeness. In summary, this study provides a reference for putting forward multi-pollutant control strategies for air quality following local conditions, to strengthen the ability of health-driven coordinated air pollution control in China.

There are still some limitations to the present study. Firstly, 8 cities with large climate differences were selected nationwide for research, which has regional representativeness to a certain extent, but its representativeness is still limited, and there may be some deviations in direct application to other cities. Secondly, as a time series analysis, this study inevitably has exposure errors. Since it is difficult to obtain the true exposure of individuals, observations from monitoring stations are used as proxies for population exposure, which leads to a certain degree of exposure error. Finally, due to data limitations, we

did not classify the population by gender, age, economy, and education level, so we could not put forward more targeted health suggestions for vulnerable populations.

5. Conclusions

This paper confirms the robust health hazards of complex air pollution and suggests that the mortality risk from exposure to the multi-pollutant type is generally higher than that of the single-pollutant type and varies regionally and seasonally. Type 7 with higher of all three pollutants ($PM_{2.5}$, O_3, and NO_2) and type 4 with higher $PM_{2.5}$ and NO_2 have a greater relative risk than other pollutant types. In most northern cities, the multi-pollutant type has a higher mortality effect in the warm season, but the single-pollutant type with only $PM_{2.5}$ above the cut-off has a higher effect in the cold season. In southeastern cities, the multi-pollutant type had a higher mortality effect in both seasons. The results also showed that the excess risk from simultaneous exposure to multiple pollutants was less than the simple sum of individual air pollutants effects, partially false conclusions would have been reached by ignoring the presence of interactions between air pollutants.

Declarations

Ethical Approval

Not applicable

Consent to Participate

Not applicable

Consent to Publish

Not applicable

Authors Contributions

All authors contributed to the study conception and design. Zhao Yuxin: Software, Visualization, Writing-Original draft preparation. An Xingqin: Conceptualization, Writing-Reviewing and Editing, Supervision. Sun Zhaobin: Methodology, Formal analysis, Project administrator. Li Yi: Data curation. Hou Qing: Validation.

Availability of data and materials

All data generated or analysed during this study are included in this article.

Competing Interests

The authors declare they have no competing financial interests in this work.

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References

1. Air Pollution Prevention and Control Action Plan (2013) http://www.gov.cn/zhengce/content/-09/13/content_4561.htm
2. Amini H, Nhung NTT, Schindler C, Yunesian M, Hosseini V, Shamsipour M, Hassanvand MS, Mohammadi Y, Farzadfar F, Vicedo-Cabrera AM, Schwartz J (2019) Short-term associations between daily mortality and ambient particulate matter, nitrogen dioxide, and the air quality index in a Middle Eastern megacity. Environmental Pollution, 254, p.113121
3. Atkinson RW, Yu D, Armstrong BG et al (2012 Oct) Concentration-response function for ozone and daily mortality: results from five urban and five rural U.K. populations. Environ Health Perspect 120(10):1411–1417. DOI: 10.1289/ehp.1104108. PMID: 22814173; PMCID: PMC3491921
4. Bell ML, Dominici F, Ebisu K, Zeger SL, Samet JM (2007) Spatial and temporal variation in $PM_{2.5}$ chemical composition in the United States for health effects studies. Environ Health Perspect 115:989–995 [PubMed: 17637911]
5. Bell ML, Kim JY, Dominici F (2006) Potential confounding of particulate matter on the short-term association between ozone and mortality in multisite time-series studies.Environ Health Perspect. ;115
6. Bell ML, McDermott A, Zeger SL, Samet JM, Dominici F (2004 Nov) Ozone and short-term mortality in 95 US urban communities, 1987–2000. JAMA 292(19):2372–2378. DOI: 10.1001/jama.292.19.2372. PMID: 15547165; PMCID: PMC3546819
7. Bobb JF, Valeri L, Henn C, Christiani B, Wright DC, Mazumdar RO, Godleski M, Coull BA (2015) Bayesian kernel machine regression for estimat¬ing the health effects of multi-pollutant mixtures. Biostatistics 16(3):493–508
8. CAA(2020).China Air 2020:Air Pollution Prevention and Control Progress in Chinese Cities
9. Cairncross EK, John J, Zunckel M (2007) A novel air pollution index based on the relative risk of daily mortality associated with short-term exposure to common air pollutants. Atmos Environ 41:8442–8454
10. Cao J, Xu H, Xu Q, Chen B, Kan H (2012) Fine particulate matter constituents and cardiopulmonary mortality in a heavily polluted Chinese city. Environ Health Perspect 120(3):373–378 PMID: 22389181. https://doi.org/10.1289/ehp.1103671
11. Chan CK, Yao X (2008) Air pollution in mega cities in China. Atmos Environ 42(1):1–42
12. Chen R, Yin P, Meng X et al (2017) Jul;196(1):73–81 Fine Particulate Air Pollution and Daily Mortality. A Nationwide Analysis in 272 Chinese Cities. American Journal of Respiratory and Critical Care Medicine. DOI: 10.1164/rccm.201609-1862oc. PMID: 28248546

13. Chen RJ 2013.The health effects of complex air pollution in 17 Chinese cities. [D] Fudan university
14. Cheng Y, Zheng G, Wei C, Mu Q, Zheng B, Wang Z, Gao M, Zhang Q, He K, Carmichael G, Poschl U, Su H (2016) Reactive nitrogen chemistry in aerosol water as a source of sulfate during haze events in China.Sci. Adv.2, No. e1601530.
15. China's Eco-Environment Status Bulletin (2017) http://www.gov.cn/guoqing/2019-04/09/content_5380689.htm
16. Chu B, Ma Q, Liu J, Ma J, Zhang P, Chen T, He H (2020) Air pollutant correlations in China: secondary air pollutant responses to NOx and SO_2 control. Environ Sci Technol Lett. doi:10.1021/acs.estlett.0c00403
17. Chu B, Wang Y, Yang W, Ma J, Ma Q, Zhang P, Liu Y, He H (2019) Effects of NO_2 and C3H6 on the heterogeneous oxidation of SO_2 on TiO2 in the presence or absence of UV-Vis irradiation. Atmos Chem Phys 19:14777–14790
18. Dastoorpoor M, Goudarzi G, Khanjani N, Idani E, Aghababaeian H, Bahrampour A (2018b) Lag time structure of cardiovascular deaths attributed to ambient air pollutants in Ahvaz, Iran, 2008–2015. Int J Occup Med Environ Health 31:459–473
19. Dominici F, Peng RD, Bell ML, Pham L, McDermott A, Zeger SL, Samet JM (2006) Fine Particulate Air Pollution and Hospital Admission for Cardiovascular and Respiratory Diseases. JAMA 295(10):1127. doi:10.1001/jama.295.10.1127
20. Dominici F, Peng RD, Barr CD, Bell ML (2010) Protecting human health from air pollution: shifting from a single-pollutant to a multi-pollutant approach. Epidemiology (Cambridge, Mass.), 21(2), p.187
21. Duan J (2020) The Practical Exploration and Prospect of China's Collaborative Governance of Transregional Atmospheric Pollution in the New Era, vol 13. JOURNAL OF CHINA EXECUTIVE LEADERSHIP ACADEMY JINGGANGSHAN, pp 45–54. 06
22. Duan Y, Liao Y, Li H, Yan S, Zhao Z, Yu S, Fu Y, Wang Z, Yin P, Cheng J, Jiang H (2019) Effect of changes in season and temperature on cardiovascular mortality associated with nitrogen dioxide air pollution in Shenzhen, China, vol 697. Science of The Total Environment, p 134051
23. Evangelopoulos D, Katsouyanni K, Schwartz J, Walton H (2021) Quantifying the short-term effects of air pollution on health in the presence of exposure measurement error: a simulation study of multi-pollutant model results. Environ Health 20(1):1–13
24. Franklin M, Koutrakis P, Schwartz JD (2008) The role of particle composition on the association between $PM_{2.5}$ and mortality. Epidemiology 19(5):680–689 PMID: 18714438. https://doi.org/10.1097/EDE.0b013e3181812bb7
25. Godzinski A, Castillo MS (2021) Disentangling the effects of air pollutants with many instruments.Journal of Environmental Economics and Management, p.102489
26. He H, Wang Y, Ma Q, Ma J, Chu B, Ji D, Tang G, Liu C, Zhang H, Hao J (2014) Mineral dust and NOx promote the conversion of SO_2 to sulfate in heavy pollution days. Sci Rep 4:04172

27. IPCC. Climate change 2014: impacts, adaptation, and vulnerability [M]. Cambridge: Cambridge University Press, in press, 2014 [2014-03-31]. http://www.ipcc.ch/report/ar5/wg2/
28. Ito K, Thurston G, Nadas A, Lippman M (2001) Monitor - to - monitor temporal correlation of air pollution and weather variables in the North-Central U.S. J Exposure Anal and Environ Epidemiol. 11:21–321
29. Jerrett M, Burnett RT, Ma R, Pope CA III, Krewski D, Newbold KB et al (2005) Spatial analysis of air pollution and mortality in Los Angeles. Epidemiology 16(6):727–736
30. Kelly FJ, Blomberg A, Frew A, Holgate ST, Sandstrom T (1996) Antioxidant kinetics in lung lavage fluid following exposure of humans to nitrogen dioxide. Am J Respir Crit Care Med 154(6 pt 1):1700–1705
31. Li X, Xiao J, Lin H, Liu T, Qian Z, Zeng W, Guo L, Ma W (2017) The construction and validity analysis of AQHI based on mortality risk: A case study in Guangzhou, China. Environmental Pollution, 220, pp.487–494
32. Lin H, Tao J, Du Y, Liu T, Qian Z, Tian L, Di Q, Rutherford S, Guo L, Zeng W, Xiao J, Li X, He Z, Xu Y, Ma W (2016) Particle size and chemical constituents of ambient particulate pollution associated with cardiovascular mortality in Guangzhou. China Environ Pollut 208:758–766
33. Lishui Ecological environment Bureau (2020) Technical Regulation for Ambient Air Quality Health Index
34. Ma Q, Wu Y, Zhang D, Wang X, Xia Y, Liu X et al (2017) Roles of regional transport and heterogeneous reactions in the $PM_{2.5}$ increase during winter haze episodes in Beijing. Sci Total Environ 599:246–253 PMID: 28477481. https://doi.org/ 10.1016/j.scitotenv.2017.04.193
35. Mauderly JL, Samet JM (2009) Is there evidence for synergy among air pollutants in causing health effects?. Environmental health perspectives, 117(1), pp.1–6
36. Olstrup H, Johansson C, Forsberg B, Tornevi A, Ekebom A, Meister KA, Multi-Pollutant (2019) Based on Short-Term Respiratory Effects in Stockholm, Sweden. Int J Environ Res Public Health 16:105. https://doi.org/10.3390/ijerph16010105. Air Quality Health Index (AQHI)
37. Ostro B, Broadwin R, Green S, Feng WY, Lipsett M (2006) Fine particulate air pollution and mortality in nine California counties: results from CALFINE. En¬viron Health Perspect 114:29–33
38. Peng RD, Bell ML, Geyh AS, McDermott A, Zeger SL, Samet JM (2009) Emergency admissions for cardiovascular and respiratory diseases and the chemical composition of fine particle air pollution. Environ Health Perspect 117:957–963 [PubMed: 19590690]
39. Rojas-Martinez R, Perez-Padilla R, Olaiz-Fernandez G, Mendoza-Alvarado L, Moreno-Macias H, Fortoul T, McDonnell W, Loomis D, Romieu I (2007) Lung function growth in children with long-term exposure to air pollutants in Mexico City. Am J Respir Crit Care Med 176:377–3854 [PubMed: 17446338]
40. Romieu I, Gouveia N, Cifuentes LA et al (2012) Oct(171):5–86 Multicity study of air pollution and mortality in Latin America (the ESCALA study). Research Report (Health Effects Institute). PMID: 23311234

41. Russell AG, McCue KF, Cass GR (1988) Mathematical- modeling of the formation of nitrogen-containing pollutants 0.2. evaluation of the effect of emission controls. Environ Sci Technol 22:1336–1347
42. Samet JM, Katsouyanni K, principle investigators for the APHENA Team (2006) Air pollution and health: a combined European and North American Approach (APHENA). Epidemiology 17(6):S19–20
43. Schwartz J, Fong K, Zanobetti A (2018) A national multicity analysis of the causal effect of local pollution, NO 2, and PM 2.5 on mortality. Environmental health perspectives, 126(8), p.087004
44. Sicard P, Lesne O, Alexandre N, Mangin A, Collomp R (2011) Air quality trends and potential health effects — development of an aggregate risk index. Atmos Environ 45:1145–1153
45. Son JY, Lee JT, Kim KH, Jung K, Bell ML (2012) Characterization of fine particulate matter and associations between particulate chemical constituents and mor-tality in Seoul, Korea. Environ Health Perspect 120(6):872–878 PMID: 22440884. https://doi.org/10.1289/ehp.1104316
46. Speizer FE, Cohen A, Mehta S (2008) Asia: Changing times and changing problems. Environ Health Perspect 116:A370–371
47. Stieb DM, Burnett RT, Smith-Doiron M, Brion O, Shin HH, Economou V (2008) A new multipollutant, no-threshold air quality health index based on short-term associations observed in daily time-series analyses. J Air Waste Manag Assoc 58:435–450
48. Strassmann A, de Hoogh K, Röösli M et al NO2 and PM2.5 Exposures and Lung Function in Swiss Adults: Estimated Effects of Short-Term Exposures and Long-Term Exposures with and without Adjustment for Short-Term Deviations.Environmental Health Perspectives. 2021Jan; 129(1):17009. DOI: 10.1289/ehp7529. PMID: 33502909; PMCID: PMC7839986.
49. Tang C, Chen Y, Song Q et al (2021) Short-term exposure to air pollution and occurrence of emergency stroke in Chongqing, China. Int Arch Occup Environ Health 94:69–76. https://doi.org/10.1007/s00420-020-01557-y
50. Tao Y, Huang W, Huang X et al (2012 Mar) Estimated acute effects of ambient ozone and nitrogen dioxide on mortality in the Pearl River Delta of southern China. Environ Health Perspect 120(3):393–398. DOI: 10.1289/ehp.1103715. PMID: 22157208; PMCID: PMC3295344
51. Three-year Action Plan to Win the Blue Sky Defense War http://www.gov.cn/zhengce/ content/2018-07/03/content_5303158.htm
52. THURSTON G, ITO K (2001) Epidemiological studies of acute ozone exposures and mortality. J Expo Sci Environ Epidemiol 11:286–294. https://doi.org/10.1038/sj.jea.7500169
53. WHO (2018) Available evidence for the future update of the who global air quality guidelines (aqgs)
54. WHO (2021) New WHO Global Air Quality Guidelines aim to save millions of lives from air pollution
55. Wong CM, Ma S, Hedley AJ, Lam TH Effect of air pollution on daily mortality in Hong Kong.Environmental Health Perspectives. 2001Apr; 109(4):335–340. DOI: 10.1289/ehp.01109335. PMID: 11335180; PMCID: PMC1240272.

56. Wong CM, Vichit-Vadakan N, Kan H, Qian Z (2008) Public Health and Air Pollution in Asia (PAPA): a multicity study of short-term effects of air pollution on mortality. Environ Health Perspect 116(9):1195–1202
57. Wong TW, Tam WWS, Yu ITS, Lau AKH, Pang SW, Wong AHS (2013) Developing a risk-based air quality health index. Atmos Environ 76:52–58
58. Xin Jiang G, Li W, Fu (2021) Government environmental governance, structural adjustment and air quality: A quasi-natural experiment based on the Three-year Action Plan to Win the Blue Sky Defense War. J Environ Manage 0301–4797 Volume 277, 2021,111470,ISSN. https://doi.org/10.1016/j.jenvman.2020.111470
59. Yan M, Wilson A, Bell ML, Peng RD, Sun Q, Pu W, Yin X, Li T, Anderson GB (2019 Jun) The Shape of the Concentration-Response Association between Fine Particulate Matter Pollution and Human Mortality in Beijing, China, and Its Implications for Health Impact Assessment. Environ Health Perspect 127(6):67007 Epub 2019 Jun 6. PMID: 31170008; PMCID: PMC6792375
60. Yin P, Chen R, Wang L, Meng X, Liu C, Niu Y, Lin Z, Liu Y, Liu J, Qi J, You J, Zhou M, Kan H (2017) Ambient Ozone Pollution and Daily Mortality: A Nationwide Study in 272 Chinese Cities. Environ Health Perspect 125(11):117006. https://doi.org/10.1289/EHP1849
61. Zhang JJ, Wei Y, Fang Z (2019) Ozone Pollution: A Major Health Hazard Worldwide. Front Immunol 10:2518. DOI: 10.3389/fimmu.2019.02518. PMID: 31736954; PMCID: PMC6834528
62. Zheng M, Salmon LG, Schauer JJ, Zeng L, Kiang CS, Zhang Y et al (2005) Seasonal trends in $PM_{2.5}$ source contributions in Beijing, China. Atmos Environ 39(22):3967–3976. https://doi.org/10.1016/j.atmosenv.2005.03.036

Figures

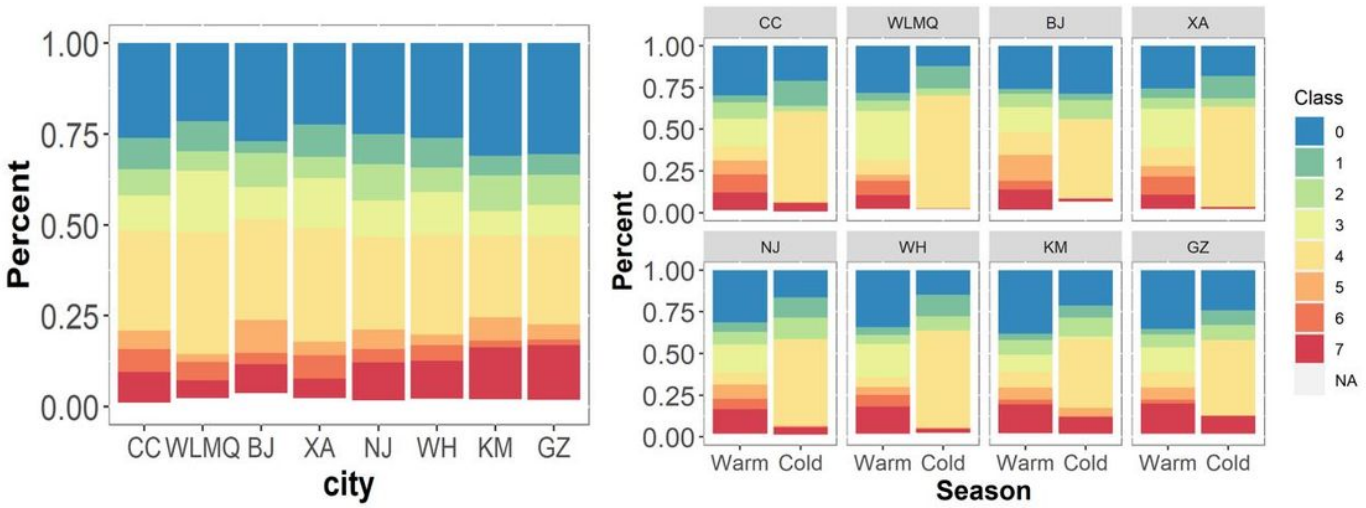

Figure 1

Frequency distribution of different pollutant types in 8 cities (left: all-year results; right: seasonal results)

0: reference type; 1: only $PM_{2.5}$ higher than cut-off; 2: only NO_2 higher than cut-off; 3: only O_3 higher than cut-off; 4: $PM_{2.5}$ and NO_2 are both above the cut-off; 5: $PM_{2.5}$ and O_3 are both above the cut-off; 6: NO_2 and O_3 are both above the cut-off; 7: $PM_{2.5}$, NO_2 and O_3 are all above the cut-off; NA: lacking values

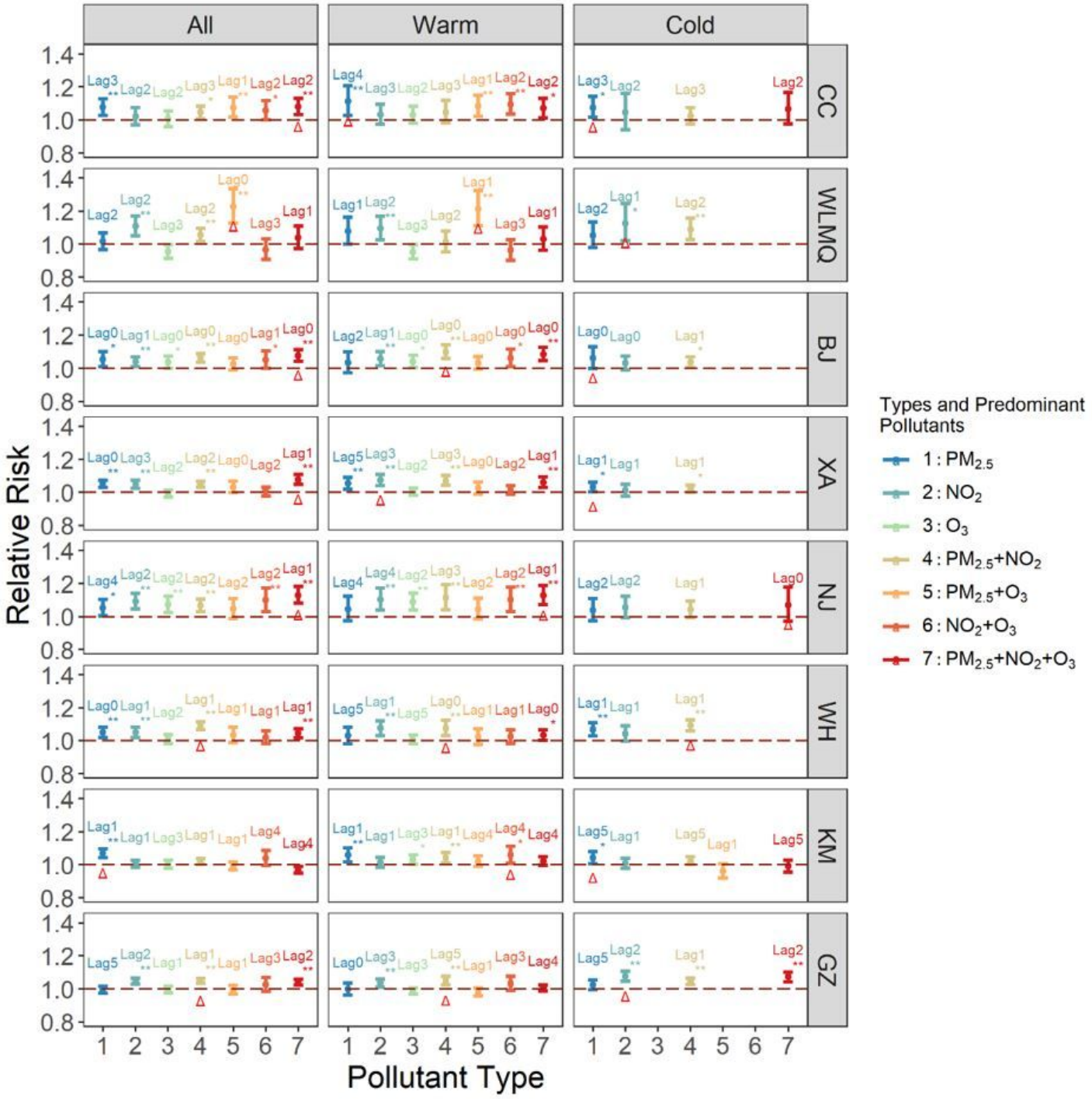

Figure 2

Association between different pollutant types and RRs (95% CIs) of mortality modified by season. Considering the lag of lag0 to lag5, the day with the highest RR value of each type was selected for analysis and comparison, and the lag day was marked above the corresponding type. The red triangle is indicated as the type with the highest RR. The eight cities are arranged north to south by latitude from top (CC) to bottom (GZ).

*P < 0.05, **P < 0.01.

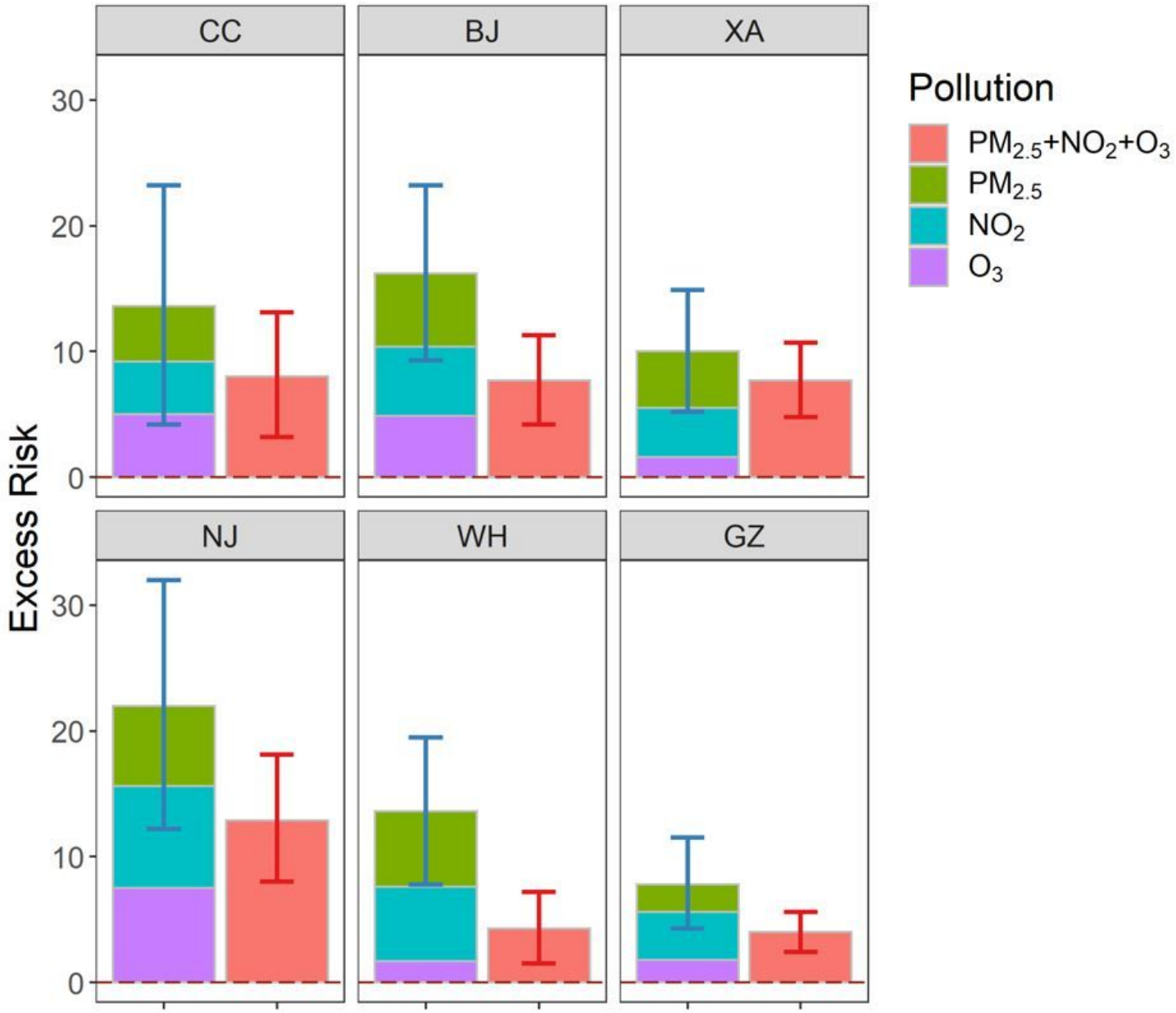

Figure 3

Comparison of the simple sum of the excess risks (95% CIs) of individual pollutants ($PM_{2.5}$, NO_2 and O_3) above the cut-off (left) with the excess risks (95% CIs) of the multiple pollution type with all three

pollutants are simultaneously higher than the cut-off (right).

Supplementary Files

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- Appendix.docx