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The burden of ambient air pollution on years of life lost in Wuxi, China, 2012–2015: A time-series study using a distributed lag non-linear model\*

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#### ABSTRACT

Ambient air pollution ranks high among the risk factors that increase the global burden of disease. Previous studies focused on assessing mortality risk and were sparsely performed in populous developing countries with deteriorating environments. We conducted a time-series study to evaluate the air pollution-associated years of life lost (YLL) and mortality risk and to identify potential modifiers relating to the season and demographic characteristics. Using linear (for YLL) and Poisson (for mortality) regression models and controlling for time-varying factors, we found that an interquartile range (IQR) increase in a three-day average cumulative (lag 0-2 day) concentrations of PM2.5, PM10, NO2 and SO<sub>2</sub> corresponded to increases in YLL of 12.09 (95% confidence interval [CI]: 2.98-21.20), 13.69 (95% CI: 3.32-24.07), 26.95 (95% CI: 13.99-39.91) and 24.39 (95% CI: 8.62-40.15) years, respectively, and to percent increases in mortality of 1.34% (95% CI: 0.67-2.01%), 1.56% (95% CI: 0.80-2.33%), 3.36% (95% CI: 2.39-4.33%) and 2.39% (95% CI: 1.24-3.55%), respectively. Among the specific causes of death, cardiovascular and respiratory diseases were positively associated with gaseous pollutants (NO2 and SO2), and diabetes was positively correlated with NO<sub>2</sub> (in terms of the mortality risk). The effects of air pollutants were more pronounced in the cool season than in the warm season. The elderly (>65 years) and females were more vulnerable to air pollution. Studying effect estimates and their modifications by using YLL to detect premature death should support implementing health risk assessments, identifying susceptible groups and guiding policy-making and resource allocation according to specific local conditions. © 2017 Elsevier Ltd. All rights reserved.

#### 1. Introduction

Ambient air pollution ranks high among the risk factors that threaten human health (Cohen et al., 2005; Lim et al., 2012) and is linked to a variety of acute and chronic morbid states, such as cardiovascular diseases (Pope et al., 2004; Rd et al., 2015; Simkhovich et al., 2008), pneumonia (Brugha and Grigg, 2014; Harris et al., 2010; Vanos et al., 2014), asthma (Newman et al., 2014), chronic obstructive pulmonary disease (COPD) (Peacock et al., 2011; Schikowski et al., 2013), neurological disorders (Chen

and Schwartz, 2008; Gatto et al., 2014; Guxens et al., 2014) and cancers (Loomis et al., 2014; Yang et al., 2015). Recent evidence has also indicated a role for air pollution in metabolic disturbances that lead to increased risks of diabetes mellitus (Krämer et al., 2010; Rajagopalan and Brook, 2012). Most previous studies were conducted in developed countries, and only a few covered Asia, where the components or sources of pollution, meteorological conditions and population demographic characteristics may vary according to geographical region. With the rapid urbanization and industrialization that has occurred in the past decades and as the most populous developing country, China is experiencing deteriorating air quality because of emissions from conventional energy consumption and vehicle exhaust (Kan et al., 2009; Petäjä et al., 2016; Rohde and Muller, 2015). Particulate matter (PM) with aerodynamic diameters <2.5  $\mu$ m (PM<sub>2.5</sub>) and <10  $\mu$ m (PM<sub>10</sub>), sulfur

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dioxide  $(SO_2)$  and nitrogen dioxide  $(NO_2)$  are the principal air pollutants in China, and their annual average concentrations are thought to be potentially harmful according to World Health Organization (WHO) air quality guidelines.

Apart from focusing on pollution patterns, interest in identifying the possible modifiers, including season (Stieb et al., 2002), pre-existing health status (Rd et al., 2015), socioeconomic status (SES) (Fecht et al., 2015; Ou et al., 2008) and demographic characteristics (Simoni et al., 2015), such as sex and age, and their association between air pollution and various health end points has arisen. However, previous findings regarding the effects of these modifiers are contradictory.

Modifiers based on varied summary measures may yield distinctive susceptibility features and should be considered cautiously. The measurement of daily death counts has been commonly used to investigate pollutant-health associations and has generated abundant evidence of environmental stressors on excess mortality (Stieb et al., 2002; Vanos et al., 2014). This approach gives equal weight to each death and is less sensitive to assessing premature death, which has a deciding effect on policy-making and resource allocation (Murray et al., 2002). In contrast, years of life lost (YLL), depending on the age at death and the number of deaths at each age, partially resolves the mismatch of disease impact derived from death numbers alone (Brustugun et al., 2014; Thun et al., 2010).

To date, YLL has been sparsely included in the practice of measuring air pollution-associated health outcomes. Therefore, the present study applied an epidemiological time-series design to derive effect estimates for air pollution on cause-specific YLL and mortality associations and to evaluate the effect of modifications by season and demographic characteristics based on a vast individual dataset of Wuxi, China.

## 2. Methods

## 1 Population and study area

Wuxi is a modernized city covering an area of 4628 km² with a population (permanent residents) of 6.50 million in 2015. The city is located in the Yangtze River Delta (31°07′ to 32°02′ North, 119°31′ to 120°36′ East) and, as a member of the largest economic zone in China (the economic zone of the Yangtze River Delta also includes Shanghai, Nanjing and Suzhou), is prosperous, with a per capita gross domestic product of US \$19,664 in 2015. The target population in this study was restricted to registered residents of the area, of which the male/female ratio was 0.98, and the elderly ( $\geq$ 65 years of age) accounted for 24.45% of the total population.

#### 2 Exposure assessment

The national standard limit of PM<sub>2.5</sub> was first implemented in 2012; thereafter, PM<sub>2.5</sub> became a regularly used monitoring indicator. In this study, the data of air pollutants (PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub> and SO<sub>2</sub>) were simultaneously collected from seven state-controlled monitoring stations distributed in different administrative districts of Wuxi from 2012 to 2015 (Supplementary Fig. S1). The results of these stations reflect the background air pollution level of the region rather than specific sources. The data from those monitoring sites were obtained from the Wuxi Municipal Environmental Monitoring Center and averaged to calculate the daily 24-h mean concentration of each pollutant and then were used to estimate exposure levels of the population. There was one missing data of PM<sub>2.5</sub> and none for the other three pollutants during the observing period. We acquired weather condition data on the daily mean temperature and relative humidity from the Wuxi Municipal

Meteorological Monitoring Center to control for potential confounding effects. The weather data were measured at a single fixed-site station in the Xishan District of Wuxi.

#### 3 Daily mortality and YLL data

Daily mortality data from 1 January 2012 to 31 December 2015 were collected from the database of the Wuxi Center for Disease Control and Prevention. This database is a part of the state-controlled network reporting system, which pools the death certificates by community doctors (for deaths at home) and hospital doctors (for deaths in hospitals). Each death must be reported by following official channels before cremation. The data in this study were coded according to *The International Classification of Diseases, Revision 10* [ICD-10] and further classified into deaths because of non-accidental causes (A00-R99), cardiovascular diseases (I00-I99), respiratory diseases (J00-J98) and diabetes mellitus (E10-E14). The mortality data were also classified by sex and age group (≤65 years and >65 years) to identify modified effects.

Chinese national life tables were obtained from WHO (Supplementary Table S1). The data from 2012 used the life expectancy in that year, and those corresponding to 2013—2015 used the life expectancy in 2013 because these data were unavailable for the past two years. YLL values were calculated for each individual death by matching the age and sex to the life tables and were then summed to yield the YLL corresponding to each day.

#### 4 Analytical strategies

For descriptive analysis, the minimum, 25% quartile, median, 75% quartile, maximum, interquartile range (IQR), mean and standard deviation were calculated using stratification factors. The associations between air pollutants and weather conditions were assessed by Spearman's rank correlation test.

To develop the basic model, we determined the distribution pattern of YLL (Supplementary Fig. S2). YLL followed a normal distribution in our study, and previously, it reported to exhibit an approximately linear association with air pollutants (Guo et al., 2013). Therefore, we used distributed lag non-linear models (DLNMs) to evaluate the effects of air pollutants on YLL (Gasparrini, 2011; Gasparrini et al., 2010) according to the following equation:

$$\begin{aligned} \textit{YLL} &= \beta T_{t,l} + \eta \textit{DOW} + ns(time, df) + ns(temperature, df) \\ &+ ns(humidity, df) + intercept \end{aligned} \tag{1}$$

DOW-day of the week;

For time-series data,  $\beta T_{t,l}$  represented the crossbasis objects used to estimate the linear effects of air pollutants; thus, T was determined for each pollutant (PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub> and SO<sub>2</sub>), and  $\beta$ was the vector of the coefficients for  $T_{t,l}$ , where t represented the observation day, and l represented the lag days. One strength of DLNM is that it create two sets of basis functions to define the relationships in two dimensions: the predictor and the lags. We used a natural cubic spline function to estimate the lag effects and a linear function to mimic the exposure-response pattern of air pollutant-death associations. Based on the Akaike information criterion (AIC) (Peng et al., 2006), the degrees of freedom (df) for the lag structure were fitted with 5 df in our model. The function ns() represents a natural spline. We controlled the long-term trends and potential confounding factors, such as time, temperature and humidity, by including natural spline functions, and we set the df values for these factors at 5 per year, 3 and 3, respectively, in accordance with previous studies (Guo et al., 2011; Liu et al., 2014b; Lu et al., 2015). The day of the week (DOW), which is another confounder, was set as a dummy variable in our model, and  $\eta$  was

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