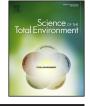
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# Air pollution and fasting blood glucose: A longitudinal study in China



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# HIGHLIGHTS

- First study to examine the air pollution impacts on fasting blood glucose in China.
- NO<sub>2</sub>, SO<sub>2</sub> and PM<sub>10</sub> were associated with the increased level of fasting blood glucose.
- The effect estimates were stronger in female, elderly, and overweight.

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## ABSTRACT

Limited studies have examined the associations between air pollutants [particles with diameters of 10  $\mu$ m or less (PM<sub>10</sub>), sulphur dioxide (SO<sub>2</sub>), and nitrogen dioxide (NO<sub>2</sub>)] and fasting blood glucose (FBG). We collected data for 27,685 participants who were followed during 2006 and 2008. Generalized Estimating Equation models were used to examine the effects of air pollutants on FBG while controlling for potential confounders. We found that increased exposure to NO<sub>2</sub>, SO<sub>2</sub> and PM<sub>10</sub> was significantly associated with increased FBG levels in single pollutant models (p < 0.001). For exposure to 4 days' average of concentrations, a 100  $\mu$ g/m<sup>3</sup> increase in SO<sub>2</sub>, NO<sub>2</sub> and PM<sub>10</sub> was associated with 0.17 mmol/L (95% CI: 0.15–0.19), 0.53 mmol/L (95% CI: 0.42–0.65), and 0.11 mmol/L (95% CI: 0.07–0.15) increase in FBG, respectively. In the multi-pollutant models, the effects of SO<sub>2</sub> were enhanced, while the effects of NO<sub>2</sub> and PM<sub>10</sub> were alleviated. The effects of air pollutants on FBG were stronger in female, elderly, and overweight people than in male, young and underweight people. In conclusion, the findings suggest that air pollution increases the levels of FBG. Vulnerable people should pay more attention on highly polluted days to prevent air pollution-related health issues.

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#### 1. Introduction

It is well recognised that modern lifestyle characteristics, including obesity and lack of physical activity, are associated with increasing 2001). Recently, more and more attention has been paid to the potential impacts of exposure to air pollution on increased incidence, prevalence, and mortality of DM (Basile and Bloch, 2012; Bhatnagar, 2009; Brook et al., 2013a; Coogan et al., 2012; Eze et al., 2014; Goldberg et al., 2000; Goldberg et al., 2006; Kan et al., 2004; Kramer et al., 2010; Raaschou-Nielsen et al., 2013; Sun et al., 2009; Tong et al., 2015; Zanobetti and Schwartz, 2001; Zanobetti and Schwartz, 2002). A meta-analysis showed that there were significant associations between long-term exposure to PM<sub>2.5</sub>, PM<sub>10</sub> and NO<sub>2</sub>, and DM morbidity and

morbidity and mortality of diabetes mellitus (DM) (Mokdad et al.,

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mortality in developed countries (USA, Canada and European countries) (Wang et al., 2014). However, it is still not clear what is the biological mechanism underlying these associations.

An increased level of fasting blood glucose (FBG) is an important indicator for DM. For example, the information on glucose levels is helpful to refine and adjust insulin dosages, leading to improved glycemic control (Welschen et al., 2005). Also, information on blood glucose is effective in improving glycaemic control in patients with type-2 diabetes who are not using insulin (Hou et al., 2014). We hypothesised that the mechanism of air pollution-related DM admissions/deaths may be explained partly by the effects of air pollution on FBG. However, limited evidence is available on the associations between air pollutants and FBG.

From 1980 to 2001, the prevalence of DM had increased sharply from 5.5% to 11.6% in China (Wang et al., 2014; Zuo et al., 2014). The prevalence of DM was 9.7% (10.6% among men and 8.8% among women) in 2006 (Yang et al., 2010), and 11.6% (12.1% among men and 11.0% among women) in 2010 (Xu et al., 2013). It is much higher than global prevalence (6.4%) in 2010 (Shaw et al., 2010). The health expenditure to treat and prevent DM and its complications is very expensive. Meanwhile, air pollution has been identified as serious environmental problem in China (Li et al., 2014; Liu et al., 2013; Wang and Hao, 2012). The adverse health impacts of air pollutants have been assessed in many cities in China (Chen et al., 2012b; Guo et al., 2010; Guo et al., 2013). However, no study has been conducted to evaluate the association between air pollution and FBG in China, which is very important for air pollution control and DM prevention.

Therefore, the present study was conducted to examine the hypothesis that high concentrations of air pollutants increase the FBG level, using data from Kailuan cohort study. In addition, we examined whether the associations were modified by individual characteristics.

# 2. Materials and methods

# 2.1. Study area and population

This study was based on longitudinal data collected by the Kailuan cohort study, which was conducted in the area of Kailuan community, Tangshan City, China. The Kailuan cohort study was a prospective population-based cohort study, which was conducted during the period of 2006 to 2010. The Kailuan community is a functional and comprehensive/intensive community owned and managed by the Kailuan Group. The original aim of Kailuan study was to investigate risk factors for chronic diseases. There are 11 hospitals responsible for the healthcare of the community. All of these hospitals are public hospitals. Out of the 155,418 residents (65.31%, 81,110 men and 20,400 women) 101,510 (aged 18–98 years old) who provided a written informed consent, were enrolled in the Kailuan study since 2006.

All participants underwent a standardized questionnaire assessment, clinical examination, and laboratory assessment every two years. Standard protocols were employed, as described previously (Brook et al., 2013b). The interviews and all examinations were performed by specifically trained medical doctors and nurses. The questionnaires collected information on basic characteristics (age, gender, blood pressure and body mass index [BMI]), life style (smoking, alcohol consumption status and physical activity), socio-economic characteristics (annual family income, work type and education levels) and other characteristics (diabetes mellitus, hypertension, hyperlipidaemia, and stroke, with the current treatments for these diseases). The health examination included physical examination and routine blood test.

Fasting blood samples were assayed for the concentrations of glucose, high-density lipoproteins (HDL), low-density lipoproteins (LDL), triglycerides, total cholesterol, and high-sensitivity C-reactive protein (hs-CRP). Blood pressure (BP) was measured on the left arm to the nearest 2 mm Hg using a mercury sphygmomanometer with a

cuff of appropriate size. The date (year, month and day) of the health examination was recorded for each participant.

# 2.2. Air pollution and weather data

Daily air pollution data on particulate matter less than 10  $\mu$ m in aerodynamic diameter (PM<sub>10</sub>), sulphur dioxide (SO<sub>2</sub>) and nitrogen dioxide (NO<sub>2</sub>) were obtained from Tangshan Environmental Monitoring Centre. We only collected air pollution data between 2006 and 2008, because of the data availability. Daily weather data including mean temperature and relative humidity were collected from Tangshan Bureau of Meteorology during 2006 and 2008.

Therefore we only used cohort data between 2006 and 2008. This means that each participant had two health examinations (once in 2006 and once in 2008). A total of 27,685 eligible participants (no missing values) were included in the analyses. Air pollution data were matched with the date of health examinations for each subject.

#### 2.3. Statistical analysis

Longitudinal analyses were performed to examine the associations between air pollutants ( $SO_2$ ,  $NO_2$  and  $PM_{10}$ ) and FBG using generalized estimating equations (GEE) to account for up to two repeated measurements on each individual. The procedure allows adjustment for withinsubject effects. Each regression model adjusted for age, sex, BMI, current drinking status, smoking status, annual family income, level of education, BP (systolic BP, diastolic BP), history of diabetes and treatment, information about exercise activity, marital status, work type, and seasonality. We controlled for seasonality using a categorical variable for months. To control for measurement bias by hospital, we included hospital as a categorical variable in the model. The models were also adjusted for weather information, including 3 days' moving average of mean temperature and relative humidity, using 4 degrees of freedom natural cubic spline.

To understand the lag pattern in associations between air pollutants and FBG, firstly, lag 0 and moving averages of lag 0-1, 0-2, 0-3 day of SO<sub>2</sub>, NO<sub>2</sub> and PM<sub>10</sub> were analysed in single pollutant models, respectively. Then, lags which produced the highest effect estimates were modelled in the multi-pollutant models. We also stratified the analyses in different groups, for example by sex (male or female), age group (<65 or  $\geq 65$  years), BMI group (<18, 18–24, 24–28, >28 kg/m<sup>2</sup>), and family income group (<600, 600-800, 800-1000, >1000 yuan/month/person). The effect estimates on FBG (mmol/L) were presented by an increase of  $100 \,\mu\text{g/m}^3$  of pollutant. Data analyses were performed using the statistical packages of SAS software (SAS Institute, Inc., Cary, NC) and R software. To control the non-linear impacts of ambient temperature and relative humidity, we used a natural cubic spline incorporated in the "splines" package of R software to transfer temperature/relative humidity to a matrix. Then the variables of the matrix were put to the SAS PROC GENMOD. We show an example in the supplemental material (Supplemental Material, Nonlinear Function for GEE).

#### 3. Results

## 3.1. Descriptive results

There were 27,685 participants during 2006 and 2008. Table 1 provides the summary statistics of these participants. Age range varied from 18 to 90 years, with mean of 47 years. A majority of the participants were male (82%). About 60% of the participants were not current smokers or drinkers in 2006. Over half (55.7%) of participants had family income ranging between 600 and 800 yuan/month/person (1 US dollar = 6.36 Chinese yuan on 17/09/2015). The prevalence of diabetes was 7.7% in 2006, but only 1.6% used treatments for diabetes. A fifth (20.9%) of participants had a history of hypertension.

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