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Associations between short-term exposure to ambient sulfur dioxide and increased cause-specific mortality in 272 Chinese cities

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ABSTRACT

Background: Ambient sulfur dioxide (SO_2) remains a major air pollutant in developing countries, but epidemiological evidence about its health effects was not abundant and inconsistent.
Objectives: To evaluate the associations between short-term exposure to SO_2 and cause-specific mortality in China.
Methods: We conducted a nationwide time-series analysis in 272 major Chinese cities (2013–2015). We used the over-dispersed generalized linear model together with the Bayesian hierarchical model to analyze the data. Two-pollutant models were fitted to test the robustness of the associations. We conducted stratification analyses to examine potential effect modifications by age, sex and educational level.
Results: On average, the annual-mean SO_2 concentrations was 29.8 μg/m^3 in 272 cities. We observed positive and associations of SO_2 with total and cardiorespiratory mortality. A 10 μg/m^3 increase in two-day average concentrations of SO_2 was associated with increments of 0.59% in mortality from total non-accidental causes, 0.70% from total cardiovascular diseases, 0.55% from total respiratory diseases, 0.64% from hypertension disease, 0.65% from coronary heart disease, 0.58% from stroke, and 0.69% from chronic obstructive pulmonary disease. In two-pollutant models, there were no significant differences between single-pollutant model and two-pollutant model estimates with fine particulate matter, carbon monoxide and ozone, but the estimates decreased substantially after adjusting for nitrogen dioxide, especially in South China. The associations were stronger in warmer cities, in older people and in less-educated subgroups.
Conclusions: This nationwide study demonstrated associations of daily SO_2 concentrations with increased total and cardiorespiratory mortality, but the associations might not be independent from NO_2.

1. Introduction

Sulfur dioxide (SO_2) is a major component of coal-smoke air pollution and also contributes to the formation of secondary particulate matters. The annual levels of SO_2 have fallen drastically below the limits considered safe for human health in developed countries in past decades because of the massive desulfurization in fuel gas, the stringent application of desulfurizers and restricted use of coal (Greenstone, 2004). However, it remains to be a severe air pollution problem in many developing countries (Guttikunda et al., 2003). As the largest developing country, China is the world's largest SO_2 emitter. In 2015, the average for annual-mean SO_2 levels in 338 Chinese cities was 25 μg/m^3 (ranging from 3 to 87 μg/m^3) (Ministry of Envinonment Protection, 2015), which was well beyond the ranges reported in developed

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countries (Kharol et al., 2017; Pope III et al., 2002).

SO_2 is a strong respiratory irritant and bronchoconstrictor. It can induce systemic inflammation and oxidative stress (Routledge et al., 2006; Zhu et al., 2014). Compared with the abundant epidemiological evidence for particulate matter (PM), limited studies have explored the health effects of SO_2, especially in regions with high SO_2 levels (Chen et al., 2012a; Deng et al., 2017). Previous studies, mainly conducted in developed countries, have demonstrated that a short-term rise in ambient SO_2 concentrations was associated with increased cardiorespiratory mortality and morbidity (Ballester et al., 2002; Stieb et al., 2002; Sunyer et al., 2003). A recent review summarized 12 studies on short-term exposure to ambient SO_2 and daily mortality in China (Shang et al., 2013), but the findings were mixed, and mainly from single cities. Furthermore, there are doubts as to the direct effects of SO_2 because the short-term associations between SO_2 and health outcomes disappeared or decreased drastically after adjustment for PM (Sunyer et al., 2003; Vanos et al., 2015) or nitrogen dioxide (NO_2) (Chen et al., 2012b). Nevertheless, a nationwide retrospective cohort study in China showed robust long-term associations of SO_2 with total and cardiorespiratory mortality even after adjustment of PM and nitrogen oxide (Cao et al., 2011). Therefore, we hypothesized that the SO_2-mortality associations in China may be different from those reported in developed countries.

China has recently established a national air quality monitoring system and a nationwide disease surveillance platform, providing a unique opportunity to examine the health effects of ambient SO_2. We therefore designed this nationwide time-series analysis to evaluate the associations between short-term exposure to SO_2 and cause-specific mortality in China.

2. Materials and methods

2.1. Health data collection

This analysis was based on China's Disease Surveillance Points System (DSPS). We extracted daily cause-specific deaths in 272 main cities from this system during the study period of January 2013 to December 2015 (Chen et al., 2017; Liu et al., 2016). In brief, these cities are dispersed over all 31 provincial administrative divisions and cover approximately 22% ($n = 220$ million) of the total population in Mainland China. According to the common regional division of China in terms of geography, climate, and culture, these cities were categorized into four regions (Fig. S1): North ($n = 107$), South ($n = 140$), Northwest ($n = 21$), and Qing-Tibet ($n = 4$, corresponding to Qinghai–Tibet Plateau).

Causes of deaths in the present study were coded by the International Classification of Disease, 10th revision (ICD-10), which included total natural causes (A00–R99, briefed as “total”),cardiovascular diseases (I00–I99, briefed as “CVD”), hypertension disease (I10–I15), coronary heart disease (CHD: I20–I25), stroke (I60–I69), respiratory diseases (J00–J98), and chronic obstructive pulmonary disease (COPD: J41–J44). We divided daily total, CVD and respiratory deaths into several strata by age ranges (5–64 years, 65–74 years and 75 years or older), sex, and educational levels (low: educated ≤9 years; high: educated > 9 years).

2.2. Environmental data

We extracted daily 24-h average concentrations of SO_2 in each city from China's National Urban Air Quality Real-time Publishing Platform (http://106.37.208.233:20035/), which is operated by the China National Environmental Monitoring Center. In brief, this platform displays real-time concentrations of criteria air pollutants in all state-controlled monitoring stations. These stations are mandated to be not in the direct vicinity of apparent emission sources, thus their measurements may well reflect the general urban background level of air pollution. All these stations were operated under the China National Quality Control (GB3095-2012). For the calculation of daily mean concentrations, at least 75% of the 1-h values must be available on that particular day. If a station had > 25% of the values missing, the entire station was excluded from the calculation. We then calculated the mean concentrations for all valid measurements of air pollutants within a city to represent the general exposure levels for all residents. To allow for adjustment of the concomitant exposure to other criteria pollutants, we additionally collected daily (24-h) average concentrations of fine particulate matter ($PM_{2.5}$), NO_2 and carbon monoxide (CO), and maximum 8-h mean concentrations of ozone (O_3) from the same monitors. Different cities entered the national monitoring system at different time. During our study period, this system included 69 cities with 3-year data, 74 cities with 2-year data, and 129 cities with 1-year data. There were no missing daily-average data during the respective study periods. To control for potential confounding of weather conditions, we also collected daily mean temperature and relative humidity in each city from the China Meteorological Data Sharing Service System (http://data.cma.cn/).

Our study protocol was approved by the Institutional Review Board at the School of Public Health, Fudan University (NO. 2014–07-0523), with a waiver of informed consent because all data were aggregated at the city level, and no subjects were contacted.

2.3. Statistical analyses

We explored the associations between SO_2 and daily cause-specific mortality using a two-stage analytic approach, which has been widely used in previous multicity studies (Chen et al., 2017; Dominici et al., 2006).

In the first stage, a generalized linear model with *quasi*-Poisson regression was used to estimate the SO_2-mortality associations in each city. We adjusted for several covariates as follows: (1) a natural spline smooth function of calendar day with 7 degrees of freedom (*df*) per year to exclude unmeasured time trends longer than 2 months in mortality; (2) an indicator variable for “day of week” to account for possible variations of mortality in a week; and (3) natural smooth functions with 6 *df* for temperature and 3 *df* for relative humidity to control for potential nonlinear confounding effects of weather conditions. We a priori used the 2-day moving average of the present- and previous- day concentrations of SO_2 (lag 01) in our main analyses, because it generally leads to the strongest effect estimates according to previous studies (Chen et al., 2012a; Li et al., 2015). To ascertain the lag patterns in the SO_2 associations, we also examined different lags periods: 1) lag 0, the present day; 2) lag 1, the previous day; 3) lag 2, the previous two day; and 4) lag 3, the previous three day.

In addition to the above single-pollutant models, we also fit two-pollutant models with one of other four criteria pollutants: $PM_{2.5}$, SO_2, CO and O_3, using their concentrations at lag 01 day. The SO_2-mortality association was considered robust if the *p*-value for the dichotomous co-pollutant variable was > 0.05 in meta-regression models with both single- and two- pollutant model estimates (Yin et al., 2017).

In the second stage, pooled estimates at the national- and regional-average level were obtained by applying the Bayesian hierarchical model. This model can combine city-specific effect estimates after accounting for within-city statistical error and for between-city variability of the “true” effect. We then reported the percentage change, including the posterior mean and 95% posterior interval (PI), in daily mortality per 10 $\mu g/m^3$ increase of SO_2 concentrations. The 95%PI is similar to the Bayesian formulation of the 95% confidence interval. We calculated the *I*-squared (I^2) statistics for the between-city heterogeneity in random-effect models.

Furthermore, we explored potential effect modifiers on the associations between SO_2 (lag 01) and total mortality deriving from single-pollutant models. First, we conducted subgroup analyses by demographic factors (i.e., age, sex and education) and by region; then, we