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Short-term exposures to $PM_{2.5}$ and cause-specific mortality of cardiovascular health in China

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ABSTRACT

Background: Many multi-center epidemiological studies have robustly examined the acute health effects of exposure to low concentrations of fine particulate matter ($PM_{2.5}$) on cardiovascular mortality in developed counties. However, data limitations have resulted in few related studies being conducted in developing counties with high levels of $PM_{2.5}$ exposure. In recent years, people in China with a heavy cardiovascular disease burden have been exposed to particularly high levels of $PM_{2.5}$.
Objective: We conducted a multi-county time series study investigating the acute effects of $PM_{2.5}$ on the increased risk of cardiovascular death across China, and explored subpopulations susceptible to $PM_{2.5}$ exposure.
Methods: Appling a county-specific Poisson regression in 30 Chinese counties, we estimated $PM_{2.5}$ effects on all-cause mortality and cause-specific mortality of cardiovascular health for 2013–2015. We also considered $PM_{2.5}$ effects on several subpopulations, including males, females, and three age groups (< 65, 65–74 and > 74 years old). We pooled the county-specific results across China using a random effects meta-analysis by cause and by subpopulation.
Results: We found a 0.13% (95% confidence interval (CI), 0.04–0.22) increase in all-cause mortality, a 0.12% increase (95% CI, 0.001–0.25) increase in cardiovascular disease (CVD), a 0.42% (95% CI, 0.03–0.81) increase in AMI, a 0.17% (95% CI, −0.04–0.40) increase in coronary heart disease, and a 0.13% (95% CI, −0.12–0.33) increase in stroke in association with a 10-μg/m^3 increase in $PM_{2.5}$ concentrations on the same day. The magnitudes of the associations were less than those reported in developed counties with lower $PM_{2.5}$ levels. A vulnerable effect on all-cause mortality was observed in the elderly population (older than 65 years) and on CVD in males.
Conclusions: This study showed the positive magnitude of $PM_{2.5}$ effects with high exposure on all natural, CVD, and cause-specific mortality and on the susceptible populations in China. The findings complemented evidence related to exposure-mortality relationships at the higher end of short-term exposure to $PM_{2.5}$ on a global scale.

1. Introduction

Short-term exposure to fine particle [Particulate Matter < 2.5 μm in aerodynamic diameter ($PM_{2.5}$)] pollution has been linked to adverse cardiovascular effects (Englert, 2004; Pope and Dockery, 2006; Brook et al., 2004). Over the last decade, efforts to understand and mitigate the effects of $PM_{2.5}$ concentrations at below-guideline levels on human health and welfare have been made through a great deal of multi-center epidemiologic research in the United States, Europe, and other developed countries (Ostro et al., 2006; Franklin et al., 2007; Zanobetti and Schwartz, 2009; Atkinson et al., 2014). The results of these studies have been well applied to improve the mitigation of local air pollution and the development of methods designed to protect the health of local populations. However, few related studies have been conducted in developing countries due to limitations of available data, funding and other reasons. In many cases, the $PM_{2.5}$ pollution levels in these countries are much higher than the levels in the developed world (Van Donkelaar et al., 2015), and this is coupled with quite distinct characteristics of the population and the socio-economic status of those societies. As a result, evidence of developed countries cannot be readily

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applied to the air pollution policy-making and related public health protection efforts of developing countries. Moreover, another critical gap in our current knowledge is whether specific individuals or population subgroups experience a greater level of risk due to short-term exposure to $PM_{2.5}$ (Pope and Dockery, 2006; Clougherty, 2010; Atkinson et al., 2014). For the reasons above, it is critical for researchers to conduct epidemiologic work on air pollution in developing countries to fill these missing gaps of knowledge.

The rapid industrialization of China, one of the largest developing countries, in the past few decades has significantly increased China's air pollution levels (Kan et al., 2012; Shang et al., 2013; Gao et al., 2011). The cities of Beijing, Shijiazhuang, Chengdu, and Xi'an have recently reported annual levels of $PM_{2.5}$ at around 87, 144, 89, and 97 μg/m^3, respectively, during 2013–2014 (Wang et al., 2014). At the same time, the Chinese population is currently experiencing a heavy burden from cardiovascular disease; in 2005, cardiovascular disease accounted for 32% of all deaths and 13% of total disability-adjusted life-years lost in China (Wang et al., 2005). In addition, with China's aging population growing, these numbers continue to increase (Ezzati et al., 2015; Moran et al., 2010). Atkinson et al. (2014) summarized the existing epidemiologic evidence related to $PM_{2.5}$ and cardiovascular mortality in the literature up to 2011 and presented estimates for various WHO regions. However, Western Pacific Area-A, which is mainly made up of China, was not included in this meta-analysis because no available studies met the eligibility criteria. Although some single-center time-series studies provided partial insight (Huang et al., 2012; Yang et al., 2012; Li et al., 2013; Chen et al., 2013), those studies had concentrated on several large cities and focused on the endpoints of all-cause death rather than addressing cardiovascular or other specific causes of death. In addition, to date, relatively few multi-center studies have been conducted in China (Shang et al., 2013; Lu et al., 2015). Compared with single-center studies, multi-center studies has several distinct advantages, especially in terms of strengthening the power of the statistical analysis and reducing the likelihood of spurious results (Anderson et al., 2005; Pope and Dockery, 2006).

Given the severe pollution situation and the knowledge gaps mentioned above, it is worth initiating more in-depth and larger epidemiological studies to understand of the acute health effects of $PM_{2.5}$ on cardiovascular death in China. Generating a complete $PM_{2.5}$-mortality exposure response relationship and determining the effect size of $PM_{2.5}$ on cause-specific cardiovascular death is also essential. Knowledge related to the subpopulations that are sensitive to $PM_{2.5}$ will be necessary for guiding future strategies designed to protect the population from the adverse effects of air pollution. Thus, in this paper, we conducted a multi-county time series analysis to investigate the short-term effects of $PM_{2.5}$ on cause-specific mortality of cardiovascular health across China, and to explore which groups are at a relatively higher risk or are more susceptible to the adverse effects of $PM_{2.5}$ exposure.

2. Materials and methods

2.1. Study site

Thirty Chinese counties with a total resident population of 23.7 million were selected for our study. These counties were located in the major cities of northern, eastern and southwestern China (Fig. 1) and includes 21 urban and 9 rural areas. Counties of interest were selected based on the availability of daily mortality data, $PM_{2.5}$ and O_3 concentration data, and meteorological factors with a baseline of at least 900 days from January 1, 2013 to December 31, 2015.

2.2. Mortality data

Daily mortality counts were obtained from the Disease Surveillance Point System of the Chinese Center for Disease Control and Prevention (China CDC). After excluding accidental deaths, we classified the deaths by sex (male and female), age groups (< 65 years, 65–74 years, and > 74 years), and cause of death according to the International Statistical Classification of Disease, 10th Revision (ICD-10; World Health Organization 2007). Classifications included all-cause mortality (A00-R99), cardiovascular disease (CVD, I00–I99), coronary heart disease (CHD, I20–I25), acute myocardial infarction (AMI, I21–I22), and stroke (I60–I64).

2.3. Air pollution data

Daily air pollution data for $PM_{2.5}$ and O_3 concentrations were collected from the National Air pollution Monitoring System. In each county, at least one fixed-site monitoring station was matched by the closest spatial distance to the county center. If multiple air pollution monitors were available for a county, the concentration data of pollutants from that county were averaged.

2.4. Meteorological data

To adjust for the effects of meteorological factors on daily mortality, data on 24-hr average temperature and relative humidity were obtained from the meteorological data network of the China Meteorological Bureau.

2.5. Analytical strategy

We applied a two-stage analysis of a multi-center time series study design. In the first stage, we used quasi-Poisson regression in a generalized linear model to estimate the county-specific relationship between daily mortality and $PM_{2.5}$ for each cause and subgroup. We controlled for time trend using a natural cubic regression spline with 7 degrees of freedom (*df*) per year, and for daily temperature and relative humidity on the same day with 3 *df* for each (Peng et al., 2006; Ostro et al., 2006; Chen et al., 2012;). The effect of day of the week was also included as a control variable. Briefly, the following model (Eq. (1)) was fitted to obtain the estimated $PM_{2.5}$ log-relative rate β:

$$LogE(Y_t) = Intercep_t + ns(time, df) + ns(temperature, df) + ns(humidity, df) + dow + \beta Z_t \quad (1)$$

where $E(Y_t)$ represents the expected number of deaths at day t, ns is the natural-spline function of time trend and meteorological factors, dow is a dummy variable for the day of the week, β represents the log-relative rate of mortality associated with a unit increase in $PM_{2.5}$, and Z_t is the concentrations of $PM_{2.5}$ at day t.

In the second-stage analysis, we conducted a random effects meta-analysis for the substantial heterogeneity that existed between counties to obtain an overall effect estimate of the relationship between $PM_{2.5}$ and mortality. This pooled analysis was completed using 30 county-specific coefficients for each cause and subgroup separately.

The current day (lag 0) exposure to $PM_{2.5}$ was entered into the core model to assess the mortality effect. Previous studies (Ostro et al., 2006; Franklin et al., 2007; Zanobetti and Schwartz, 2009) reported strong relationships between mortality and $PM_{2.5}$ lagged 1 or 2 days or with cumulative exposures over several days. Therefore, the present study also examined a single-day lag of 1 (lag 1) and 2 days (lag 2) as well as the period lag for $PM_{2.5}$ exposure, including the 2-day average of current- and previous-day concentrations (lag 01) and 3-day average of current day and the previous 2 days concentrations (lag 02) for each cause of death.

We examined the sensitivity of key findings with respect to (1) specification of degrees of freedom in the smooth functions of time (df = 5, 6) and meteorological indicators (df = 5) to observe model stability; (2) inclusion of ozone in the statistical model as a potential confounder to structure a two-pollutant model and estimate the potential modified effect. In addition, we combined the relationship