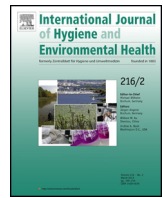




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## Differentiating the effects of characteristics of PM pollution on mortality from ischemic and hemorrhagic strokes

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### ABSTRACT

Though increasing evidence supports significant association between particulate matter (PM) air pollution and stroke, it remains unclear what characteristics, such as particle size and chemical constituents, are responsible for this association. A time-series model with quasi-Poisson function was applied to assess the association of PM pollution with different particle sizes and chemical constituents with mortalities from ischemic and hemorrhagic strokes in Guangzhou, China, we controlled for potential confounding factors in the model, such as temporal trends, day of the week, public holidays, meteorological factors and influenza epidemic. We found significant association between stroke mortality and various PM fractions, such as PM<sub>10</sub>, PM<sub>2.5</sub> and PM<sub>1</sub>, with generally larger magnitudes for smaller particles. For the PM<sub>2.5</sub> chemical constituents, we found that organic carbon (OC), elemental carbon (EC), sulfate, nitrate and ammonium were significantly associated with stroke mortality. The analysis for specific types of stroke suggested that it was hemorrhagic stroke, rather than ischemic stroke, that was significantly associated with PM pollution. Our study shows that various PM pollution fractions are associated with stroke mortality, and constituents primarily from combustion and secondary aerosols might be the harmful components of PM<sub>2.5</sub> in Guangzhou, and this study suggests that PM pollution is more relevant to hemorrhagic stroke in the study area, however, more studies are warranted due to the underlying limitations of this study.

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### Introduction

A great number of epidemiological studies have demonstrated a consistent increased risk from stroke with short term exposure to ambient particulate matter (PM) air pollution, which was generally measured as particulate matter with aerodynamic diameter

≤10 μm (PM<sub>10</sub>) or ≤2.5 μm (PM<sub>2.5</sub>) (Dominici et al., 2006; Williams et al., 2014). Previous studies mainly evaluated the relationship of stroke occurrence with total mass concentration of the particles, fewer have examined the stroke effects of different characteristics of the particles, such as particle size and their chemical constituents (Kettunen et al., 2007), and more importantly limited studies have been conducted to differentiate the effects of these PM characteristics on different stroke types, which presented an obstacle to a better understanding of the biological mechanisms of their association.

Epidemiological and toxicological studies suggest that smaller particles might be more harmful to human health (Lin et al., 2015). Only limited epidemiological studies, however, have examined the association between stroke and these smaller particles with inconsistent findings. For example, a study examined the relationship between stroke mortality and three size fractions (PM<sub>2.5–10</sub>, PM<sub>1–2.5</sub>

**Abbreviations:** PM, particulate matter; OC, organic carbon; EC, elemental carbon; PM<sub>10</sub>, particulate matter with aerodynamic diameter ≤10 μm; PM<sub>2.5</sub>, particulate matter with aerodynamic diameter ≤2.5 μm; QA, quality assurance; QC, quality control; ICD-10, International Classification of Diseases Tenth Revision; SO<sub>2</sub>, sulfur dioxide; NO<sub>2</sub>, nitrogen dioxide; GAM, generalized additive model; PH, public holidays; DOW, day of the week; df, degree of freedom; ER, excess risk; CI, confidence interval; IQR, interquartile range.

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and PM<sub>1</sub>) in Barcelona, Spain, and found that PM<sub>1</sub> and PM<sub>2.5–10</sub>, rather than PM<sub>1–2.5</sub>, was associated with stroke mortality (Perez et al., 2009). A study from Helsinki, Finland only detected significant stroke effects of PM<sub>2.5</sub> and ultrafine particles (PM<sub>0.1</sub>) in warm season, but not in cold season (Kettunen et al., 2007). And in Copenhagen, Denmark, ultrafine particle, rather than PM<sub>10</sub>, was found to be associated with ischemic stroke hospitalization without atrial fibrillation (Andersen et al., 2010). One recent systematic review suggested that PM<sub>2.5</sub> and PM<sub>10</sub>, rather than PM<sub>2.5–10</sub>, were associated with stroke mortality (Wang et al., 2014).

On the other hand, the current air pollution control guidelines/regulations generally use total mass concentration as the indicator. Although it is important to protect human health, more targeted air quality standards need to incorporate PM chemical constituents or emission sources that are more directly related to the health impacts, and this has been viewed as the ultimate goal of air pollution control policies. However, such standards have been hindered by limited information on the toxicity of PM constituents (Dai et al., 2014). PM consists of many chemical components that originate from different sources, such as industrial emission, traffic, biomass burning and coal combustion. Exploring which specific PM component was associated with a given health outcome will also help to explain the underlying mechanism of the PM health effects (Li et al., 2014).

The objective of this study was to investigate the relationship between PM pollution with different particle sizes (PM<sub>10</sub>, PM<sub>2.5–10</sub>, PM<sub>2.5</sub>, PM<sub>1–2.5</sub> and PM<sub>1</sub>), PM<sub>2.5</sub> constituents and mortalities from ischemic and hemorrhagic strokes in Guangzhou, China.

## Materials and methods

### Study setting

Guangzhou, the capital city of Guangdong Province, is an economic center of south China. Due to the rapid economic development and corresponding rise in energy consumption over the past decades, this city has experienced serious air pollution. Guangzhou has a typical subtropical humid-monsoon climate with an average annual temperature of 22 °C and average rainfall of 1500–2000 mm. The residents in urban districts of Guangzhou were selected as the subjects of this study, with a population of about 5.5 million, accounting for 69.7% of the whole population of this city. The urban areas were chosen for two reasons. First, they were close to the air monitoring stations. Second, the mortality data were of high quality because most of the residents living in these districts are permanent residents (Yu et al., 2012).

### Data collection

Daily mortality data from 1st January 2007 to 31st December 2011 were obtained from the death registry system, which included the information of sex, date of death, age at death, residential address and the underlying cause of death. In Guangzhou, all deaths were obliged to be reported to the death registry system. Hospital or community doctors were requested to report the cause of death on a death certificate. The government has mandated detailed quality assurance (QA) and quality control (QC) for the death registry. The cause of death was coded using the International Classification of Diseases, Tenth Revision (ICD-10). Mortality from stroke (ICD-10: I60–I66), and sub-categories, including ischemic stroke (ICD-10: I63–I66), and hemorrhagic stroke (ICD-10: I60–I62) were extracted to construct the time series. We also compiled stroke mortality data among the residents near the air monitoring station to evaluate the impact of potential exposure misclassification.

The air pollution data were collected from two different air monitoring stations. The two stations were surrounded by residential

areas where there were neither major industrial sources nor local fugitive dust sources (Fig. 1). An automatic air monitoring system was installed on the rooftop of Panyu Meteorological Centre (Station 1) to measure daily air pollution from 1st January 2009 to 31st December 2011, including PM<sub>10</sub>, PM<sub>2.5</sub> and PM<sub>1</sub>, and also gaseous air pollutants including sulfur dioxide (SO<sub>2</sub>) and nitrogen dioxide (NO<sub>2</sub>). Measurements of PM<sub>10</sub>, PM<sub>2.5</sub> and PM<sub>1</sub> were performed using a GRIMM Aerosol Spectrometer (Model 1.108, Grimm Aerosol Technik GmbH, Ainring, Germany). Details about the air pollution collection and quality control have been introduced elsewhere. In brief, the GRIMM model 1.108 monitor is designed to measure particle size distribution and the mass concentration based on a light scattering measurement of individual particles in the collected air samples. Thus, the particle density, determined by chemical composition, could affect the concentration of PM mass. However, the PM mass concentrations are converted to a mass distribution using a density factor corresponding to the GRIMM established “urban environment” factor. Thus, the measured PM mass should be accurate (Grimm and Eatough, 2009). We estimated PM<sub>2.5–10</sub> concentrations by subtracting daily PM<sub>2.5</sub> from PM<sub>10</sub> and PM<sub>1–2.5</sub> by subtracting PM<sub>1</sub> from PM<sub>2.5</sub>. When no concentration was measured on some observation days, they were treated as missing data; during the measurement period of 2009–2011, the proportion of missing data for the particle concentration was very low (ranging from 1% to 2%).

Daily PM<sub>2.5</sub> chemical composition data were obtained from another automatic monitoring system, which was located on the rooftop of the South China Institute of Environmental Sciences (Station 2). PM<sub>2.5</sub> samples were collected on 47 mm quartz microfiber filters (Whatman International Ltd., Maidstone, England, QMA) using a sampler (BGI Incorporated, Waltham, MA, US, Model PQ200) operating at a flow rate of 16.7 L min<sup>-1</sup>. For this study, we measured seven major PM<sub>2.5</sub> chemical constituents for four months (January, April, July and November) of each year from 2007 to 2010. These measures included organic carbon (OC), elemental carbon (EC), and five water-soluble ions (nitrate (NO<sub>3</sub><sup>-</sup>), sulfate (SO<sub>4</sub><sup>2-</sup>), ammonium (NH<sub>4</sub><sup>+</sup>), sodium ions (Na<sup>+</sup>) and chloride ion (Cl<sup>-</sup>). Details of the measurement and QA/QC procedure can be found elsewhere (Tao et al., 2012).

We also collected daily meteorological data, including daily mean temperature (°C) and relative humidity (%) from Guangzhou Weather Station. Approval to conduct this study was granted by the Medical Ethics Committee of Guangdong Provincial Centre for Disease Control and Prevention.

### Statistical analysis

Due to different time periods to measure the concentrations of different particle fractions and PM<sub>2.5</sub> chemical constituents, we constructed two datasets for the data analyses. The first one involved daily mass concentrations of PM<sub>10</sub>, PM<sub>2.5–10</sub>, PM<sub>2.5</sub>, PM<sub>1–2.5</sub> and PM<sub>1</sub> for 1st January 2009 through 31st December 2011 and the second included daily concentrations of PM<sub>2.5</sub> chemical constituents for January, April, July and November of 2007–2010.

We examined the short-term association between daily PM pollution and stroke mortality using generalized additive models (GAM) with a quasi-Poisson link function to account for overdispersion in stroke mortality. In the model, we controlled for public holidays (PH) and day of the week (DOW) using categorical variables. To reduce the issues associated with multiple testing and model specifications, we followed some previous studies to select model specification a priori and the degree of freedom (df) for seasonal patterns and long-term trends and other meteorological variables (Peng et al., 2006). We applied 8 df per year for time trends to filter out the information at time scales of longer than two months, 6 df for mean temperature of the current day (Temp<sub>0</sub>) and moving average of previous 3 days (Temp<sub>1–3</sub>) to account for

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