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# The cold effect of ambient temperature on ischemic and hemorrhagic stroke hospital admissions: A large database study in Beijing, China between years 2013 and 2014—Utilizing a distributed lag non-linear analysis<sup>☆</sup>

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## ABSTRACT

The effects of ambient temperature on stroke death in China have been well addressed. However, few studies are focused on the attributable burden for the incident of different types of stroke due to ambient temperature, especially in Beijing, China. We purpose to assess the influence of ambient temperature on hospital stroke admissions in Beijing, China. Data on daily temperature, air pollution, and relative humidity measurements and stroke admissions in Beijing were obtained between 2013 and 2014. Distributed lag non-linear model was employed to determine the association between daily ambient temperature and stroke admissions. Relative risk (RR) with 95% confidence interval (CI) and Attribution fraction (AF) with 95% CI were calculated based on stroke subtype, gender and age group. A total number of 147,624 stroke admitted cases (including hemorrhagic and ischemic types of stroke) were documented. A non-linear acute effect of cold temperature on ischemic and hemorrhagic stroke hospital admissions was evaluated. Compared with the 25th percentile of temperature (1.2 °C), the cumulative RR of extreme cold temperature (first percentile of temperature, -9.6 °C) was 1.51 (95% CI: 1.08–2.10) over lag 0–14 days for ischemic type and 1.28 (95% CI: 1.03–1.59) for hemorrhagic stroke over lag 0–3 days. Overall, 1.57% (95% CI: 0.06%–2.88%) of ischemic stroke and 1.90% (95% CI: 0.40%–3.41%) of hemorrhagic stroke was attributed to the extreme cold temperature over lag 0–7 days and lag 0–3 days, respectively. The cold temperature's impact on stroke admissions was found to be more obvious in male gender and the youth compared to female gender and the elderly. Exposure to extreme cold temperature is associated with increasing both ischemic and hemorrhagic stroke admissions in Beijing, China.

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## 1. Introduction

Over the past two decades, stroke has gained public health concern on a global scale (Feigin et al., 2016). Stroke incidence varies by races and countries, especially in economically low income and developing countries (Carandang et al., 2006; Tsai et al.,

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2013; Wu et al., 2013; Zhang et al., 2012). According to the Global Burden of Disease Study in 2013, more than 90% of the stroke burden is attributable to the modifiable risk factors, including adopted lifestyle as well as low physical activity and metabolic status (Feigin et al., 2016). It is a remarkable fact that environmental conditions and meteorological factors, particularly ambient temperature and air pollution have significantly and affectedly shifted the global stroke burden, currently accounting for approximately 29.2% (Feigin et al., 2016).

Despite the consistent evidence of extreme weather conditions associated with an increased risk of cardiovascular diseases (Phung et al., 2016) and respiratory diseases (Lavigne et al., 2014), previously reported studies have demonstrated conflicting results on the correlation of ambient temperature and the incidence of stroke (Cevik et al., 2015; Jeong et al., 2013). Several published works suggest that a decline in ambient temperature is evidently linked with a higher susceptibility to ischemic stroke (Cevik et al., 2015; Hong et al., 2003; Mostofsky et al., 2014; Rakers et al., 2016). However, another research conducted in the United States about 6 years ago, reported no significant association between ambient temperature and any stroke subtype from 155 hospitals in 20 different States over a five-year study period (Cowperthwaite and Burnett, 2011). Furthermore, two recent meta-analyses have also concluded that a lower mean ambient temperature was significantly related to a higher risk of stroke incidence (Wang et al., 2016; Zorrilla-Vaca et al., 2016). Nevertheless, the meta-analyses by Wang et al. (2016) which included three studies from Taiwan (Chen et al., 1995; Fang et al., 2012; Lee et al., 2008) and one study from Hong Kong (Goggins et al., 2012). The other meta-analyses by Zorrilla-Vaca et al. (2016) only entailed one study from Taiwan (Chen et al., 1995) and one study from Shanghai, China (Meng et al., 2015). Therefore, suggesting that a reproducible large population-based and high quality evidence study from Beijing, China is certainly lacking.

The relationship between ambient temperature and stroke mortality has been reported in different areas of China (Chen et al., 2013b; Yang et al., 2012; Yang et al., 2016). However, the effect of ambient temperature on hospital stroke admissions is rarely addressed and inadequately accounted for. Recently, Guo et al. (2016) found that cold temperature is attributed to stroke hospital admission in Guangzhou, China. Comparably, ambient temperature in Beijing (North) is much lower than observed in Guangzhou (South), China (Chen et al., 2013b). Additionally, the effect of ambient temperature on stroke may differ by the stroke subtype (Ding et al., 2016). For instance, one study reported that a higher temperature was more detrimental to ischemic stroke than to hemorrhagic stroke (Lim et al., 2013), while another study reported a conflicting result (Guo et al., 2016). It is therefore critically important to investigate the relationship between ambient temperature and hospital admissions for different stroke subtypes.

The impacts of ambient temperature on hospital stroke admissions in Beijing, China, between 2013 and 2014 were investigated using distributed lag non-linear models (DLNMs) (Gasparrini et al., 2010; Gasparrini and Leone, 2014), and whether the associations differed by gender, age group and the stroke subtype were explored in this large population-based study.

## 2. Method

### 2.1. Study setting

Beijing, the capital of China, is an international metropolis with a population of over 20 million. It is in the Northern China Plain (39°26' to 41°03' north latitude, 115°25' to 117°30' east longitude) with an estimated area of about 16410 km<sup>2</sup>. Beijing belongs to a

somewhat humid continental monsoon climate with an average temperature of 11.6 °C within the study period.

### 2.2. Data collection

Daily meteorological data from 1 January 2013 to 31 December 2014 were collected from the Chinese Meteorological Bureau, which included daily mean temperature (°C) and relative humidity (%). Daily mean levels of particulate matter with an aerodynamic diameter <2.5 μm (PM<sub>2.5</sub>) for the same period were collected from the Centre of City Environmental Protection Monitoring Website Platform of Beijing.

Daily count of stroke admissions from 1 January 2013 to 31 December 2014 was extracted from the databases maintained by the Beijing Public Health Information Center. These databases encompassed 63 hospitals in Beijing which are highly recognized and approved by the Chinese government to diagnose and treat cardiovascular and cerebrovascular related diseases. Stroke was defined according to the International Classification of Diseases 10th Revision (ICD-10). The count of stroke admissions by stroke subtype (ischemic stroke, ICD10: I63 and hemorrhagic stroke, ICD10: I60–61) were also documented. A flowchart showing how these counts of stroke admissions were composed of was in the Supplementary materials (Fig. S1).

This study's protocol was approved by the School of Public Health, Capital Medical University Institutional Review Board (IRB00009511). Informed consent from patients was not necessary since only aggregated data was used in this study.

### 2.3. Statistical analysis

Descriptive statistics was used to describe for the participant's characteristics including gender, age group, and stroke subtype in this study. Time-series line figure was utilized to evaluate the long-term trends and seasonal patterns of stroke admissions, weather variables and air pollution. A distributed lag non-linear model (DLNM) was applied to investigate the delayed and non-linear effects of temperature on stroke admissions, after controlling the potential co-variates. A “cross-basis” function was used to evaluate the two-dimensional relationship between different number of lag days and temperature change by DLNM (Gasparrini et al., 2010). Specifically, according to the previous studies (Gasparrini and Leone, 2014), a natural cubic spline with three degrees of freedom (*df*) for the lag dimension and four *df* for the temperature change dimension were utilized in the “cross-basis” function. As from the prior knowledge, the impact of cold temperature on stroke mortality and emergency hospitalization could last for two or three weeks, however, the effect of hot temperature was shorter (Gasparrini et al., 2015b; Tian et al., 2016). Because the hot effects of temperature cannot be assessed by the short lags adequately due to the harvesting effects (Guo et al., 2011; Lavigne et al., 2014). The maximum lag period was chosen to 21 days to adequately capture the long-term delay effect of cold temperature effect and hot effect while also taking harvesting effect into account (Guo et al., 2014; Yang et al., 2015, 2016). A quasi-likelihood Poisson generalized additive model was used to model the natural logarithm of everyday stroke admission counts as functions of predictors, and is displayed as follows:

$$\begin{aligned} \text{Log}[E(Y_t)] = & \alpha + \beta_1 \times \text{Temp}_{t,l} + ns(t, df = 7 \times 2) \\ & + ns(RH_t, df = 3) + \beta_2 \times PM_{2.5(t)} + \beta_3 \times DOW_t \\ & + \beta_4 \times \text{Holiday}_t \end{aligned}$$

Here,  $E(Y_t)$  is the expected daily counts of stroke hospital admission

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