Science of the Total Environment 851 (2022) 158046

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Associations of ambient temperature with mortality for ischemic and hemorrhagic stroke and the modification effects of greenness in Shandong Province, China

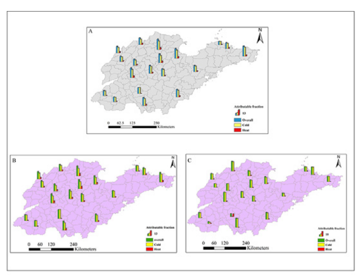
Fenfen He [a,1], Jing Wei [b,1], Yilin Dong [a], Chao Liu [a], Ke Zhao [a], Wenjia Peng [c], Zilong Lu [d], Bingyin Zhang [d], Fuzhong Xue [e,f,*], Xiaolei Guo [d,**], Xianjie Jia [a,***]

[a] Department of Epidemiology and Statistics, Bengbu Medical College, Bengbu, China
[b] Department of Atmospheric and Oceanic Science, Earth System Science Interdisciplinary Center, University of Maryland, College Park, MD, USA
[c] School of Public Health, Fudan University, Shanghai, China
[d] Shandong Center for Disease Control and Prevention, Jinan, China
[e] Department of Biostatistics, School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan, China
[f] Healthcare Big Data Research Institute, Cheeloo College of Medicine, Shandong University, Jinan, China

HIGHLIGHTS

- Moderate and extreme temperatures cause substantial stroke subtypes death burdens.
- Ischemic stroke mortality is more attributable to cold than Hemorrhagic stroke.
- The higher the latitude, the less adaptable to heat based on multicenter findings.
- Greenness alleviate stroke mortality risks from heat using NDVI, SAVI, EVI as exposures.

GRAPHICAL ABSTRACT



Greenness modifications (β)				
Summer	Stroke		Ischemic stroke	
	Moderate heat	Extreme heat	Moderate heat	Extreme heat
NDVI	-0.070 (-0.135, -0.005)	-0.162 (-0.312, -0.013)	-0.112 (-0.200, -0.023)	-0.239 (-0.428, -0.049)
SAVI	-0.080 (-0.163, 0.003)	-0.194 (-0.384, -0.004)	-0.135 (-0.246, -0.023)	-0.296 (-0.535, -0.058)
EVI	-0.039 (-0.094, 0.016)	-0.017 (-0.233, 0.019)	-0.070 (-0.142, 0.002)	-0.168 (-0.325, -0.011)

ARTICLE INFO

Editor: Scott Sheridan

Keywords:
Ambient temperature
Ischemic stroke
Hemorrhagic stroke
Mortality
Attributable fraction
Greenness

ABSTRACT

Background: Evidence is scant on the relative and attributable contributions of ambient temperature on stroke subtypes mortality. Few studies have examined modification effects of multiple greenness indicators on such contributions, especially in China. We quantified the associations between ambient temperature and overall, ischemic, and hemorrhagic stroke mortality; further examined whether the associations were modified by greenness.

Methods: We conducted a multicenter time-series analysis from January 1, 2013 to December 31, 2019. we adopted a distributed lag non-linear model to evaluate county-specific temperature-stroke mortality associations. We then applied a random-effects meta-analysis to pool county-specific effects. Attributable mortality was calculated for cold and heat, defined as temperatures below and above the minimum mortality temperature (MMT). Finally, We conducted a multivariate meta-regression to determine associations between greenness and stroke mortality risks for

Abbreviations: Q-AIC, quasi-Akaike information criterion; MMT, minimum mortality temperature; NDVI, normalized difference vegetation index; SAVI, soil adjusted vegetation index; EVI, enhanced vegetation index; RR, relative risk; OR, odds ratio; AF, attributable fraction; CI, confidence interval; eCI, empirical confidence interval; DLNM, distributed lag non-linear model; BLUP, best linear unbiased prediction.

* Correspondence to: F. Xue, Department of Biostatistics, School of Public Health, Shandong University, 44 Culture West Road, Jinan 250012, China.
** Correspondence to: X. Guo, Shandong Center for Disease Control and Prevention, 16992 Jingshi Road, Jinan 250012, China.
*** Correspondence to: X. Jia, Department of Epidemiology and Statistics, School of Public Health, Bengbu Medical College, No. 2600 Donghai Avenue, Longzihu District, Bengbu 233000, China.
E-mail addresses: xuefzh@sdu.edu.cn (F. Xue), guoxiaolei@126.com (X. Guo), jiaxianjie@bbmc.edu.cn (X. Jia).

[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.scitotenv.2022.158046
Received 26 May 2022; Received in revised form 28 July 2022; Accepted 11 August 2022
Available online 17 August 2022

cold and heat, using normalized difference vegetation index (NDVI), soil adjusted vegetation index (SAVI), and enhanced vegetation index (EVI) as quantitative indicators of greenness exposure.
Results: In the study period, 138,749 deaths from total stroke were reported: 86,873 ischemic and 51,876 hemorrhagic stroke. We observed significant W-shaped relationships between temperature and stroke mortality, with substantial differences among counties and regions. With MMT as the temperature threshold, 17.16 % (95 % empirical CI, 13.38 %–19.75 %) of overall, 20.05 % (95 % eCI, 16.46 %–22.70 %) of ischemic, and 12.55 % (95 % eCI, 5.59 %–16.24 %) of hemorrhagic stroke mortality were attributable to non-optimum temperature (combining cold and heat), more mortality was caused by cold (14.94 %; 95 % eCI, 11.57 %–17.34 %) than by heat (2.22 %; 95 % eCI, 1.54 %–2.72 %). Higher levels of NDVI, SAVI and EVI were related to mitigated effects of non-optimum temperatures—especially heat.
Conclusions: Exposure to non-optimum temperatures aggravated stroke mortality risks; increasing greenness could alleviate that risks. This evidence has important implications for local communities in developing adaptive strategies to minimize the health consequences of adverse temperatures.

1. Introduction

In 2019, stroke was the second—leading cause of death worldwide after ischemic heart disease (Roth et al., 2020). Age-standardized mortality and disability-adjusted life year (DALY) rates due to stroke have decreased; however, the global burden of stroke has increased substantially from 2013 to 2019. That development is evidenced by a 70 % increase in absolute numbers, a 43 % increase in mortality, and a 36 % increase in DALYs; the bulk of the burden occurred in low- and lower-middle-income countries (GBD 2019 Stroke Collaborators, 2021). As the world's largest developing country, China has a disproportionately higher stroke burden: in 2018, stroke accounted for 22.6 % of the total mortality (Wang et al., 2020). From 1990 to 2019, stroke-related mortality increased by 59 %, with a greater increment in ischemic stroke (171.1 %) than hemorrhagic stroke (37.4 %) (Ma et al., 2021).

To reduce the growing burden of stroke, it is essential to identify modifiable risk factors. Epidemiological evidence suggests that approximately 90 % of the stroke burden is attributable to lifestyle and environmental exposures (GBD 2019 Risk Factors Collaborators, 2020; Zhou et al., 2019). Well-known conventional factors, such as high blood pressure, smoking, and unhealthy dietary habits, can increase the risk of stroke (Aigner et al., 2017; van Alebeek et al., 2018; Xia et al., 2019). However, the associations and mechanisms between environmental risk factors and stroke mortality have not been fully elucidated (Chen et al., 2013a, 2013b; Cheng et al., 2019; de Bont et al., 2022). World Health Day on April 7, 2022, was an essential reminder that the global crisis is entwined with climate change–primarily in the form of global warming and ongoing climate, which are increasing various health risks, including the burden of disease (The Lancet Public Health, 2022). Nevertheless, the association and mechanism of ambient temperature with the burden of stroke deaths has not been well understood.

On the one hand, although previous studies have largely agreed that both extreme cold and extreme heat affect overall stroke mortality, their relative importance is still controversial and other details of the association remain unexplored (Chen et al., 2013a, 2013b; Mazidi and Speakman, 2020; Polcaro-Pichet et al., 2019; Saucy et al., 2021; Yang et al., 2019; Zafeiratou et al., 2021). For example, previous research has mostly focused on extreme events, neglecting the contribution of moderately low and high temperatures. The association has been quantified in terms of risk ratio, e.g., relative risk (RR) and odds ratio (OR); however, few studies have provided estimates of the attributable burden, such as attributable fraction (AF) (Lei et al., 2022; Luan et al., 2017; Ma et al., 2020). Moreover, little research has examined the associations between ambient temperature and subtypes of stroke (i.e., ischemic and hemorrhagic stroke) with high heterogeneity across the results. For example, one study found that both low and high temperatures increased the mortality risks of stroke subtypes; it did so based on 272 cities in China: it reported higher AF values for hemorrhagic stroke (18.10 %, empirical confidence interval [eCI], 15.30 %–20.45 %) than for ischemic stroke (14.09 %, 95 % eCI: 10.90 %–17.04 %) owing to non-optimum temperature (Chen et al., 2018). However, heat was found to have no effect on ischemic stroke in Hong Kong (Goggins et al., 2012). A beneficial effect of heat on hemorrhagic stroke mortality was observed in four cities in South Korea (Lim et al., 2013). One study of 155 cities in the United States reported that cold and heat were unrelated to stroke subtypes (Cowperthwaite and Burnett, 2011).

On the other hand, studies have demonstrated that the temperature-mortality association could be modified by various environmental characteristics, including greenness, which has been shown to alleviate heat stress in different populations (Dang et al., 2018; De Lombaerde et al., 2022; Zellweger et al., 2019). Vegetation can absorb solar radiation to achieve a cooling effect on the surroundings; living areas with higher greenness levels could increase opportunities for physical activity, enhance social interaction, relieve stress, and reduce air pollution, which may buffer the adverse impacts of cold and heat temperatures (Avellaneda-Gómez et al., 2022; Kondo et al., 2018; Zhang et al., 2020). However, potential modifying effects of greenness on heat-related RRs were observed in limited studies using only one greenness indicator, i.e., normalized difference vegetation index (NDVI). For example, one report in South Korea used NDVI to assess the modified effect of greenness on the temperature-mortality association; it found that less vegetation had a stronger effect of heat on mortality (Son et al., 2016); An investigation in Thailand observed that each 0.1-unit increase in NDVI was associated with a 0.47 % [−0.47 % (95 % CI: −0.89 %, 0.02 %)] reduction in cardiovascular mortality burden caused by non-optimal temperature (Denpetkul and Phosri, 2021). NDVI is the best indicator of vegetation growth status and vegetation cover; it is the most used global-based index. That is partly due to the ability of NDVI to offset some of the influences of radiation variations associated with atmospheric conditions caused by solar angles, satellite observation angle, topography, and clouds or shadow. However, the sensitivity of NDVI to soil and canopy remains a serious challenge (Rhew et al., 2011; Donovan et al., 2022). Thus, the soil-adjusted vegetation index (SAVI) and enhanced vegetation index (EVI) have received attention. SAVI can minimize soil background influence on the vegetation signal (Zhen et al., 2021). EVI is considered an improvement to NDVI in that it can simultaneously correct for atmospheric aerosols or residual aerosols scattering and decouple canopy background, thereby improving sensitivity for high biomass regions and vegetation monitoring capability (Liu and Huete, 1995).

In the context of a global climate change that may lead to a more burden of stroke deaths, investigating an effective adaptation and mitigation strategy would have significant public health implications. From the above evidence, it is reasonable to assume that higher greenness levels are associated with lower RRs of mortality for cold- and heat-related stroke. To the best of our knowledge, however, no studies have combined NDVI, SAVI, and EVI to estimate the effect modifications of greenness on temperature-stroke mortality in China and enhanced the robustness of the results.

Thus, to quantify the corresponding attributable burdens caused by cold and heat based on multicenter, we examined the associations between ambient temperature and stroke mortality at county, regional and provincial levels in China. Moreover, we investigated whether greenness (NDVI, SAVI, and EVI) could have potential effect modifications on those associations.

2. Material and methods

2.1. Study sites

Located on the eastern coast of China, Shandong Province has a total land area of 158,000 km^2 and population of approximately 101.53 million in 17 cities. The province has a complex landscape: the east is mainly the hilly area of Shandong Peninsula; the center is mountainous; and the northwest and southwest are both plains. Shandong has a warm temperate monsoon climate with a short spring and autumn as well as a long winter and summer; however, this has regional variations owing to geographic and environmental factors, such as differences in landform and sea-land distribution. Specifically, the average temperature increases gradually from the east coast to the southwest; regional differences in average temperature are greater between the east and west than between the north and south. Accordingly, we selected 19 counties from Shandong Province by stratified random sampling according to the above characteristics. We divided the 19 countries into four regions: central (Feicheng, Huaiyin, Laiwu, Yiyuan, Zhangdian), Shandong Peninsula (Fushan, Gaomi Penglai, Shouguang, Wenden); southwest (Chengwu, Junan, Mudan, Xuecheng, Zoucheng) and northwest (Bincheng, Gaotang, Leling, Wucheng) (Zhu et al., 2016). The locations of the study areas are appeared in Fig. 1.

2.2. Data collection

We obtained daily stroke death records (January 1, 2013 to December 31, 2019) of the 19 counties from the Death Register system of Shandong Provincial Center for Disease Prevention and Control (CDC). In China, death certificates are first completed by hospital doctors at the time of death; they are then reported to the CDC via the Internet, which better ensures accuracy of the data. The death information mainly includes age, sex, date of death, and primary cause of death coded according to the International Classification of Diseases, 10th Revision (ICD–10). As in a previous study (Zhou et al., 2017), we categorized the stroke mortality data into three cause-specific counts following ICD-10: overall stroke deaths (codes I60–I67); ischemic stroke deaths (codes I63–I67); and hemorrhagic stroke deaths (codes I60–I62).

Based on the daily source data of total 131 meteorological monitoring stations in Shandong Province and its neighboring provinces (i.e., Anhui, Beijing, Hebei, Henan, Jiangsu, Shanxi, Shanghai, and Tianjin) from the China Meteorological Data Sharing Service System (http://data.cma.cn/), we applied a thin-plat smooth spline function to interpolate daily average temperature and relative humidity grid at 0.01° * 0.01° resolution for all Shandong Province for 2013—2019, with longitude and latitude as independent spline variables, and elevation as a covariate considered in the function (Hutchinson and Xu, 2013). To verify the prediction accuracy, we further applied the 10-fold cross-validation method to calculate correlation coefficients (R^2) and root mean square error(RMSE) for temperature (R^2 = 0.99, RMSE = 0.86 °C) and relative humidity (R^2 = 0.86, RMSE = 5.88 %) (Hu et al., 2021; Lv et al., 2020). Finally, we extracted the daily mean temperature and relative humidity corresponding to the study areas by averaging the grid values covered at each location.

We obtained daily air pollution data during the study period from the ChinaHighAirPollutants (CHAP) dataset (https://wei-jing-rs.github.io/product.html). Specifically, daily SO_2, NO_2, CO and O_3 were estimated by Wei et al. over a 10 km × 10 km using an extended ensemble learning of the space-time extremely randomized trees model together with ground-based observations, remote sensing products, atmospheric reanalysis, and an emission inventory (Wei et al., 2022a, 2022b). The results showed

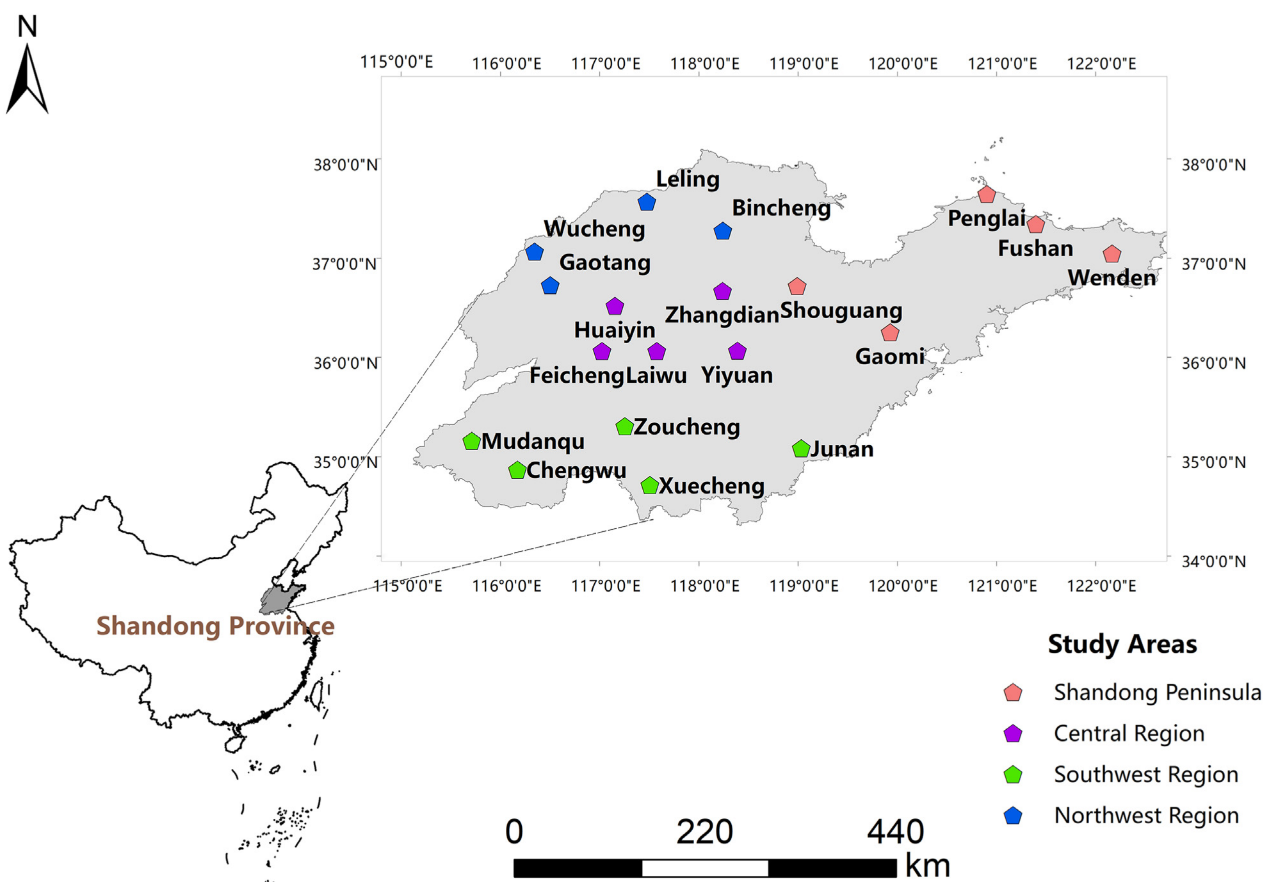


Fig. 1. The geographical location of the 19 counties of Shandong Province in China.

high predictive ability; 10-fold cross-validation R^2 (RMSE) values for the daily predictions of SO_2, NO_2, CO and O_3 were 0.84 (10.07 μg/m^3), 0.84 (7.99 μg/m^3), 0.80 (0.29 mg/m^3) and 0.87 (17.1 μg/m^3), respectively. Meanwhile, We acquired high-resolution (1 km) daily fine particulate matter ($PM_{2.5}$) in Eastern China also from the CHAP dataset (R^2 = 0.92, RMSE = 10.76 μg/m^3) (Wei et al., 2020; Wei et al., 2021). Ultimately, We did not regard O_3 as a confounder because of its strong covariance with average temperature in the main models (Spearman correlation coefficient, $r_s \geq$ 0.70).

We quantitatively assessed greenness using NDVI (Tucker, 1979), SAVI (Huete, 1988) and EVI (Jarchow et al., 2018): we derived the data from Landsat 8 Operational Land Imager (OLI) satellite images at a resolution of 30 m × 30 with <10 % cloud cover (http://earthexplorer.usgs.gov). With those data, we estimated NDVI and SAVI based on the land surface reflectance of visible red (RED) and near-infrared (NIR) parts of the light spectra; they were calculated respectively according to the following equations:

$$\mathrm{NDVI} = (\mathrm{NIR} - \mathrm{RED})/(\mathrm{NIR} + \mathrm{RED})$$

and

$$\mathrm{SAVI} = (1 + \mathrm{L}) \times (\mathrm{NIR} - \mathrm{RED})/(\mathrm{NIR} + \mathrm{RED} + \mathrm{L})$$

where L is correction factor to reduce the impact of soil background. We calculated EVI by adding blue light bands (BLUE) to compensate for the influence of atmospheric correction being incomplete and soil brightness when vegetation density was sparse with the following equation:

$$\mathrm{EVI} = 2.5 \times (\mathrm{NIR} - \mathrm{RED})/(\mathrm{NIR} + 6\mathrm{RED} - 7.5\mathrm{BLUE} + 1)$$

That had a higher response to canopy structure. The above three indexes ranged from −1 to 1; higher values represented densely vegetated areas. We computed the county-specific NDVI, SAVI and EVI for summer (June–August) and winter (December–February) by taking the cumulative average of summer and winter over 7 years in each village during the study periods.

Other environmental and regional characteristics could confound the modification effects of greenness on the RRs of stroke mortality from cold and heat. Thus, we obtained data for population density and GDP per capita for 2013–2019 from statistical yearbooks at the county level (He et al., 2020). We calculated the road density of each county using road vector data up-dated in real-time by Open Street Map. Further, we considered the averages of mean temperature, relative humidity, and $PM_{2.5}$ as potential confounders.

2.3. Statistical analysis

We adopted a two-stage statistical analysis to investigate the effects of cold and heat on mortality risks of overall, ischemic and hemorrhagic stroke at the county, regional and provincial levels.

2.3.1. First-stage analysis

To determine the delayed and non-linear effects of temperature on overall, ischemic, and hemorrhagic stroke mortality at the county-specific level, we applied a distributed lag non-linear model (DLNM) combined with quasi-Poisson regression (Gasparrini et al., 2010). By means of a "cross-basis" function, the DLNM can simultaneously evaluate the non-linear exposure-response relationship and the additional lag-response association. In accordance with previous studies (Luo et al., 2018; Zhang et al., 2014), we applied a natural cubic spline with 4 degrees of freedom (df) for the temperature dimension and natural cubic splines with 3 df for the lag dimension; we did so to fit the model by minimizing the quasi-Akaike Information Criteria (Q-AIC). We adopted the maximum lagged period over 14 days (Li et al., 2021). The final model was as follows:

$$\begin{aligned}\mathrm{Log}\left[\mathrm{E}(\mathrm{Y_t})\right] = \alpha &+ \mathrm{cb}\left(\mathrm{Tmean}_{t,l}\right) + \mathrm{ns}\left(\mathrm{Time}, 7^{*}7\right) + \mathrm{ns}\left(\mathrm{Humidity}, 3\right)\\ &+ \mathrm{ns}\left(\mathrm{PM_{2.5}}, 3\right) + \mathrm{ns}\left(\mathrm{SO_2}, 3\right) + \mathrm{ns}\left(\mathrm{NO_2}, 3\right) + \mathrm{ns}\left(\mathrm{CO}, 3\right)\\ &+ \beta_1 \mathrm{Dow_t} + \beta_2 \mathrm{Holiday_t}\end{aligned}$$

where, Y_t is daily number of stroke mortality at day; α signifies the intercept; β_1 and β_2 are the regression coefficient; cb ($\mathrm{Tmean}_{t,l}$) denotes the cross-basis matrix of daily average temperature, l is the number of lag days; ns (.) signifies a natural cubic spline function. We use 7 df per year for the time variable to adjust for the long-term trend and seasonality and 3 df to adjust for confounders (relative humidity, $PM_{2.5}$, SO_2, NO_2 and CO) in line with previous research (Guo et al., 2017; Royé et al., 2019). Both $\mathrm{Dow_t}$ and $\mathrm{Holiday_t}$ are categorical variables to control for weekdays and public holidays, respectively (Sun et al., 2021).

2.3.2. Second-stage analysis

We conducted a multivariate random-effect meta-analysis to obtain pooled estimates and derive the best linear unbiased prediction (BLUP) of the county-specific cumulative exposure-response associations at the regional and provincial levels (Gasparrini et al., 2012). The BLUP represents a trade-off between the city-specific association and second-stage pooled estimations; it can thus provide more accurate estimates, especially in cities with low numbers of deaths (Gasparrini et al., 2015). In accordance with a previous study (Sera et al., 2019), we first defined the minimum mortality temperature (MMT) as the reference temperature; and if that could not be identified, we used the median temperature as the temperature threshold instead. We further calculated the RRs of stroke mortality under extreme cold (1st percentile of temperature), moderate cold (10th percentile), moderate heat (90th percentile) and extreme heat (99th percentile) (Ban et al., 2017). Finally, we applied the Cochran *Q*-test and I^2 statistics to test residual heterogeneity.

Then, we used the cumulative BLUP estimates corresponding to each day's temperature in each county to calculate the mortality fractions of stroke-specific (i.e., overall, ischemic, and hemorrhagic stroke) caused by non-optimal temperatures using a previously introduced method (Gasparrini and Leone, 2014). The total attributable number of stroke-specific deaths due to non-optimum temperature was given by summing the contributions from all the days of the study period; the total AF was obtained by the ratio of attributable deaths and the total mortality of corresponding cause. We further calculated the AFs of stroke mortality caused by cold and heat by summing the subsets corresponding to the days with temperatures lower or higher MMT, respectively. We calculated the empirical CIs (eCIs) through Monte Carlo simulations, assuming a multivariate normal distribution of the BLUP estimates of the reduced coefficients. The algebraic equations we applied and other details were reported elsewhere (Gasparrini and Leone, 2014; Greenland, 2004).

2.3.3. Assessment of greenness effects

Using greenness indicators (NDVI, SAVI, and EVI) and county-specific characteristics as meta-predictors, we developed a multivariate meta-regression model to examine the associations between greenness and BLUP RRs of stroke mortality from cold and heat. Considering the different levels of vegetation in different seasons, we applied the cumulative averages of NDVI, SAVI, and EVI during summer to examine the associations between greenness and the BLUP relative risks from moderate and extreme heat; the cumulative averages of NDVI, SAVI, and EVI during winter to assess the relationship between greenness and BLUP estimates from moderate and extreme cold.

2.3.4. Sensitivity analysis

To check the robustness of the results, we performed sensitivity analyses for the main model by changing the df for the lag variable (4–6), time-long trends(8–10 per year), humidity and air pollution(4–6), and changing the maximum lag days (14, 21 and 28 days). In particular, we controlled the model residual autocorrelation at lag 1 day to observe the stability of the estimates(Bhaskaran et al., 2013).

All statistical analysis depended on R software (version 4.0.4), with the "dlnm" and "mvmeta" packages. Two-sided P values <0.05 were considered as statistically significant.

3. Results

Table 1 describes the summary statistics for stroke deaths, meteorological characteristics, air pollution and greenness coverages for 19 counties from 2013 to 2019. A total of 138,749 stroke deaths were recorded, with 86,873 (62.6 %) from ischemic stroke and 51,876 (37.4 %) from hemorrhagic stroke. The daily average temperature (range) and relative humidity were 14.28 °C (−14.44 to 33.45 °C) and 64.12 % (13.00–100 %), respectively. There was regional variation during the study period, where the lowest values of $PM_{2.5}$, O_3 and other air pollutants were evident in the Shandong Peninsula region (Fig. S1). The average NDVI, SAVI, and EVI, respectively, were as follows: 0.46 (0.34–0.60), 0.32 (0.22–0.43) and 0.54 (0.38–0.74) during summer; 0.20 (0.12–0.30), 0.13 (0.07–0.15) and 0.37 (0.13–0.37) during winter; the highest values mainly in the southwest region and the lowest values in the central region (Fig. S1). Further details about average temperature, relative humidity, $PM_{2.5}$, and greenness variation in 19 counties are shown in Tables S2–S3.

Fig. 2 presents the county-specific RRs associated with extreme temperatures at different lag periods, and the RRs for moderate temperatures are supplemented in Fig. S2. Generally, compared with temperature thresholds (i.e., minimum mortality temperature or median temperature), the RRs of overall ($I^2 = 32.9.\%, p < 0.01$), ischemic ($I^2 = 26.8\,\%, p < 0.05$) and hemorrhagic stroke mortality ($I^2 = 24.2\,\%, p < 0.05$) were observed to vary significantly among the counties over lag 0–14 days. The effects of extreme temperatures were higher than those of moderate temperatures; significant RRs associated with extreme heat were evident in some counties for overall and ischemic stroke deaths and also in a few counties for hemorrhagic stroke death. The county-specific and BLUP RRs for different temperature cut-offs and different lag periods are shown in Tables S4–S9. Moreover, the associations between ambient temperature and overall, ischemic or hemorrhagic stroke mortality varied across regions (Figs. S4–S6). Specifically, for overall and ischemic strokes mortality, the central was more susceptible to non-optimum temperatures–especially heat, it was followed by the northwest; for hemorrhagic stroke mortality, the southwest seemed to be more susceptible to cold than the other three regions.

Fig. 3 demonstrates the pooled cumulative temperature-stroke mortality associations with the approximately W-shaped curves on the relationships between temperature and mortality risk of overall, ischemic and hemorrhagic stroke. The pooled RRs of stroke mortality at moderate and extreme temperature levels with different lag periods are reported in Table 2. Specifically, the effects of heat on stroke mortality were the strongest at cumulative lag 0–7 days and attenuated along the lag period, while effects of cold persisted over lag 0–14 days (Fig. S3). The cumulative RRs of overall stroke mortality from extreme cold at lag 0–14 days and extreme heat at lag 0–7 days relative to MMT were 1.49 (95 % CI, 1.24–1.78) and 1.48 (95 % CI, 1.28–1.72), respectively. The RRs of ischemic stroke mortality were corresponding 1.56 (95%CI, 1.26–1.92) and 1.71 (95%CI, 1.41–2.04); and the mortality RRs of hemorrhagic stroke were 1.37 (95% CI, 1.03–1.81) and 1.18 (95%CI, 1.02–1.37), respectively. Moreover, the cumulative effects of extreme temperatures(1st and 99th percentiles) were higher than of moderate temperatures(10th and 90th percentiles); the RRs of ischemic stroke mortality associated with moderate and extreme temperatures were stronger than of hemorrhagic stroke mortality at lag 0–14 days.

Table 3 presents the AFs for stroke mortality associated with non-optimum temperatures at the pooled level. The total AF for the effect of the non-optimum temperature on overall stroke mortality was 17.16 % (95 % eCI, 13.38 %–19.75 %) at lag 0–14 days. However, the total AF of ischemic stroke mortality caused by non-optimum temperature was higher than that of hemorrhagic stroke mortality, with the value of 20.05 % (95 % eCI, 16.46 %–22.70 %) and 12.55 % (95 % eCI, 6.59 %–16.24 %), respectively. In addition, cold was responsible for the most of the AF compared with heat, with 14.94 % (95 % eCI, 11.57 %–17.34 %) and 2.22 % (95 % eCI, 1.54–2.72 %) of overall stroke mortality caused by cold and heat, respectively; the AFs of ischemic stroke mortality caused by cold and heat was 17.09 % (95 % eCI, 13.47 %–19.45 %) and 2.96 % (95 % eCI, 2.07 %–3.64 %), respectively; 11.21 % (95 % eCI, 5.57–14.56 %) and 1.34 % (95 % eCI, −1.35 % to 2.98 %) of hemorrhagic stroke mortality AFs, respectively, was due to cold and heat. The stroke mortality burdens attributable to heat were the highest in a week, while that due to cold lasted over lag 0–14 days. Moreover, the AFs for overall and ischemic stroke attributable to heat were higher in the central and northwest regions, whereas a higher mortality fraction for hemorrhagic stroke due to cold was evident in the southwest (Fig. S7). The numerical values for county-specific mortality fraction attributable to non-optimum temperatures over different lag days are supplemented in Tables S10–S12.

Fig. 4 shows the associations between greenness and BLUP RRs for overall and ischemic stroke mortality from extreme heat before and after adjusting for potential confounders at lag 0–14 days. The non-significant negative associations between greenness and RRs of overall and ischemic stroke mortality from cold are supplemented in Table S13. The results are expressed as changes in RR for each 0.1–unit increase in NDVI, SAVI, and EVI. Generally, NDVI, SAVI, and EVI were significantly and negatively associated with RRs for overall and ischemic stroke mortality from heat; an exception was hemorrhagic stroke mortality (Table S14); the modifying effects of NDVI, SAVI, and EVI on extreme-heat-related risks were stronger than on moderate-heat-related risks (Fig. S8). In particular, for each 0.1–unit increase in NDVI, the RRs for overall and ischemic stroke mortality from extreme heat decreased by 0.162 [−0.162 (95 % CI, −0.312 to −0.013)] and 0.239 [−0.239 (95 % CI, −0.428 to −0.049)], respectively; for each 0.1–unit increase in SAVI, the RRs associated with extreme heat decreased by 0.194 [−0.194 (95 % CI, −0.384 to −0.004)] and 0.296 [−0.296 (95%CI, −0.535 to −0.058)]; and for each 0.1–unit increase in EVI, the RRs from heat reduced by 0.107 [−0.107 (95 % CI, −0.233 to 0.019)] and 0.168 [−0.168 (95 % CI, −0.325 to −0.011)], respectively. More significant associations between greenness and stroke mortality were evident after adjusting for average temperature and $PM_{2.5}$.

The effect estimates of temperature on stroke mortality were relatively robust in the main model. There, the curves for the temperature-stroke

Table 1
Descriptive statistics of stroke death counts and environmental variables during 2013–2019 in Shandong, China.

Variables		Min	P25	P50	P75	Max	Mean	SD
Death counts								
Stroke		0	1	2	4	33	2.86	2.35
IS		0	1	1	3	16	1.79	1.69
HS		0	0	1	2	24	1.07	1.24
Ambient environment								
Average temperature (°C)		−14.44	4.76	15.58	23.53	33.45	14.28	10.35
Relative humidity (%)		13.00	52.00	65.08	77.00	100.00	64.12	16.40
$PM_{2.5}$ (μg/m^3)		3.31	39.87	59.33	87.31	508.38	70.31	45.14
NO_2 (μg/m^3)		5.92	26.85	36.39	49.20	271.25	39.48	17.11
SO_2 (μg/m^3)		1.81	16.05	24.77	46.91	600.86	36.34	29.93
CO (mg/m^3)		0.15	0.82	1.11	1.45	47.00	1.23	0.62
O_3 (μg/m^3)		5.45	65.14	100.66	138.75	323.56	104.98	48.02
greenness								
Summer	NDVI	0.34	0.42	0.45	0.50	0.60	0.46	0.07
	SAVI	0.22	0.28	0.31	0.36	0.43	0.32	0.06
	EVI	0.38	0.48	0.53	0.60	0.74	0.54	0.09
Winter	NDVI	0.12	0.16	0.21	0.23	0.30	0.20	0.05
	SAVI	0.07	0.10	0.12	0.15	0.20	0.13	0.03
	EVI	0.13	0.16	0.21	0.25	0.37	0.22	0.07

Notes: IS and HS refer Ischemic stroke and Hemorrhagic stroke, respectively; Min and Max are minimum and maximum value, respectively; P_{25}, P_{50}, P_{75} define 25th, 50th, and 75th percentiles, respectively; SD is standard deviation.

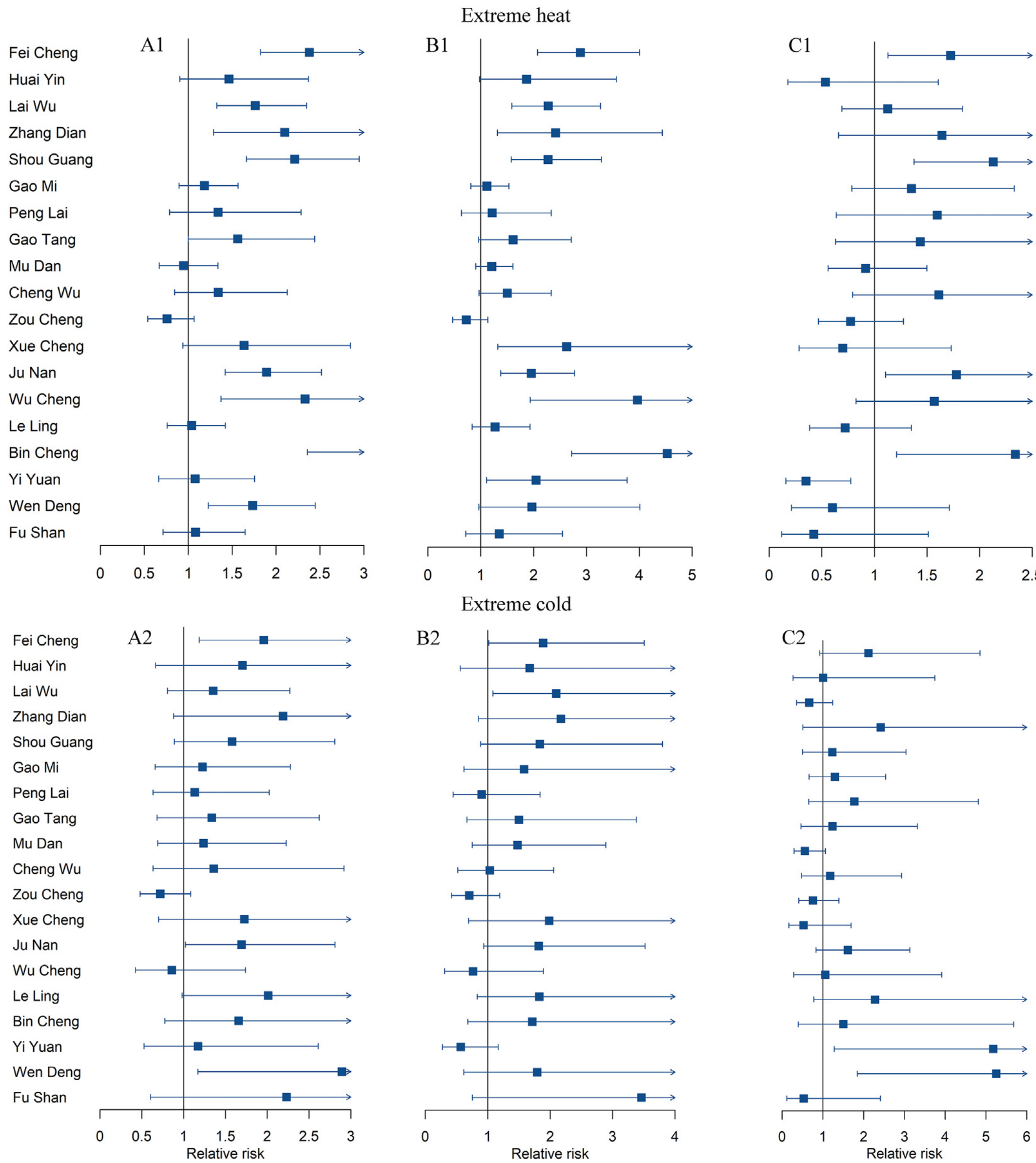


Fig. 2. County-specific RRs of stroke mortality for extreme heat over lag of 0–7 days and for extreme cold over lag of 0–14 days. A1, B1, and C1 represent overall, ischemic and hemorrhagic stroke mortality associated with extreme heat; A2, B2, and C2 represent overall, ischemic and hemorrhagic mortality associated with extreme cold; The rectangles are the effect estimates and the horizontal lines represent the 95 % confidence intervals. Extreme cold is defined as the 1st percentiles of temperature and extreme heat as the 99th percentiles, both compared with the temperature thresholds (minimum-mortality temperatures or median temperatures).

mortality relationships were similar after changing df of the natural cubic spline for time trend, confounders and lag variable, extending maximum lag period and controlling for autocorrelation (Figs. S9–S13).

4. Discussion

Using multiple centers data, we found that exposure both moderate and extreme temperatures were significantly associated with increased mortality risks of stroke, including RRs and AFs; there were greater effects with extreme temperatures. The effects of cold and heat varied across the counties and regions, with the central and northwest regions bearing higher heat burden for overall and ischemic stroke; the southwest region having a higher cold burden for hemorrhagic stroke. Furthermore, we determined that higher levels of greenness (NDVI, SAVI, and EVI) were all significantly associated with decreased impact of heat-related on overall and ischemic stroke mortality; thus, there could have been be lower related–heat risks through stroke mortality in counties with higher levels of vegetation density, especially after adjusting average temperature and $PM_{2.5}$.

Consistent with previous epidemiological studies, our results suggested that moderate and extreme temperatures exposures strongly increased the risk of overall stroke mortality, and that extreme temperatures effects were higher than those for moderate temperatures (Bunker et al., 2016; Lv et al., 2020; Rodrigues et al., 2019). We found that 17.16 % of overall stroke mortality burden was attributable to non-optimum temperature and identified a significant difference in the relative importance of heat and cold effects. Specifically, in line with previous findings (Yang et al., 2015; Yang et al., 2016), our analysis revealed that almost 90 % of overall stroke mortality burden was attributable to cold, which may be explained by the presence of a right-shifting trend in the MMT selection and a more pronounced delayed effect of cold than heat (Gasparrini et al., 2015; Ingole et al., 2022). We also observed that cold and heat were significantly, positively associated with both ischemic and hemorrhagic stroke mortality burdens; that the burden attributable to non-optimum temperatures was higher with the former than the latter. Our findings on ischemic stroke mortality concur with those of studies from multiple-cities in China (Hu et al., 2021) and Brazil (Ikefuti et al., 2018); however, they differed from a

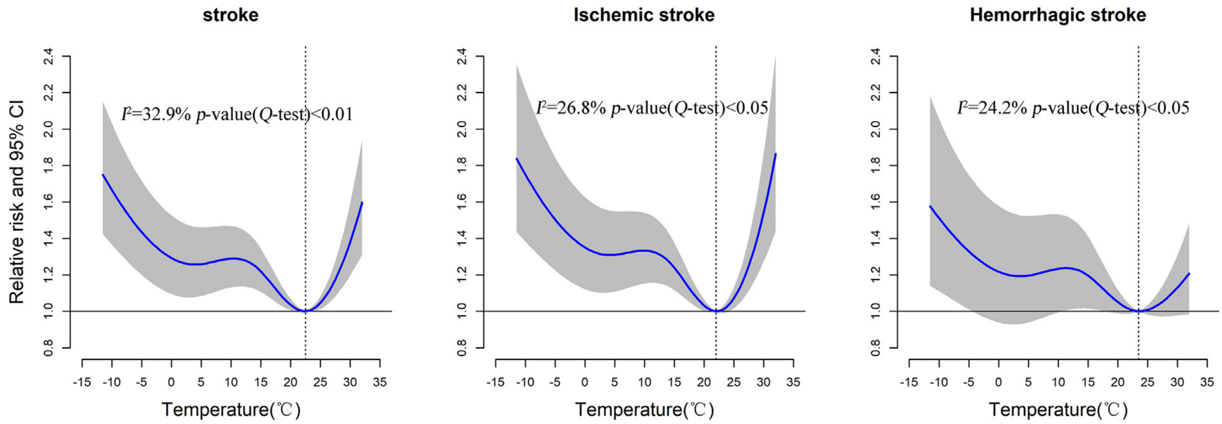


Fig. 3. The pooled cumulative temperature-stroke mortality response curves based on 19 counties in Shandong province over lag 0–14 days. The blue lines are the maximum likelihood estimate of RRs and the gray regions are pointwise 95 % confidence intervals; The vertical dotted lines indicate minimum mortality temperatures (MMT) (22.3 °C for overall stroke mortality, 22.1 °C for ischemic mortality, and 23.2 °C for hemorrhagic mortality). I^2 and *p*-value (*Q*-test) indicate the residual heterogeneity across counties.

Table 2
The pooled cumulative RRs (95 % CI) of different temperature levels effect on stroke mortality over different lag days.

Temperature percentiles (°C)	Lag 0–3 days	Lag0–7 days	Lag0–14 days
Stroke			
Extreme cold (−6.25)	1.07 (0.98, 1.17)	1.25 (1.11, 1.41)	1.49 (1.24, 1.78)
Moderate cold (−1.00)	1.02 (0.94, 1.10)	1.14 (1.02, 1.27)	1.31 (1.11, 1.55)
Moderate heat (25.90)	1.15 (1.08, 1.22)	1.14 (1.07, 1.21)	1.08 (1.03, 1.14)
Extreme heat (29.85)	1.45 (1.28, 1.65)	1.48 (1.28, 1.72)	1.36 (1.19, 1.57)
IS			
Extreme cold (−6.25)	1.00 (0.91, 1.09)	1.21 (1.05, 1.38)	1.56 (1.26, 1.92)
Moderate cold (−1.00)	0.96 (0.89, 1.03)	1.11 (0.98, 1.25)	1.37 (1.14, 1.66)
Moderate heat (25.90)	1.19 (1.06, 1.33)	1.20 (1.11, 1.31)	1.12 (1.04, 1.21)
Extreme heat (29.85)	1.60 (1.33, 1.94)	1.71 (1.41, 2.04)	1.52 (1.26, 1.83)
HS			
Extreme cold (−6.25)	1.16 (0.96, 1.41)	1.32 (1.05, 1.65)	1.37 (1.03, 1.81)
Moderate cold (−1.00)	1.09 (0.94, 1.26)	1.19 (0.98, 1.44)	1.23 (0.95, 1.60)
Moderate heat (25.90)	1.04 (1.00, 1.08)	1.04 (0.99, 1.10)	1.02 (0.98, 1.07)
Extreme heat (29.85)	1.16 (1.03, 1.30)	1.18 (1.02, 1.37)	1.12 (0.98, 1.29)

Notes: Extreme cold, Moderate cold, Moderate heat, and Extreme heat refer the 1st, 10th, 90th, and 99th percentile of daily temperature distribution, respectively, compared with minimum mortality temperature.

hospital admission study in Jinan, China (Wang et al., 2013); accordingly, heat could be a protective factor for ischemic stroke occurrence. Further, zero associations between ischemic stroke mortality and temperature change were reported in the United States (Cowperthwaite and Burnett, 2011). One study in China observed that heat increased risk of hemorrhagic stroke mortality (Zhou et al., 2017), which was similar to the present study. No association was found between high temperature and hemorrhagic stroke (Lavados et al., 2018); whereas one study did observe a beneficial effect of heat on death from hemorrhagic in South Korea (Lim et al., 2013). Moreover, one report revealed that hemorrhagic stroke mortality was more affected by cold and less affected by heat than ischemic stroke mortality; that was at odds with our results (Chen et al., 2018).

These different findings are difficult to explain. However, in addition to varying characteristics in the study cities, such as climate adaptation, use of air conditioning, housing types, socioeconomic status, and population vulnerability (Cho et al., 2018; Ma et al., 2014; Medina-Ramón et al., 2006; Shen and Lung, 2020; Urban et al., 2014), they could be due to different study designs, definitions for thresholds of temperature exposure, model choices, and health outcomes (Lian et al., 2015). For example, studies in Australia and Hong Kong applied a linear term for temperature to describe the association between temperature and ischemic or hemorrhagic stroke mortality (Goggins et al., 2012; Wang et al., 2009). By contrast, the present study employed a DLNM to clearly demonstrate non-linear associations between ambient temperature and stroke subtypes. Further, inadequate control for seasonality or other confounding factors could lead to incorrect temperature–mortality estimates. In the context of global warming and climate change, our findings provides an accurate reference for governments and sectors (such as public health) that should expand adaptation policies with a focus on both the hazards of heat and primarily preventing the adverse effects of cold.

In the present study, we also observed variations in county-specific and region-specific analyses. For the mortality burdens of overall and ischemic

Table 3
Attributable fractions of stroke mortality at different lag structures.

Lag days	Mortality	Attributable fraction (%, 95 % empirical CI)		
		Overall	Cold	Heat
Lag0–3 days				
	Stroke	6.14 (3.56, 8.01)	2.12 (0.12, 3.80)	4.02 (3.08, 4.79)
	IS	1.23 (−0.52, 2.57)	−1.78 (−2.62, −1.07)	3.01 (1.64, 4.00)
	HS	9.29 (4.45, 12.41)	5.43 (2.37, 7.72)	3.86 (0.21, 6.38)
Lag0–7 days				
	Stroke	10.44 (7.13, 12.70)	7.30 (4.60, 9.34)	3.14 (2.44, 3.71)
	IS	10.72 (8.87, 12.18)	6.48 (4.88, 9.92)	4.25 (3.29, 5.02)
	HS	12.23 (7.53, 15.40)	9.06 (5.41, 11.81)	3.17 (0.28, 4.96)
Lag0–14 days				
	Stroke	17.16 (13.38, 19.75)	14.94 (11.57, 17.34)	2.22 (1.54, 2.72)
	IS	20.05 (16.46, 22.70)	17.09 (13.47, 19.45)	2.96 (2.07, 3.64)
	HS	12.55 (6.59, 16.24)	11.21 (5.57, 14.56)	1.34 (−1.35, 2.98)

Notes: Overall indicates stroke mortality fractions attributable to non-optimum temperature (both cold heat effect combining), cold and heat represent stroke mortality fractions caused by low temperatures (blow MMT) and high temperatures (above MMT), respectively.

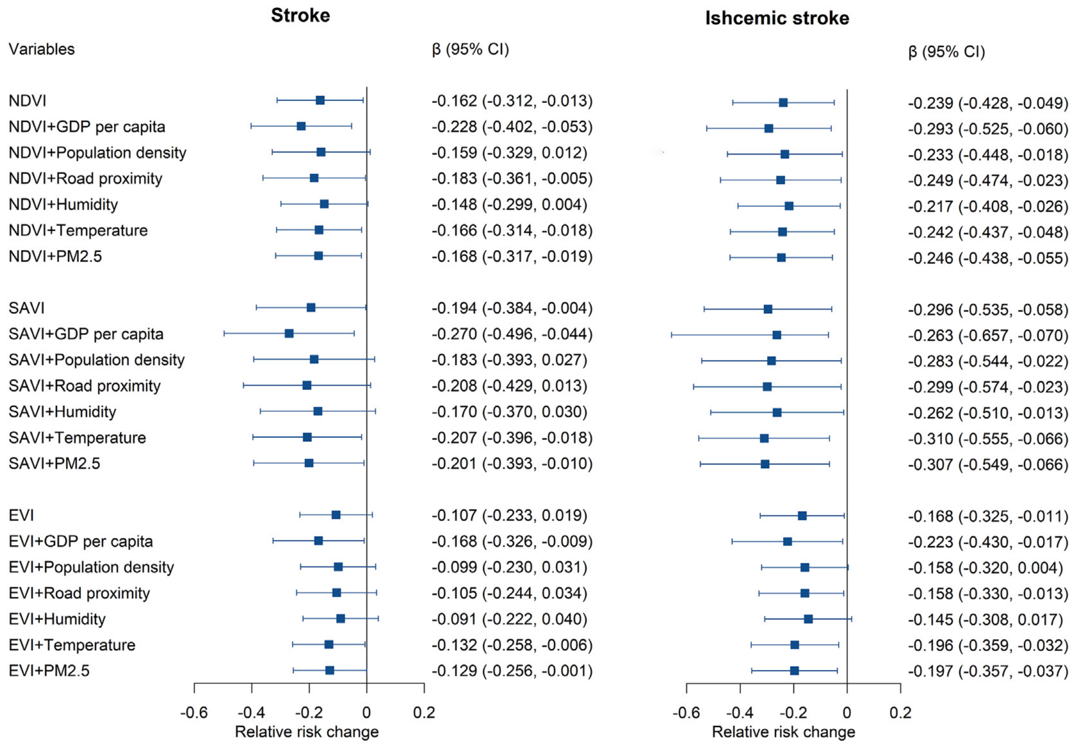


Fig. 4. Estimated relationships between greenness and effects of extreme heat on overall and ischemic stroke mortality, before and after the adjustment of confounders. The numeric results indicate with changes in RR associated with each 0.1-unit increase in NDVI, SAVI and EVI value.

stroke, the central and northwest regions were more vulnerable to moderate and extreme heat than other regions. That could be mainly related to the urban heat island effect and temperature adaptation: the central region is characterized by accelerated urbanization, with the provincial capital (Jinan) at its core and lower greenness levels (Chen et al., 2021; Heaviside et al., 2017; Lee et al., 2021); the higher latitude in the northwest meant lower optimal temperature and a greater impact of high temperature (Kim et al., 2016; Moghadamnia et al., 2017; Wang et al., 2017). For the mortality burden of hemorrhagic stroke, we found that cold-related mortality fraction was higher in the southwest: that could be explained by the lower latitude and poorer adaptation to cold (Lee et al., 2019; Song et al., 2017); however, it could also be due to a less developed economy, inadequate allocation of medical resources, and poor heating conditions (Barnard et al., 2008; Li and Gu, 2020; Liu et al., 2020).

The potential biological mechanisms that could account for burdens of stroke mortality attributable to cold and heat are not the same. With the cold, thrombogenic factors (such as red blood cell count, platelet count, plasma cholesterol, and fibrinogen increase), and an increased inflammatory response could trigger cerebral ischemia (Cheng and Su, 2010; Gordon et al., 1988; Manfredini et al., 1997). Further, cold easily leads to vasoconstriction of peripheral blood vassals and blood transfer to other vital organs (Kawahara et al., 1989; Park et al., 2020; Yu et al., 2020), which in turn produces increased blood pressure and hypertension, which is one of the most important causes of hemorrhagic stroke (Lewington et al., 2012). To dissipate heat when exposed to high temperatures, the body may mediate the adverse effects by sweating, dilating blood vessels, and increasing the heart rate: that may lead to dehydration, increased blood viscosity, higher cholesterol levels, and further increase the likelihood of thrombosis (Keatinge et al., 1986). In hot weather, blood vessels in the skin dilate, which reduces blood flow to the brain and causes possible blood pressure fluctuations (Liu et al., 2015). Moreover, hot weather can make people more nervous and irritable, which increase their stress reactions: blood pressure suddenly rising can cause blood vessel rupture and may induce brain hemorrhage or even death (Zafeiratou et al., 2021). High temperatures have been found to be associated with endothelial dysfunction, which can contribute to the increased stroke mortality (Nawrot et al., 2005).

Identification of the different lag structures of low and high temperatures could be useful for policy makers to develop early response plans to prevent the adverse effects of climate change. Previously, most studies demonstrated cold cumulative effects lasting 2 weeks or longer, whereas heat effects generally occurred within 1 week (Breitner et al., 2014; Deng et al., 2019; Mohammadi et al., 2021); those findings are in accordance with our own. Using either a longer lag period to determine the effects of heat or a shorter one to assess the effects of cold could produce underestimation of the results. For example, we obtained the following results: the mortality burden of ischemic stroke through cold at lag 0–14 days (17.09 %; 95 % eCI, 13.47–19.45 %) was greater than at lag 0–7 days (6.48 %; 95 % eCI, 4.88–9.92 %); while that attributable to heat at lag 0–7 days (4.25 %; 95 % eCI, 3.29–5.02 %) was higher than at lag 0–14 days (2.96 %; 95 % eCI, 2.07–3.64 %). Various potential mechanisms could explain those differences. The difference in duration of some physiological stress responses at low and high temperatures may be a contributing factor (Cheshire, 2016; McArthur et al., 2010). For example, with exposure to cold, it may take days to weeks for the accumulation of causative factors for less acute stroke events, such as the formation of thrombotic factors, increased blood viscosity, elevated inflammatory response, and changes in some microorganisms, e.g., influenza (Warren-Gash et al., 2009); By contrast, heat exposure may result in a series of immediate physiological responses—particularly when the body temperature exceeds regulatory thresholds. Examples here are salt depletion, dehydration, increased body surface circulation, increased heart rate, decreased cerebral blood flow, and raised blood pressure; they may directly lead to acute stroke events and even death (Keatinge et al., 1986). Aging has also been associated with attenuated sweat gland output during heat exposure. The elderly are the most sensitive group for stroke; heat exposure may cause much greater heat production than heat dissipation, further contributing to acute stroke complications and death (Balmain et al., 2018). The choice of the optimal lag for the temperature effect is unclear: different studies made a relatively arbitrary choice based on their own model fits, which could have led to false estimates. Moreover, to date, the underlying environmental and physiological mechanisms for various lag effects of heat and cold exposure remain to be clarified (Gronlund et al., 2018). Each mortality outcome has its own induction period in response to non-optimum temperature stress; in term of environment, that phenomenon may be related to differences in geographic, climatological, socioeconomic, and demographic factors. Evidence suggests that people's adaptation to climate may be modified by socioeconomic and education levels, intensity of the heat island effect, greenness level, housing characteristics, and access to air conditioning; they could alter the lag effects of temperature on local population health (Lay et al., 2021; Sera et al., 2019; Zhao et al., 2021). In terms of physiological mechanisms, those factors may involve different thermoregulation and physiological feedback at low and high temperatures. As noted above regarding the mechanism of temperature-stroke mortality associations, cold is associated with cardiovascular stress(Fares, 2013). Similarly, cold can induce some immunological and inflammatory reactions and increase the risk of infection; those physiological changes persist (Woodhouse et al., 1994); By contrast, heat can cause sudden physiological reactions that result in a loss of control of the core body temperature, producing a significant increase in body temperature within a short period; that may lead to organ dysfunction and structural damage and eventually cause failure or even death (Kenny and Jay, 2013). Studies have revealed that extra heat load may have fatal consequences for patients with cardiovascular disease (Rowell, 1983). In short, future studies should develop a criterion for the optimal lag time and investigate potential mechanisms to further explain the different lag effects.

Although some studies have explored factors that may contribute to the heterogeneity of cold or heat effects across countries or regions: they include geographic indicators (longitude and latitude), demographic and socioeconomic indicators (population density and GDP); however, the results have been inconsistent (Gasparrini et al., 2012; Rodrigues et al., 2019). To date, few studies have reported that greenness may ameliorate the adverse health effects of non-optimum temperatures (moderate and extreme), particularly the cooling effect of high temperatures (Bao et al., 2021; Burkart et al., 2016; Qiu et al., 2021). Greenness may modify local micro- and meso-climate through various mechanisms: shading, evapotranspiration and albedo. On the one hand, vegetation plays a vital role in inducing cooling effects in the warm seasons: it does so through biophysical effects, which emphasize interactions between leaves and the atmosphere; it also does so through biochemical effects, which depend mostly on changes in vegetation biomass (Lian et al., 2022). Regarding biophysical effects, trees allow evapotranspiration to absorb long-wave radiation, thereby converting liquid water to water vapor and replacing sensible heat with latent heat; Canopy provides shade to intercept incoming short-wave radiation, which traps heat fluxes and reduces the ground and wall surface temperatures; greenery enhances the surface albedo of urban environments, which increases the proportion of reflected incident radiation, decreases the absorbed fraction, and further reduces surrounding temperature (Wong et al., 2021). Regarding biochemical effects, vegetation performs photosynthesis, thereby promoting carbon uptake and indirectly relieving local thermal stress (Piao et al., 2020). On the other hand, the cooling effects of greenness diminish or even turns to net warming owing to snow cover and lower vegetation density. That results in weakened evapotranspiration and enhanced albedo and water vapor feedbacks in the cold season (Alkama et al., 2022).

Consistent with previous research (Dang et al., 2018; Denpetkul and Phosri, 2021), the present study primarily found negative associations between greenness and risks of overall and ischemic stroke mortality from moderate or extreme temperatures; this result implied that increasing greenness levels can mitigates stroke mortality from non-optimum temperatures, especially heat. However, the role of greenness in modifying the vulnerability of stroke patients to unsuitable temperatures remains unclear. In addition to the natural cooling effects of greenness described above, exposure to greenness may alter indoor and outdoor activity patterns, thereby influencing exposure at a given temperature (Markevych et al., 2017; Nieuwenhuijsen, 2021). For example, as we explained in the introduction, living in greener areas could relieve stress, increase opportunities for physical activity and social interaction, enhance well-being and diminish air pollution hazards, which may relieve non-optimal temperature—especially heat stress, and ultimately may also alleviate the burdens of temperature-related cardiovascular and cerebrovascular disease in various populations (Crouse et al., 2021; Gianfredi et al., 2021; Liu et al., 2022). Moreover, increasing greenness could decrease a number of physiological stress response, such as reducing sweating frequency, maintaining a steady heart rate, and preventing dehydration, thereby keeping blood and cholesterol at normal levels (Orioli et al., 2019). Greenery can also moderate vascular aging and reduce aortic extension and sclerosis, which helps mitigate the risk of hypertension, a major cause of stroke (Dzhambov and Dimitrova, 2018).

We observed slight differences in the results of the association between the three vegetation indices and the heat-related RR for overall stroke mortality; however, the differences were not statistically significant. We believe this variation is due to differences in the inherent characteristics of the indexes. For example, NDVI is calculated based on the reflectance of the infrared and near-infrared light bands; it has “ratio” properties, which allows it to eliminate some of the effects of solar radiation, such as topography and clouds (Huete and Justice, 1999). SAVI has a correction factor (L), which reduces the effect of soil brightness (Huete, 1988). EVI includes a blue light band, mainly for atmospheric correction (Huete et al., 2002). The sensitivity of the three indexes to vegetation varies precisely because of their particularly properties. NDVI is commonly used to monitor the growth state of healthy vegetation owing to its insensitivity to densely vegetated areas and its oversensitivity to soil background; SAVI is suitable for assessing areas with low vegetation cover; while EVI is often used in densely vegetated areas, such as tropical forests, because its saturation point is above NDVI (Jiang et al., 2006; Zeng et al., 2022). Nevertheless, all three indicators were essentially designed to assess quantitatively the level of greenness exposure.

We also found that the modifying effects of greenness differed between summer and winter at extreme and moderate temperatures. In summer, high levels of greenness significantly alleviate the adverse effects of heat, especially extreme heat, highlighting that greenness may be more sensitive to extreme heat and bridging this knowledge gap has important implications for development public health programs to prevent the burden of stroke (Dang et al., 2018; Xu et al., 2022). However, in winter, we found that low levels of greenness do not appear to have a significant protective effect against cold or extreme cold. That result is perhaps related to the fact that the insulating effect of vegetation is offset by the heat-absorbing nature of snowmelt. Thus, to reduce cold hazards, public health and other relevant authorities should consider anthropogenic mitigation as the primary means and natural mitigation as a supplementary measure (Leng et al., 2020). Generally, authorities should consider increasing green vegetation cover to mitigate the adverse effects of non-optimum temperatures a good strategy to promote health–especially with stroke prevention.

Our study has several advantages. First, previous studies focused on the relative contributions (e.g., RR and OR) of extreme temperatures; however, we expanded the research basis and found that moderate and extreme temperatures increased mortality risks for stroke subtypes based on multicenter; we observed that cold accounted for greater stroke mortality burden (AFs) than heat. Second, we identified a spatial distribution variability in the temperature-stroke mortality associations; that could help policy makers recognize high-risk areas. Third, our relatively comprehensive control for potential confounders (which included other air pollutants in models in addition to adjusting for PM2.5) enhanced the interpretability of our results. Finally, to the best of our knowledge, this study is the first to use multiple indicators (i.e., NDVI, SAVI and EVI) as greenness exposure; it is the first to examine comprehensively the effects of greenness modifications on temperature-stroke mortality associations, which have important implications for public health interventions.

Several limitations ought to be acknowledged. First, this research was biased toward ecological study: we may not have completely ruled out potential confounding at the individual level. Second, exposure measurement errors were inevitable in accordance with the monitoring site data; the lack of indoor temperature data could have underestimated the true effect of temperature on mortality. Third, owing to data availability, we did not conduct subgroup analyses by sex, age, education, and other factors. We also failed to fully examine other potential sources of estimated heterogeneity among the counties: they should be addressed in future studies. Fourth, owing to regional limits, our findings may not directly apply to different climatic zones or socioeconomic environments.

5. Conclusions

This study provides strong evidence that ambient temperature is associated with increased mortality risks for overall, ischemic, and hemorrhagic stroke. Combining data from multiple centers we found that unlike with hemorrhagic stroke, ischemic stroke mortality burden was more attributable to non-optimum temperatures and was mostly caused by cold temperature. Cold and heat effects on stroke mortality varied spatially across the investigated regions: the central and northwest regions were more sensitive to heat for overall and ischemic stroke; the southwest was more vulnerable to cold for hemorrhagic stroke. A higher greenness level could significantly alleviate the effects of heat on overall and ischemic stroke mortality. Our findings can provide important assistance when developing and implementing targeted, adaptive strategies to address climate change. However, more studies involving different urban characteristics and climate zones are needed to yield more comprehensive information.

CRediT authorship contribution statement

Fenfen He: Formal analysis, Data Curation, Writing-Original draft, Visualization.
Jing Wei: Methodology, Resources, Software, Validation.
Yilin Dong: Investigation, Resources.
Chao Liu: Investigation, Resources.
Ke Zhao: Investigation, Resources.
Wenjia Peng: Methodology, Writing-Review and Editing.
Zilong Lu: Resources, Supervision.
Bingyin Zhang: Investigation, Supervision.
Fuzhong Xue: Supervision, Project administration, Writing-Review & Editing.
Xiaolei Guo: Resources, Supervision.
Xianjie Jia: Conceptualization, Writing-Review & Editing, Supervision, Funding acquisition.

Funding

The work was supported by the National Key Research and Development Program of China [No. 2020YFC2003500] and the 512 Talent Cultivation Plan of Bengbu Medical College [by51201202], China.

Data availability

The authors do not have permission to share data.

Declaration of competing interest

We declare that all authors have no competing interests.

Acknowledgements

We would like to thank the Shandong Centers for Disease Control and Prevention (CDC), the Dr. Jing Wei's team, the China Meteorological Data Sharing Service System, and the U.S. Geological, providing mortality, air pollutants, meteorological and greenness data, respectively, for all analyses in present study. We also thank Liwen Bianji (Edanz) (www.liwenbianji.cn/), for editing the English text of a draft of this manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2022.158046.

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