Associations between non-optimum temperatures and cardiovascular hospital admissions and effect modification by ambient particulate air pollution: a two-stage time-series study in China

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Summary

Background It remains unclear whether non-optimum temperatures are associated with hospital admissions for subtypes of cardiovascular events, and how $PM_{2.5}$ and black carbon (BC) modify these associations.

Methods Hospital admission data of major cardiovascular events were obtained from two major national health insurance systems across 270 cities of prefecture-level or above in China during 2013–2017. A two-stage time-series study was conducted using a generalized additive model with a quasi-Poisson family, combined with a distributed lag nonlinear regression model, to explore the exposure-response associations of non-optimum temperatures with hospital admissions. Effect modification was investigated by stratifying ambient particulate air pollution levels into quartile groups.

Findings In a total of 24,564,921 hospital admission records for major cardiovascular events, compared with the minimum morbidity temperature (18.3 °C), the relative risks (RRs) of hospital admissions for total major cardiovascular events associated with extreme cold temperature (−3.1 °C, 2.5th percentile) and extreme hot temperature (27.9 °C, 97.5th percentile) were 1.69 [95% confidence interval (CI): 1.46–1.96] and 1.27 (95% CI: 1.15–1.41), respectively. Such temperature-hospital admission associations were amplified at high BC levels, especially under extreme hot temperature, with RR increased from 1.14 (95% CI: 1.02–1.28) in the first quartile to 1.53 (95% CI: 1.31–1.78) in the fourth quartile group of BC levels.

Interpretation Our study suggests that both extreme cold and hot temperatures contribute to elevated hospital admission risks for major cardiovascular events, with high BC levels further exacerbating the risks associated with extreme hot temperature.

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Research in context

Evidence before this study

Extensive epidemiological evidence has consistently demonstrated significant associations between non-optimum temperatures and increased risks of cardiovascular morbidity, as well as fine particulate matter ($PM_{2.5}$) pollution and cardiovascular outcomes. However, current evidence presents inconsistent findings regarding the specific relationships between non-optimum temperatures and a wide range of cardiovascular disease (CVD) subtypes. Notably, there remains a critical gap in examining potential effect modifications by $PM_{2.5}$ and its major constituents, particularly black carbon (BC). We searched PubMed, Web of Science, and Google Scholar without language restrictions, using the term ("non-optimum temperatures" OR "non-optimal temperatures) AND ("hospital admission" OR "hospitalization") AND ("cardiovascular disease" OR "CVD") AND ("modification" OR "modify") AND ("black carbon" OR "BC"). No study has explored the effect modification by BC on the associations between non-optimum temperatures and hospital admissions for extensive CVD subtypes in a general population.

Added value of this study

Utilizing data from two major medical insurance systems in China, covering 270 Chinese cities of prefecture-level or above and comprising 24,564,921 hospital admission records for major cardiovascular events, we evaluated temperature-related hospital admission associations, as well as effect modifications by $PM_{2.5}$ and BC. Our findings demonstrate statistically significant increased risks of hospital admissions for major cardiovascular events under both extreme cold and extreme hot conditions. Notably, the extreme hot temperature-related admission risks were particularly pronounced under high BC exposure scenarios.

Implications of all the available evidence

These findings provide critical evidence for the development of targeted public health interventions that address temperature-related cardiovascular risks in the context of concurrent exposure to ambient particulate air pollution. Our results underscore the necessity for integrating mitigation strategies that simultaneously address both extreme hot temperature and ambient particulate air pollution. Additionally, it highlights the importance of incorporating BC monitoring into existing air quality frameworks. These insights are particularly relevant for policymakers developing climate adaptation strategies in rapidly urbanizing regions with both rising temperatures and complex ambient particulate air pollution profiles.

Introduction

Cardiovascular diseases (CVDs) remain the leading cause of mortality and morbidity, accounting for 32% of deaths in 2019 and 24% of hospital admissions globally.[1] Although CVD mortality declined between 1990 and 2019 due to advances in prevention and treatment,[2] non-optimum temperatures, one of the significant risk factors for CVDs,[3] may undermine this progress in the context of global warming.[4] Growing epidemiological evidence highlights a rising climate-attributable CVD burden from extreme temperatures.[4,5] In China, the population attributable fractions for cold and hot reached 4.3% and 0.4%, respectively, during 1990–2019, which were most pronounced compared with other countries globally.[4] Previous temperature-mortality studies have focused on absolute temperatures or defined extreme events (e.g., cold spells/heat waves) and have consistently reported associations with elevated CVD mortality risks.[6,7] Whereas, studies on CVD morbidity have generally been focused on CVD as a whole in specific regions of China,[8] or targeted particular subpopulations, such as the elderly.[9] Critical gaps persist in understanding the associations between non-optimum temperatures and hospital admissions, a more sensitive indicator capturing the temporal sequence of environmental factors and clinical presentation of diseases, across diverse CVD subtypes in the general population.[10]

Ambient fine particulate matter ($PM_{2.5}$), a well-established risk factor for CVD, has been extensively studied and is consistently associated with increased risks of CVD mortality and morbidity.[10,11] Previous findings have shown that both ambient particulate air pollution and extreme temperature events can synergistically increase the risk of cardiovascular mortality.[6,12] However, emerging evidence regarding the effect modification by $PM_{2.5}$ on the associations between ambient temperature and CVD morbidity remains limited and inconclusive, especially under hot temperature condition.[13] As a complex mixture, $PM_{2.5}$ contains various hazardous constituents, among which black carbon (BC) has been identified as one of the key contributors to adverse cardiovascular effects.[14] As a potent global warming agent, BC absorbs sunlight, heats the air, and prolongs extreme hot temperature.[15] These toxicological and climatic properties of BC suggest a plausible mechanism by which BC may amplify the adverse cardiovascular effects associated with extreme hot temperature.

Therefore, we conducted a large-scale time-series study using nationwide hospital admission data from two major medical insurance systems across 270 Chinese cities of prefecture-level or above during 2013–2017. The study aimed to comprehensively quantify the hospital admission risks for major cardiovascular events associated with non-optimum temperatures and to explore whether $PM_{2.5}$ and BC modify these associations.

Methods

Data collection

Hospital admission data for major cardiovascular events were collected from two major national health insurance systems in China, the urban employee-based basic medical insurance scheme (UEBMI) and the urban resident-based basic medical insurance scheme (URBMI), during 2013–2017.[16] Briefly, the UEBMI covers urban employees and retirees, funded primarily through payroll taxes. The URBMI covers urban residents, including children, students, elderly individuals without prior employment, and the unemployed, with government subsidies as the primary funding source. The urban basic medical insurance schemes in China target the entire urban population for fundamental health benefits and do not serve any specific subpopulations (details are presented in Supplementary eMethods). The number of daily hospital admissions for major cardiovascular events was extracted from the centralized health insurance system and aggregated by age, sex, and insurance type in each city. In accordance with personal privacy protection policies, individual identifying information, such as name and national ID number, was omitted during data collection.

A total of 293 Chinese cities of prefecture-level or above (including prefecture-level cities, regions, autonomous prefectures, leagues, and municipalities directly under the central government) from the UEBMI and URBMI are available of daily hospital admission data for major cardiovascular events during 2013–2017 (out of 338 such cities in China by the end of 2017). To ensure a reliable analysis, 23 cities were excluded due to the average daily admissions were fewer than three. The final dataset included 270 cities, covered 668 million urban residents (accounting for 82.12% of the total urban population in China) at the end of 2017. A flowchart of the city selection process is shown in Supplementary Figure S1. To explore heterogeneity in different climatic zones, the included cities were categorized into five climatic zones according to previous literature.[7]

Exposure assessment

To ensure spatial consistency with the hospital admission data, temperature and air pollution exposures were also matched at the city level. Daily mean temperature data were obtained from the China Meteorological Data Sharing Service System. For cities with more than one monitoring station, daily mean temperature was averaged across all stations within the city. Daily maximum and minimum temperatures were also obtained. Missing values were omitted from subsequent analyses. Daily mean concentrations of $PM_{2.5}$ and BC at 1 × 1 km spatial resolution during 2013–2017 were derived from the ChinaHighAirPollutants (CHAP) database,[17] which were averaged across grid cells within each city's boundary.

Ascertainment of outcomes

Hospital admissions for major cardiovascular events were identified based on the principal discharge diagnoses according to the International Classification of Diseases, 10th Revision (ICD-10), and related text (details are presented in Supplementary eMethods). In this study, major cardiovascular events are defined as cardiac arrhythmias, coronary heart disease (CHD) and its major subtypes [including acute coronary syndrome (ACS), acute myocardial infarction (AMI), and angina pectoris], heart failure, stroke, and its subtypes (including hemorrhagic stroke and ischemic stroke). According to previous literature, the total number of major cardiovascular events is the sum of admissions for CHD, cardiac arrhythmias, heart failure, and stroke.[10] Detailed ICD-10 codes for major cardiovascular events included in the study are presented in Supplementary Table S1.

Statistical analysis

A two-stage time-series analysis was conducted. In the first stage, the overdispersed generalized additive model (GAM) with a quasi-Poisson link function was applied in combination with a distributed lag nonlinear regression model (DLNM) within each city. This approach accounts for overdispersion in the hospital admission data and captures the nonlinear and lagged effects of temperature on hospital admission risks.[18] To assess potential effect modification, an interaction term of a cross-basis function for daily mean temperature and city-specific quartile groups of $PM_{2.5}$ or BC (denoted as *pol* in the following formula) was incorporated in the model:

$$Y_{it} \sim quasiPoisson\left(\mu_{it}\right)$$

$$\begin{aligned} E(Y_{it}) = {} & \alpha_i + cb\left(Temp_{it}, lag = 28\right) + cb\left(Temp_{it}, lag = 28\right) \\ & \times Quartile_{pol} + \beta_i pol_{it} + ns\left(rhu_{it}, df = 3\right) \\ & + ns\left(Time_{it}, df = 8 \big/ year\right) + \gamma_i\left(DOW_{it}\right) + \delta\left(Holiday_{it}\right) \end{aligned}$$

where Y_{it} is the number of daily hospital admissions for major cardiovascular events in city i on day t; cb ($Temp_{it}$, $lag = 28$) represents the cross-basis function generated by the DLNM for daily mean temperature, with a maximum lag period up to 28 days. This lag period was selected based on prior knowledge and is designed to capture overall temperature effects and adjust for the potential harvesting effect.[19] As proposed in previous studies, the nonlinear exposure-response function was built by a natural cubic B-spline function with three degrees of freedom (dfs), and the lag-response function was built by a natural cubic B-spline function with three equally spaced knots in the log scale, which allows for more flexible effects with shorter delays.[18,20,21] $Quartile_{pol}$ is a dummy variable representing groups of $PM_{2.5}$ or BC categorized by city-specific quartiles. As the short-term effect of $PM_{2.5}$ generally occurs within several days, the moving average of the current day and the previous day (lag0-1) for $PM_{2.5}$ or BC was used as the main time window in the effect modification analyses.[22] pol_{it} is the linear term of $PM_{2.5}$ or BC at lag0-1 in city i on day t. rhu_{it} represents the present-day relative humidity in city i on day t, which was adjusted as a natural cubic spline function with three dfs.[23] Furthermore, natural cubic spline function for time with eight dfs per year was adjusted to control for long-term trend and seasonality.[18] Day of week (DOW) and public holidays were also included in the model. To improve model fitting and minimize the influence of tail-sparse data and potential outliers, arising from occasional equipment malfunctions, measurement errors, or data transmission issues, we excluded extreme daily temperatures lower than 0.5th percentile or higher than 99.5th percentile within each city, consistent with previous literature.[24]

In the second stage, the random-effects meta-analysis models were utilized to pool the city-specific associations.[25] The minimum morbidity temperature (MMT) was defined as the temperature associated with the lowest hospital admission risk for major cardiovascular events based on the overall cumulative exposure–response relationship (bounded between the means of minimum and maximum temperature in each city, which could generate a uniform distribution of temperatures at the national level).[7,18] City-specific MMT was derived from the best linear unbiased prediction (BLUP).[26] The relative risks (RRs) and 95% confidence intervals (CIs) in hospital admissions for major cardiovascular events associated with non-optimum temperatures (extreme cold and hot temperatures defined as 2.5th and 97.5th percentiles of temperature distribution across included cities, respectively) were estimated with the reference to MMT.[7] RR represents the cumulative risk of hospital admissions associated with a specific level of an exposure (e.g., 2.5th percentile of temperature distribution across 270 Chinese cities) compared to a predefined reference level (e.g., MMT) over the entire lag period.[25] The calculation of the RR is presented in Supplementary eMethods according to previous literature.[27]

According to a previously described method based on forward perspective,[28] the number of hospital admissions for total major cardiovascular events attributable to non-optimum temperatures at the nationwide level was calculated by summing the contributions from all the days with non-optimum temperatures in each city, and the attributable fraction was obtained by dividing the total number of attributable hospital admissions by the total number of hospital admissions. Attributable fractions associated with cold (lower than city-specific MMT), hot (higher than city-specific MMT), extreme cold (lower than 2.5th percentile of city-specific temperature distribution), and extreme hot temperature (higher than lower than 97.5th percentile of city-specific temperature distribution) were calculated by summing the subsets of days within relevant temperature ranges at the city level. Empirical CIs were estimated through Monte Carlo simulations (n = 1000).

To examine differences in exposure-response curves for temperature-admission associations stratified by $PM_{2.5}$ and BC quartile groups, we applied random-effects meta-analysis models with quartile groups as the only meta-predictor.[29] Additionally, we assessed the effect modifications by $PM_{2.5}$ and BC by testing the differences between the effect estimates of the first quartile (Q1) and the fourth quartile (Q4) by calculating the 95% CIs as:

$$\left(Q_1 - Q_4\right) \pm 1.96\sqrt{\left(SE_1\right)^2 + \left(SE_4\right)^2}$$

where Q1 and Q4 represent the estimates for the first and fourth quartile groups, respectively, and SE_1 and SE_4 denote corresponding standard errors.[30] We focused on the comparison between Q1 and Q4 of air pollution strata because they capture the extremes of the air pollution distribution and are informative for assessing effect modification by ambient particulate air pollution. The attributable number and fraction were also calculated in each quartile group of ambient particulate air pollution.

We also estimated whether the associations between non-optimum temperatures and hospital admissions for major cardiovascular events, as well as the effect modifications by $PM_{2.5}$ and BC, varied across climatic zones (tropical monsoon zone, subtropical monsoon zone, temperate continental zone, temperate monsoon zone, and alpine zone) and subgroups stratified by age (<40, 40–64, 65–74 and $\geq$ 75 years old), sex (self-reported male and female), region (north and south, divided by the Qingling Mountains-Huaihe River Line), and insurance type (UEBMI and URBMI). Differences among the subgroups were tested by the 2-sample Z-test.[30]

To test the robustness of the results, a series of sensitivity analyses were performed to ensure the robustness of the main findings, and more details are presented in the eMethods section. All analyses were performed using R Software version 4.3.0, with the “dlnm”, “mgcv”, and “mvmeta” packages. A two-tailed *P* value lower than 0.05 was considered statistically significant for all analyses.

Ethics approval

This study was exempted from institutional review board approval by the Biomedical Ethics Committee of the Xi’an Jiaotong University Health Science Center because no data with any individual identifiers were extracted for this study (No. 2021-1604).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Descriptive statistics

A total of 24,564,921 hospital admission records for major cardiovascular events were obtained from the UEBMI and the URBMI over the study period, among which 55.18% were male (Supplementary Table S2). On average, there were 56 daily hospital admissions per city for total major cardiovascular events. Daily hospital admissions per city for specific cardiovascular events ranged from 3 for AMI and hemorrhagic stroke to 29 for CHD. Daily mean ([standard deviation, SD]) temperature, relative humidity, $PM_{2.5}$, and BC concentrations across the 270 Chinese cities were 13.7 (11.3) °C, 67.6 (17.8) %, 48.7 (31.4) $\mu g/m^{3}$, and 2.8 (1.6) $\mu g/m^{3}$, respectively (Table 1). Geographical locations, city-specific daily mean temperature, daily mean hospital admissions per city for total major cardiovascular events, and daily mean concentrations of $PM_{2.5}$ and BC are presented in Supplementary Figures S2 and S3. Time trend plots for daily mean temperature, number of daily hospital admissions per city, and daily mean $PM_{2.5}$ and BC concentrations are presented in Supplementary Figure S4. We also observed moderate inverse correlations between daily mean temperature and $PM_{2.5}$ or BC, and a strong positive correlation between daily mean $PM_{2.5}$ and BC (Supplementary Figure S5).

Associations between non-optimum temperatures and hospital admissions

The cumulative exposure-response curves depict inverse J-shaped patterns with elevated hospital admission risks for total major cardiovascular events

Variables	Mean (SD)	2.5th percentile	25th percentile	50th percentile	75th percentile	97.5th percentile
Daily hospital admissions per city						
Total major cardiovascular events[a]	56 (43)	5	15	27	59	253
Cardiac arrhythmias	5 (4)	1	2	2	4	26
CHD	29 (23)	3	6	12	25	130
ACS	5 (3)	1	1	2	3	15
AMI	3 (2)	1	1	1	2	10
Angina pectoris	5 (4)	1	1	2	3	29
Heart failure	5 (4)	1	2	2	4	29
Stroke	22 (16)	2	6	12	25	97
Hemorrhagic stroke	3 (2)	1	1	2	3	12
Ischemic stroke	20 (14)	2	5	11	23	88
Daily meteorological conditions						
Temperature (°C)	13.7 (11.3)	−12.2	6.5	15.7	22.6	29.9
Relative humidity (%)	67.6 (17.8)	28.2	56.0	70.5	81.0	95.0
Daily ambient particulate air pollution						
$PM_{2.5}$ ($\mu g/m^{3}$)	48.7 (31.4)	15.0	27.9	40.5	59.7	132.1
BC ($\mu g/m^{3}$)	2.8 (1.6)	0.9	1.7	2.5	3.5	7.1

Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; BC, black carbon; CHD, coronary heart disease; $PM_{2.5}$, ambient fine particulate matter; SD, standard deviation. [a]Total major cardiovascular events include coronary heart disease, cardiac arrhythmias, heart failure, and stroke.

***Table 1:* Summary descriptive statistics on cause-specific hospital admissions for major cardiovascular events, temperature and ambient particulate air pollution in 270 Chinese cities of prefecture-level or above, 2013–2017.**

and specific subtypes associated with non-optimum temperatures (Fig. 1). The MMTs were comparable across different major cardiovascular events, ranging from 18.1 °C for ischemic stroke to 22.3 °C for hemorrhagic stroke. Cold temperature was associated with higher risk of hospital admissions for all major cardiovascular events than hot temperature. Specifically, with reference to MMT, the RRs for daily hospital admissions associated with extreme cold temperature ranged from 1.20 (95% CI: 1.06–1.36) for cardiac arrhythmias to 1.69 (95% CI: 1.43–1.98) for CHD. For extreme hot temperature, the RRs ranged from 1.12 (95% CI: 1.02–1.22) for cardiac arrhythmias to 1.27 (95% CI: 1.15–1.41) for total major cardiovascular events (Table 2). As shown in Supplementary Table S3, the overall fraction of hospital admissions for total major cardiovascular events attributable to non-optimum temperatures was 24.77% (95% empirical CI: 20.84%–25.43%). Compared with hot temperature, cold temperature was associated with many more hospital admissions for total major cardiovascular events (5112.95 thousand hospital admissions attributable to cold temperature versus 972.23 thousand attributable to hot temperature).

Heterogeneities were observed in the associations between non-optimum temperatures and hospital admissions for major cardiovascular events across different climatic zones. Generally, across the five climatic zones, stronger associations between extreme cold temperature and hospital admissions were primarily observed in the tropical monsoon zone. For extreme hot temperature, stronger associations were observed in the subtropical monsoon zone (Supplementary Table S4). Geographical heterogeneity was also observed in city-specific MMT across different climatic zones, with higher MMTs in warmer zones (Supplementary Figure S6). In addition, both extreme cold and hot temperatures were associated with elevated hospital admission risks for total major cardiovascular events across all age groups, with stronger associations observed among middle-aged individuals (aged 40–64 years) and individuals covered by the URBMI (Fig. 2).

Lag patterns for the associations between non-optimum temperatures and hospital admissions

Lag patterns for the associations with extreme cold temperature (−3.1 °C on average) and extreme hot temperature (27.9 °C on average) are illustrated in Supplementary Figures S7 and S8. Generally, the associations between extreme cold temperature and hospital admissions for total major cardiovascular events appeared on lag day one (lag1), peaked at lag3, dramatically declined until lag5, and became minimal in subsequent lag days after lag5. For extreme hot temperature, the associations were strongest on the present day (lag0), then dramatically declined to their lowest levels at lag2 or lag3. During the period of lag2 to lag4, RRs fell below 1.0, and the associations nearly vanished after lag5 (i.e., RRs almost equal to 1.0). As shown in Supplementary Figures S9, sliced exposure–response relationships between daily mean

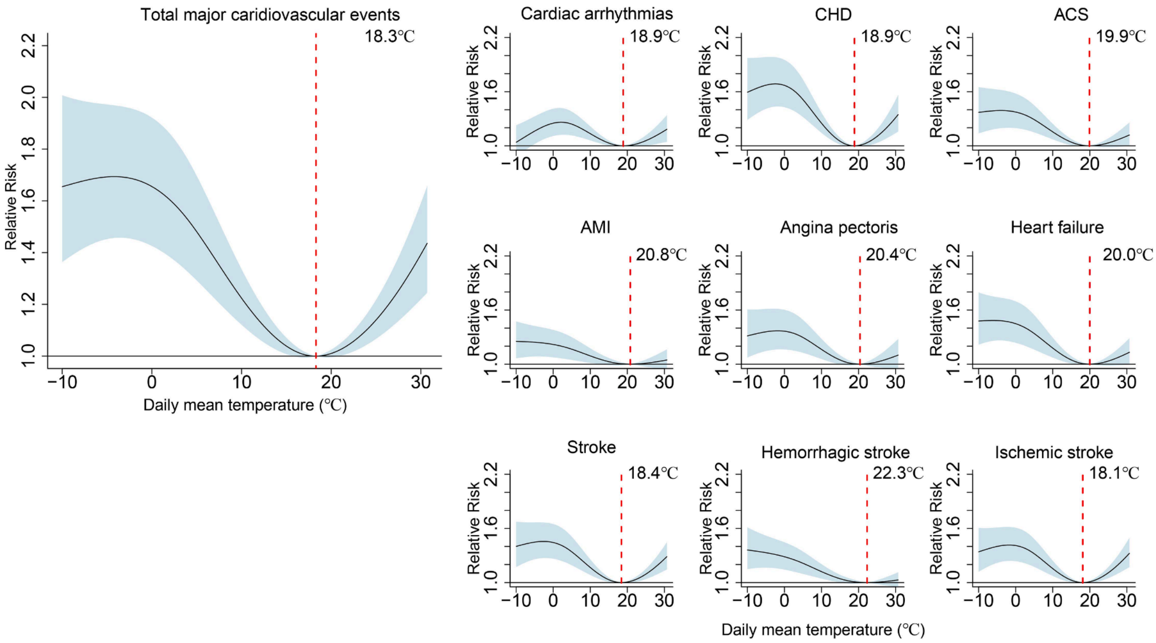


Fig. 1: **Exposure-response curves for the associations between daily mean temperature and cause-specific hospital admissions for major cardiovascular events.** Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; CHD, coronary heart disease.

Cause-specific hospital admission	Relative risk (95% CI)[a]		Minimum morbidity temperature (°C)
	Extreme cold temperature[b]	Extreme hot temperature[c]	
Total major cardiovascular events[d]	1.69 (1.46, 1.96)[e]	1.27 (1.15, 1.41)[e]	18.3
Cardiac arrhythmias	1.20 (1.06, 1.36)[e]	1.12 (1.02, 1.22)[e]	18.9
CHD	1.69 (1.43, 1.98)[e]	1.21 (1.09, 1.35)[e]	18.9
ACS	1.39 (1.20, 1.61)[e]	1.07 (0.99, 1.16)	19.9
AMI	1.24 (1.09, 1.41)[e]	1.03 (0.95, 1.10)	20.8
Angina pectoris	1.37 (1.16, 1.61)[e]	1.06 (0.95, 1.18)	20.4
Heart failure	1.48 (1.26, 1.73)[e]	1.08 (0.99, 1.18)	20.0
Stroke	1.46 (1.27, 1.67)[e]	1.18 (1.09, 1.29)[e]	18.4
Hemorrhagic stroke	1.32 (1.16, 1.49)[e]	1.01 (0.96, 1.07)	22.3
Ischemic stroke	1.41 (1.24, 1.61)[e]	1.21 (1.11, 1.32)[e]	18.1

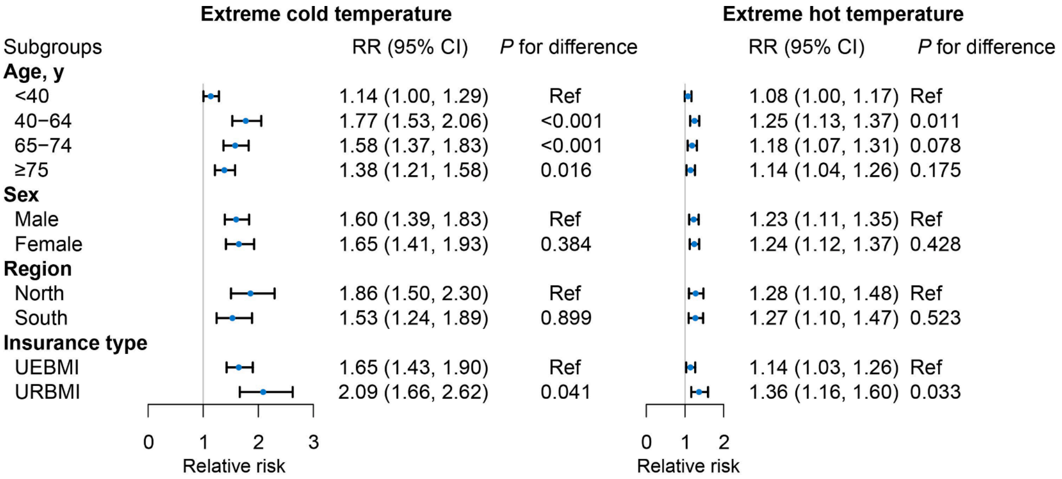
Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; CHD, coronary heart disease; CI, confidence interval. [a]Relative risks were estimated using a generalized additive model with a quasi-Poisson family combined with distributed lag non-linear models after adjusting for long-term trend, day of the week, public holidays, and relative humidity. [b]Extreme cold temperature: 2.5th percentile of temperature distribution across 270 Chinese cities (−3.1 °C on average), and the reference temperature is the minimum morbidity temperature. [c]Extreme hot temperature: 97.5th percentile of temperature distribution across 270 Chinese cities (27.9 °C on average), and the reference temperature is the minimum morbidity temperature. [d]Total major cardiovascular events include coronary heart disease, cardiac arrhythmias, and stroke. [e]Benjamini-Hochberg corrected $P < 0.05$.

Table 2: **Relative risks of daily cause-specific hospital admissions for major cardiovascular events associated with non-optimum temperatures.**

temperature and hospital admissions for total major cardiovascular events at specific lag days further validated the above lag patterns of the delayed effect of cold temperature and the immediate effect of hot temperature.

Effect modification by ambient particulate air pollution

As shown in Supplementary Figure S10, both $PM_{2.5}$ and BC were associated with elevated risks of hospital admissions for major cardiovascular events, with BC exhibiting stronger associations than $PM_{2.5}$. Fig. 3 illustrates that the exposure-response curves differed across $PM_{2.5}$ and BC quartiles, with higher hospital admission risks for total major cardiovascular events associated with non-optimum temperatures at higher pollution levels. Specifically, the RRs of hospital admissions for total major cardiovascular events associated with extreme hot temperature increased from 1.14 (95% CI: 1.02–1.28) in Q1 to 1.53 (95% CI: 1.31–1.78) in Q4 of BC levels (P for difference between Q1 and Q4 <0.05). A similar effect modification by



Subgroups	Extreme cold temperature RR (95% CI)	Extreme cold temperature P for difference	Extreme hot temperature RR (95% CI)	Extreme hot temperature P for difference
Age, y				
<40	1.14 (1.00, 1.29)	Ref	1.08 (1.00, 1.17)	Ref
40–64	1.77 (1.53, 2.06)	<0.001	1.25 (1.13, 1.37)	0.011
65–74	1.58 (1.37, 1.83)	<0.001	1.18 (1.07, 1.31)	0.078
≥75	1.38 (1.21, 1.58)	0.016	1.14 (1.04, 1.26)	0.175
Sex				
Male	1.60 (1.39, 1.83)	Ref	1.23 (1.11, 1.35)	Ref
Female	1.65 (1.41, 1.93)	0.384	1.24 (1.12, 1.37)	0.428
Region				
North	1.86 (1.50, 2.30)	Ref	1.28 (1.10, 1.48)	Ref
South	1.53 (1.24, 1.89)	0.899	1.27 (1.10, 1.47)	0.523
Insurance type				
UEBMI	1.65 (1.43, 1.90)	Ref	1.14 (1.03, 1.26)	Ref
URBMI	2.09 (1.66, 2.62)	0.041	1.36 (1.16, 1.60)	0.033

Fig. 2: **Relative risks of daily hospital admissions for total major cardiovascular events associated with non-optimum temperatures classified by age, sex, region, and insurance type.** Extreme cold temperature: 2.5th percentile of temperature distribution across 270 Chinese cities (−3.1 °C on average), and the reference temperature is the minimum morbidity temperature. Extreme hot temperature: 97.5th percentile of temperature distribution across 270 Chinese cities (27.9 °C on average), and the reference temperature is the minimum morbidity temperature. Regions are classified into the northern region and the southern region according to the city location, divided by the Qingling Mountains-Huaihe River Line. *P* for difference was used to evaluate the differences among subgroups. Abbreviations: CI, confidence interval; UEBMI, urban employee-based basic medical insurance; URBMI, urban resident-based basic medical insurance; RR, relative risk.

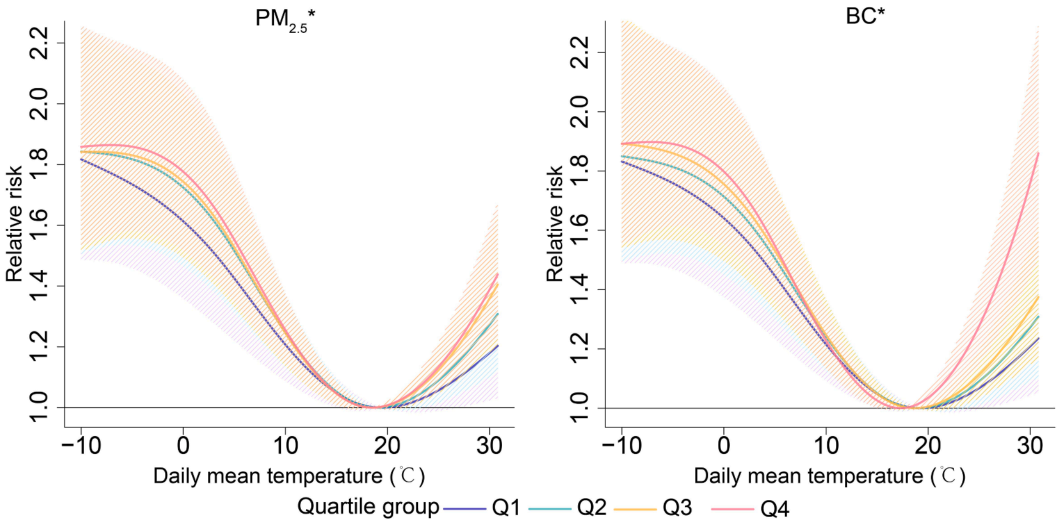


***Fig. 3:* Exposure-response curves for daily mean temperature and hospital admissions for total major cardiovascular events stratified by quartile groups of $PM_{2.5}$ and black carbon.** *The differences among the four curves stratified by quartiles of $PM_{2.5}$ and black carbon were tested to be statistically significant. Abbreviations: BC, black carbon; $PM_{2.5}$, ambient fine particulate matter; Q1, the 1st quartile; Q2, the 2nd quartile; Q3, the 3rd quartile; Q4, the 4th quartile.

$PM_{2.5}$ was also observed on the associations between extreme hot temperature and hospital admissions for angina pectoris and stroke (*P* for difference between Q1 and Q4 <0.05); however, no consistent evidence was found for the effect modification by $PM_{2.5}$ on the association between extreme cold temperature and hospital admissions for major cardiovascular events (Supplementary Figure S11). Maximum attributable fractions due to hot temperature were observed under Q4 of $PM_{2.5}$ and BC levels (Supplementary Table S5). The fraction attributable to hot temperature under Q4 of BC [9.67% (5.35%–10.22%)] was higher than that under Q4 of $PM_{2.5}$ [7.33% (3.56%–8.01%)].

Across the five climatic zones, the most pronounced differences in the associations between extreme hot temperature and hospital admissions for total major cardiovascular events across quartile groups of BC were observed in the temperate monsoon zone (Supplementary Table S6). Subgroup analyses showed that residents aged 65–74 years, female, cities located in the North, and those covered by the UEBMI were particularly vulnerable to extreme hot temperature under high BC levels, compared to other subgroups (Table 3).

Results of sensitivity analyses

Comparisons between the main analyses and sensitivity analyses are presented in Supplementary Figures S12 and S13. First, using different definitions of extreme temperatures showed minimal changes in the RRs. Second, using daily maximum temperature may slightly underestimate the associations between non-optimum temperatures and hospital admissions. The effect modifications by $PM_{2.5}$ and BC on temperature-admission associations were robust and slightly enhanced when alternating daily temperatures, including daily minimum and maximum temperatures (Supplementary Tables S7 and S8). Third, the results were broadly similar when changing knots for lag-response associations. Fourth, the results generally remained consistent and robust across different time windows for $PM_{2.5}$ and BC (Supplementary Figures S14 and S15). Fifth, without removing extreme daily temperatures lower than 0.5th percentile or higher than 99.5th percentile in each city, the associations between non-optimum temperatures and hospital admissions for major cardiovascular events, as well as the effect modifications by $PM_{2.5}$ and BC, were similar to those of the main analysis (Supplementary Table S9). Sixth, population-weighted exposures yielded results consistent with the main analyses, with the MMT increasing by a maximum of 2.7 °C for AMI (Supplementary Figures S16 and S17). Finally, as shown in Supplementary Figure S18, when ambient particulate air pollution concentrations were modeled as continuous variables, we also observed a consistent pattern that hospital admission risks for total major cardiovascular events peaked when both $PM_{2.5}$ or BC and temperature were at high levels. This pattern remained consistent across alternative temperature lag windows.

Discussion

Based on a large-scale nationwide medical insurance dataset in China, our findings provide evidence for the associations between both extreme cold and hot

Subgroups	Extreme cold temperature[b]				Extreme hot temperature[c]			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Age								
<40	1.20 (1.03, 1.39)	1.19 (1.03, 1.38)	1.22 (1.06, 1.40)	1.26 (1.10, 1.45)	1.06 (0.97, 1.16)	1.07 (0.98, 1.17)	1.12 (1.02, 1.24)	1.30 (1.11, 1.54)[d]
40–64	1.77 (1.50, 2.10)	1.83 (1.55, 2.16)	1.87 (1.59, 2.19)	1.86 (1.60, 2.17)	1.12 (1.02, 1.24)	1.18 (1.06, 1.30)	1.21 (1.09, 1.33)	1.44 (1.25, 1.67)[d]
65–74	1.64 (1.39, 1.93)	1.69 (1.43, 1.98)	1.70 (1.45, 2.00)	1.70 (1.47, 1.98)	1.13 (1.01, 1.26)	1.17 (1.04, 1.31)	1.20 (1.07, 1.35)	1.54 (1.32, 1.80)[d]
≥75	1.50 (1.29, 1.75)	1.52 (1.31, 1.77)	1.54 (1.33, 1.78)	1.55 (1.34, 1.78)	1.11 (0.99, 1.23)	1.13 (1.01, 1.26)	1.16 (1.04, 1.29)	1.34 (1.17, 1.54)[d]
Sex								
Male	1.64 (1.40, 1.93)	1.68 (1.44, 1.97)	1.71 (1.47, 2.00)	1.75 (1.52, 2.02)	1.14 (1.02, 1.26)	1.17 (1.04, 1.31)	1.18 (1.06, 1.31)	1.45 (1.26, 1.68)[d]
Female	1.65 (1.39, 1.96)	1.74 (1.47, 2.06)	1.77 (1.50, 2.09)	1.76 (1.51, 2.06)	1.12 (1.01, 1.25)	1.18 (1.06, 1.32)	1.26 (1.12, 1.42)	1.56 (1.32, 1.84)[d]
Region								
North	1.99 (1.55, 2.56)	2.07 (1.65, 2.59)	2.13 (1.71, 2.67)	2.13 (1.75, 2.59)	1.08 (0.94, 1.24)	1.11 (0.95, 1.30)	1.21 (1.03, 1.42)	1.64 (1.30, 2.06)[d]
South	1.52 (1.19, 1.95)	1.56 (1.21, 2.01)	1.57 (1.24, 2.00)	1.63 (1.29, 2.04)	1.24 (1.05, 1.48)	1.30 (1.09, 1.55)	1.26 (1.06, 1.51)	1.44 (1.16, 1.79)
Insurance type								
UEBMI	1.51 (1.29, 1.78)	1.51 (1.29, 1.76)	1.56 (1.34, 1.82)	1.56 (1.36, 1.79)	1.13 (1.01, 1.27)	1.15 (1.01, 1.31)	1.14 (1.02, 1.27)	1.52 (1.26, 1.84)[d]
URBMI	1.92 (1.50, 2.44)	2.01 (1.59, 2.54)	2.11 (1.67, 2.66)	2.15 (1.71, 2.72)	1.26 (1.07, 1.49)	1.25 (1.07, 1.46)	1.42 (1.17, 1.71)	1.68 (1.24, 2.29)

Abbreviations: BC, black carbon; CI, confidence interval; Q1, the 1st quartile; Q2, the 2nd quartile; Q3, the 3rd quartile; Q4, the 4th quartile; UEBMI, urban employee-based basic medical insurance; URBMI, urban resident-based basic medical insurance. [a]Relative risks were estimated using a generalized additive model with a quasi-Poisson family combined with distributed lag non-linear models across quartile groups of black carbon after adjusting for long-term trend, day of the week, public holidays, and relative humidity. [b]Extreme cold temperature: 2.5th percentile of temperature distribution across 270 Chinese cities (−3.1 °C on average), and the reference temperature is the minimum morbidity temperature. [c]Extreme hot temperature: 97.5th percentile of temperature distribution across 270 Chinese cities (27.9 °C on average), and the reference temperature is the minimum morbidity temperature. [d]Significant difference between Q1 and Q4 ($P < 0.05$) based on two-sample Z-test.

***Table 3:* Relative risks of daily cause-specific hospital admissions for total major cardiovascular events associated with non-optimum temperatures stratified by quartile groups of black carbon in different subgroups.**[a]

temperatures and elevated hospital admission risks for several major cardiovascular events. The exposure-response curves exhibited inverse J-shaped patterns for major cardiovascular events and related subtypes. Furthermore, ambient particulate air pollution modified the associations between non-optimum temperatures and hospital admissions for major cardiovascular events. Compared to low BC levels (Q1), high BC levels (Q4) amplified the risks of hospital admissions for total major cardiovascular events associated with extreme hot temperature by 34%. Subgroup analysis further identified that cities located in the temperate monsoon zone and people aged 65–74 were particularly vulnerable to extreme hot temperature under high BC levels.

The inverse J-shaped exposure-response curves for short-term non-optimum temperatures exposure and hospital admissions for major cardiovascular events are consistent with previous studies.[7,31,32] In line with our results, cold temperature exposure is an important risk factor associated with elevated CVD morbidity.[33] In contrast, the associations between extreme hot temperature and CVD morbidity vary across studies and locations and remain inconclusive.[31,32,34,35] For example, a previous meta-analysis based on 28 studies found that short-term heat exposure was associated with increased risks of CVD mortality but not morbidity.[32] Whereas a meta-analysis of 266 studies revealed that a 1 °C rise in short-term temperature exposure was associated with a 0.5% increased risk of CVD morbidity.[36] These discrepancies may be partially explained by the different morbidity indicators used across studies (e.g., hospital admissions, emergency department visits, and ambulance attendance). These indicators reflect varying severities of cardiovascular outcomes and may influence the temperature-admission associations.[37]

When classifying cities into climatic zones, we observed pronounced cold temperature effects in the tropical zone. This can be partially attributed to differences in temperature adaptation across climatic zones. Residents in tropical areas have limited physiological and behavioral adaptation to cold conditions, making them more vulnerable when temperatures fall below their usual thermal norms, temperatures that would be considered mild in colder regions. In addition, housing characteristics and heating infrastructure in the tropical zone are typically not designed for low temperatures,[38] which may further exacerbate cold-related health risks. Furthermore, consistent with previous studies, we observed geographical heterogeneity in city-specific MMT across different climatic zones, with lower MMTs found in colder zones.[39] This can be explained by long-term adaptation to cold temperature and greater temperature variability in these regions.

Consistent with previous findings, we also found that the associations between short-term exposure to extreme cold temperature and CVD morbidity persisted for five days, whereas the associations with extreme hot temperature appeared immediately and persisted for only two or three days.[7,18] Due to harvesting effects, we observed a period during which the RRs for hospital admissions associated with extreme hot temperature were lower than 1.0.[40] This suggests that while hot temperature may increase hospital admission risk in high-risk individuals, it has minimal adverse effects on healthy individuals. As the high-risk pool is depleted by hot temperature, a subsequent reduction in hospital admissions can occur in subsequent days until the high-risk pool is replenished. In line with another study,[41] we found that the harvesting effects of extreme hot temperature on hospital admission for cardiovascular events ceased after lag5. More discussions on the associations between non-optimum temperatures and hospital admissions for specific subtypes are presented in Supplementary eDiscussion.

To date, existing studies have primarily focused on the effect modification by short-term exposure to $PM_{2.5}$ on the associations between non-optimum temperatures and CVD mortality, but have not reached an agreement yet.[42,43] Furthermore, little is known about the effect modification by BC, one of the major constituents of $PM_{2.5}$, on CVD morbidity. A time-series study conducted across 620 cities in 36 countries found that the association between temperature and all-cause mortality became stronger with 10 $\mu g/m^3$ increments of $PM_{2.5,}$ especially at temperatures higher than the 90th quantile.[43] Another study conducted in eight European urban areas found that the risk of all-cause mortality associated with hot temperature was more pronounced on days with high short-term $PM_{2.5}$ exposure levels than on days with low $PM_{2.5}$ levels; however, this effect modification was not observed for cardiovascular mortality.[44] To date, no study has estimated the effect modification by BC on the associations between short-term exposure to non-optimum temperatures and hospital admissions for major cardiovascular events and related subtypes. Our study obtained novel findings that the associations between extreme hot temperature and cause-specific hospital admissions for major cardiovascular events were more pronounced under high BC levels. However, comparisons between high and low $PM_{2.5}$ levels did not suggest a clear difference in the associations between extreme hot temperature and hospital admissions for total major cardiovascular events. This may be because some $PM_{2.5}$ constituents, such as sulfate and nitrate, can reflect sunlight, helping to cool the air.[45] The light-scattering effect of these $PM_{2.5}$ constituents may outweigh the warming effect of BC when considering total $PM_{2.5}$ mass rather than BC alone. Even though the proportion of BC in $PM_{2.5}$ was small, the contribution of BC radiative forcing to aerosol radiative forcing is substantial.[46] It is worth noting that although little evidence of the association between extreme hot temperature and hospital admission for angina pectoris was observed, a stronger positive association was observed at high $PM_{2.5}$ and BC levels. This suggests that individuals with angina pectoris may be susceptible to extreme hot temperature exposed to high levels of ambient particulate air pollution.

Subgroup analyses found that middle-aged residents (40–64 years old) were more vulnerable to non-optimum temperatures than other age groups, which is in line with findings from another study on emergency room visits among adults across the full age spectrum in the United States.[34] Compared with individuals younger than 40 years old, middle-aged individuals showed greater vulnerability, likely due to their higher risks of cardiovascular events. Meanwhile, compared to the elderly (over 64 years old), middle-aged individuals are more likely to be exposed to non-optimum temperatures due to occupational and recreational outdoor activities. However, when considering the modification by BC on the associations between extreme hot temperature and hospital admissions for major cardiovascular events, individuals aged 65–74 years (followed by middle-aged individuals aged 40–64 years old) were more sensitive to extreme hot temperature under high BC levels than other age groups. This implies that individuals aged 65–74 years are particularly vulnerable to short-term exposure to extreme hot temperature in the context of BC pollution. Compared with the elderly older than 75 years old, who may tend to stay indoors to avoid such extreme exposure, individuals aged 65–74 engage in outdoor activities and opportunities to be exposed to extreme hot temperature and ambient particulate air pollution. On the other hand, the elderly, especially those with severe cardiovascular impairments, may experience fatal outcomes before reaching the hospital for treatment after acute exposure to non-optimum temperatures and ambient particulate air pollution, thus resulting in lower hospital admission rates.[36] These findings expand upon the previous knowledge and underscore that the adverse health impacts of non-optimum temperatures are as important among middle-aged individuals as among the elderly.

From a climatic perspective, near-surface BC heats the air, a phenomenon often referred to as the “stove effect”, with this warming effect intensifying as the BC and $PM_{2.5}$ ratio increases.[47] Although the Air Pollution Prevention and Control Action Plan effectively decreased the overall concentrations of $PM_{2.5}$ and BC,[14] the BC/$PM_{2.5}$ ratio rose from 5.66% in 2013 to 6.36% in 2017, potentially amplifying near-surface temperature through BC-induced “strove effect”. Physiological responses to hot temperature, such as increased sweating, blood flow, and cardiac output, tend to enhance the uptake and distribution of air pollutants in the body.[48] Our findings support the viewpoint that BC, one of the constituents in $PM_{2.5,}$ should be paid more attention in the context of global warming.

Our findings have several implications for urban design and public health policies. Firstly, urban design policies should be optimized to reduce traffic-related emissions, particularly BC, and to establish clear emission-control targets. Secondly, land-use planning should aim to minimize residential proximity to high-traffic corridors to reduce exposure to traffic-related air pollutants. Third, nature-based solutions, such as expanding urban green spaces, can improve microclimatic conditions and dilute ambient particulate air pollution. In addition, although climate-related health early-warning services in China already cover a large proportion of the population (587.97 million people in 2024),[49] local systems should further consider city-specific characteristics and integrate meteorological indicators with air pollution metrics, including key hazardous $PM_{2.5}$ constituent(s). Finally, from a healthcare perspective, integrating meteorological forecasts into health surveillance systems may therefore enhance the ability to anticipate short-term fluctuations in healthcare demand. Such forecasting approaches could support timely resource allocation, improve hospital preparedness, and strengthen the resilience of healthcare systems under varying environmental conditions.

Several limitations should be mentioned. First, the use of city-level daily mean temperature data obtained from weather monitoring stations may introduce exposure misclassification, as individual information was not available due to ethical concerns and privacy reasons. However, the use of city-level exposure data conforms to develop climate change adaptation and air pollution control policies. Meanwhile, misclassification and coding errors of the outcome are inevitable in such a large-scale time-series study. However, such errors are unlikely to be related to ambient temperature and air pollution levels and are expected to reduce the statistical precision and potentially bias the RR toward the null.[50] Second, we were unable to access updated medical insurance data from 2018 onward due to the restructuring of China's health administration system.[51] Third, as an ecological study, individual-level confounders such as occupation, health behaviors, and air conditioning usage were not controlled for due to the lack of individual-level information. Therefore, we could not assess potential differences in temperature-admission associations across these characteristics. Fourth, the generalizability of the results to the overall population may be limited, as the study included only urban residents, who may generally have better access to healthcare services than rural residents. Because of limited healthcare resources for rural residents, the exposure-outcome associations among them may be more pronounced than urban residents. Finally, because of ethical concerns and privacy reasons, individual identifiers were unavailable to obtain readmissions or in-hospital deaths.

Our study suggests that both extreme cold and hot temperatures contribute to elevated hospital admission risks for major cardiovascular events. Additionally, high levels of ambient BC amplified the associations under extreme hot temperature. Heterogeneities across the climatic zones and different demographic characteristics were also observed. Our findings highlight the importance of mitigating exposures to both hot temperature and ambient particulate air pollution in order to reduce hospital admission risks of major cardiovascular events and help raise awareness on the consideration of not only the total mass of $PM_{2.5}$ but also major $PM_{2.5}$ constituents, such as BC, amidst ongoing global warming mitigation and adaptation efforts in CVD prevention.

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Data sharing statement

Air pollution data used in this study can be applied from the ChinaHighAirPollutants (CHAP) dataset at https://weijing-rs.github.io/product.html. Meteorological data are available from the China Meteorological Data Sharing Service System at http://data.cma.cn/. Governmental policies regulate the medical insurance data analyzed in this study and cannot be made available to the public for ethical and privacy reasons. Application for collaborative research purposes based on the data used in the study can be addressed by contacting the corresponding authors. The analytical code with example dataset is deposited in GitHub at: https://github.com/hmliu123/Temperature-and-modification-by-PM2.5/tree/main.

Declaration of interests

The authors declare no conflict of interest for this article.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2026.101829.

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