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Association between ambient temperature and cause-specific mortality: An individual-level case-crossover study in Suzhou, China

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ABSTRACT

The changing climate poses a growing challenge to the population health. The objective of this study was to assess the association between ambient temperature and cause-specific mortality in Suzhou. Based on the non-accidental mortality data collected during 2008–2022 in Suzhou, China, this study utilized an individual-level case-crossover design to evaluate the associations of temperature with cause-specific mortality. We applied a distributed lag nonlinear model with a maximum lag of 14 days to account for lag effects. Mortality risk due to extreme cold (<2.5th percentile) and extreme heat (>97.5th percentile) was analyzed. A total of 634,530 non-accidental deaths were analyzed in this study. An inverse J-shaped exposure-response relationship was observed between ambient temperature and non-accidental mortality, with the minimum mortality temperature (MMT) at 29.1°C. The relative risk (RR) of mortality associated with extreme cold (2.5th percentile) was 1.37 [95 % confidence interval (CI): 1.30, 1.44], higher than estimate of 1.09 (95 %CI: 1.07, 1.11) for extreme heat (97.5th percentile) relative to the MMT. Heat effect lasted for 2–3 days, while cold effect could persist for almost 14 days. Higher mortality risk estimates were observed for cardiorespiratory deaths compared to total deaths, with statistically significant between-group differences. Consequently, this study provides first-hand evidence on the associations between ambient temperatures and mortality risks from various causes, which could help local government and policy-makers in designing targeted strategies and public health measures against the menace of climate change.

1. Introduction

Along with the intensified global climate change, non-optimum temperature is becoming a greater threat to public health worldwide (GBD 2019 Risk Factors Collaborators, 2020). The Global Burden of Disease Study included non-optimum temperature in the top ten leading causes of death worldwide (GBD 2019 Risk Factors Collaborators, 2020). Increasing epidemiological studies have provided evidence of temperature-related mortality (The Lancet, 2021; Gasparrini et al., 2015; Guo et al., 2014; Chen et al., 2018). For instance, a global systematic evaluation on the temperature-mortality association in 306 communities from 12 countries or regions showed an increased risk of total mortality in non-optimum ambient temperatures (Guo et al., 2014). Another national study in China found that non-optimum temperatures were associated with increased mortality from non-accidental causes, cardiovascular diseases, and respiratory diseases (Chen et al., 2018).

Evidence showed that the temperature-mortality associations vary by specific causes and locations, which might be explained by differential mechanisms, regional climates, human adaptability, and different distributions of vulnerability factors such as socioeconomic status (Yin et al., 2019). It is therefore of practical importance to quantitatively

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assess the impacts of non-optimum temperatures on a wide range of diseases using local data. However, most studies have focused on the effect of temperature on total mortality or mortality from a single cause (Xing et al., 2022). Furthermore, most of these studies have collected data within a short time span.

Suzhou is a prefecture-level city located in Jiangsu province of eastern China, with a subtropical monsoon maritime climate. The local population may be more susceptible to the detrimental health effects of non-optimum temperatures, as exposed to heatwaves in summer and clammy winters without central heating (Wang et al., 2014). However, there remains a knowledge gap between local evidence and practice to manage heath risk of non-optimum temperatures.

Our study aimed to evaluate the short-term association between temperature and cause-specific mortality in Suzhou from 2008 to 2022, using an individual-level case-crossover design with a large sample. We also assessed the impact of sociodemographic characteristics on this association. Our findings can provide evidence-based guidance for policymakers to protect citizens against climate change.

2. Methods

2.1. Study design

We applied a time-stratified case-crossover study design to evaluate the temperature-mortality association at the individual level (Zhang et al., 2022). Specifically, each death date was defined as a case and matched with controls on the same day of the week, month, and year. For example, the control days will be all the remaining Mondays in the same month (i.e., 10th, 17th, 24th and 31st) of January 2022 if a case day falls on the first Monday (January 3rd). In this design, each case serves as its own control and the within-subject comparison could control for time-invariant confounders at the individual level, such as demographic factors (e.g., age, sex, and genetic factors) and socioeconomic status (Maclure, 1991). Additionally, by selecting control days in the same month and spaced 7 days or integral multiples of 7 days apart from the case day, this study design controls for day-of-week effects, seasonality, and long-term time trends.

2.2. Data collection

The cause-specific mortality data of all registered residents in Suzhou from January 1st, 2008, to November 31st, 2022, was obtained from the Suzhou Center for Disease Control and Prevention. To avoid the impact of the COVID-19 pandemic, we have excluded mortality data of December 2022, which was collected after the lifting of the lockdowns in Suzhou. The death data was cross-checked with information from the Public Security Bureau, the Funeral Department, and the Municipal Medical Insurance Bureau. To protect patient privacy and ensure data confidentiality, the study removed personally identifiable information.

Based on the International Classification of Diseases 10th Revision (ICD-10) codes, the individual-level data were categorized into the following groups: non-accidental causes (referred to as 'total' in this study; ICD-10: A00-R99), cardiovascular disease (ICD-10: I00-I99), including ischemic heart disease (ICD-10: I20-I25) and stroke (ICD-10: I60-I69), which further comprised hemorrhagic stroke (ICD-10: I60-I61) and ischemic stroke (ICD-10: I63), and respiratory disease (ICD-10: J00-J99), encompassing pneumonia (ICD-10: J10-J18) and chronic obstructive pulmonary disease (ICD-10: J41-J44). The death records collected individual characteristics, including age, sex, and education.

We collected the meteorological data (i.e., daily mean temperature, relative humidity, air pressure, and wind speed) from the fixed-site monitoring station closest to the location of each case, based on the National Meteorological Data Network of the Chinese Meteorological Bureau (Chen et al., 2018). The address at the time of death of each case was obtained from the death record and standardized, then those records with missing or incorrect addresses were excluded from the analyses. Additionally, we obtained the data on daily average concentrations of six criteria pollutants, including particulate matter with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$), particulate matter with an aerodynamic diameter of less than 10 μm (PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), ozone (O_3) and carbon monoxide (CO) from the nearest station to the individual location.

2.3. Statistical analyses

We utilized a conditional logistic regression model to examine the temperature-mortality association. The dependent variable in the model was defined as a dichotomous variable, with 1 representing the case day and 0 denoting the control day. To account for the delayed and non-linear health effect of the ambient temperature, an independent variable was introduced using a cross-basis matrix of temperature, constructed through the distributed lag non-linear model (DLNM) (Gasparrini et al., 2010). We constructed the cross basis function of daily temperature, and used a quadratic B spline with knots positioned at the 10th, 50th, and 90th percentiles of the temperature distributions. A maximum lag of 14 days was chosen to explore the lag effect of temperature, based on previous fundings indicating lagged effect of cold and our prior data analysis (Dimitrova et al., 2021). The spline of lags included two internal knots positioned at equally spaced values on the logarithmic scale. Additionally, the model accounted for holidays and relative humidity.

The minimum mortality temperature (MMT) was defined as the optimal temperature with the lowest mortality risk, which derived from the lowest point of the temperature-mortality exposure-response relationship curve. Extreme cold and hot temperatures referred to the 2.5th and the 97.5th percentiles of the temperature distributions, respectively (Gasparrini et al., 2015). Exposure-response curves were generated to illustrate the associations of temperature with both total and cause-specific mortality. In addition, relative risks (RRs) and 95 % confidence intervals (CIs) were computed for extreme cold and hot temperatures compared to the MMT.

We conducted several stratified analyses by sex (male and female), age ($<$65 years and $\geq$65 years), and educational attainment ($\leq$9 years and $>$9 years) to identify the potentially susceptible subgroups. Additionally, several sensitivity analyses were conducted to examine the robustness of the temperature-mortality association. First, we changed the maximum lag periods to 5 and 7 days to provide estimates in shorter lag days. Second, we specified the knot placement as the 10th, 75th, 90th and 25th, 50th, 75th percentiles of temperature distributions in the DLNM construction. Third, we included each of the six criteria air pollutants (PM_{10}, $PM_{2.5}$, NO_2, SO_2, O_3, and CO) in the model. Finally, we included weather conditions (i.e., air pressure and wind speed) in the model, and excluded the relative humidity from the model to examine the confounding effects of the non-temperature variables. Z-tests were applied to assess the between-group differences in the stratified analyses by causes of death and subgroups.

Statistical analyses were conducted using R software (Version 4.1.1), with statistical significance set at two-sided p-values < 0.05. The "dlnm" and "survival" packages were utilized to construct DLNM and perform conditional logistical regression analysis, respectively.

3. Results

3.1. Descriptive data

Table 1 presents a summary of statistics on cause-specific deaths and meteorological factors in Suzhou, China from 2008 to 2022. The study period had a daily mean temperature of 16.6℃ (SD=9.2) and a mean relative humidity of 74.2 % (SD=13.8). A total of 634,530 deaths were identified, including 233,799 deaths from all-cause cardiovascular disease, 34,962 deaths from ischemic heart disease, 141,032 overall stroke deaths, 30,718 deaths from hemorrhagic stroke, 28,456 deaths from

Table 1
Summary descriptive statistics on cause-specific deaths and meteorological conditions in Suzhou, China.

Disease	ICD codes	Cases, n	Temperature, mean (SD), °C	Relative Humidity, mean (SD), %
Total	A00-R99	634,530	16.6 (9.2)	74.2 (13.8)
Cardiovascular disease	I00-I99	233,799	16.2 (9.2)	74.1 (13.8)
Ischemic heart disease	I20-I25	34,962	16.2 (9.2)	74.3 (13.9)
Stroke	I60-I69	141,032	16.3 (9.2)	74.1 (13.8)
Hemorrhagic stroke	I60-I61	30,718	16.3 (9.2)	74.1 (13.8)
Ischemic stroke	I63	28,456	16.3 (9.2)	74.3 (13.8)
Respiratory disease	J00-J99	79,689	15.6 (9.3)	74.1 (13.8)
Pneumonia	J10-J18	19,156	15.5 (9.3)	73.9 (13.7)
COPD	J41-J44	48,906	15.6 (9.2)	74.2 (13.8)

Abbreviation: SD, standard deviation; COPD, chronic obstructive respiratory disease.

ischemic stroke, 79,689 deaths from all-cause respiratory disease, 19,156 deaths from pneumonia, and 48,906 deaths from chronic obstructive respiratory disease.

3.2. Regression results

Fig. 1 presents the cumulative exposure-response relationships between daily mean temperature and cause-specific mortality in Suzhou, China. The overall exposure-response curves exhibited a consistent inverse J-shaped, indicating elevated mortality risk associated with both cold and hot temperatures. Table 2 summarizes the estimated RRs and 95 % confidence intervals of cause-specific mortality linked to ambient temperature. The MMT for total deaths as 29.1℃, ranging from 25.0℃ to 30.5℃ for different causes of death. The total mortality risk for extreme low temperature (RR=1.37, 95 %CI: 1.30, 1.44) was higher than that for extreme heat (RR=1.09, 95 %CI: 1.07, 1.11) with the MMT as the reference.

Different causes of death exhibited various temperature-related mortality risks (Table 2). Higher mortality risk estimates were observed for cardiorespiratory deaths compared to total deaths, with statistically significant between-group differences. For instance, the corresponding RRs for extreme cold temperature were 1.67 (95 %CI: 1.41, 1.99) for respiratory diseases and 1.61 (95 %CI: 1.47, 1.76) for cardiovascular diseases. The RRs of extreme hot temperature were 1.17 (95 %CI: 1.09, 1.25) and 1.12 (95 %CI: 1.09, 1.16), respectively. Furthermore, we observed differential patterns across specific causes. For extreme cold effects, a higher risk of chronic obstructive respiratory disease was observed, with RR of 1.75 (95 %CI: 1.40, 2.19). For extreme hot effects, pneumonia might be more susceptible, with RR of 1.23 (95 %CI: 1.05, 1.45).

Fig. 2 displays the lagged associations between extreme low temperatures and cause-specific mortality risks. The effect of extreme low temperatures generally occurred on lag 1 day and lasted up to 12 days. The effect estimates were largest on lag 2–3 days. In contrast, the effects of extreme heat on mortality risks were strongest on the present day, decreased gradually to lag day 4, and then tended to be non-significant (Fig. 3). Apparently, we observed more lagged and stronger effects for extreme cold for each cause of death.

Table S1 displays that the MMTs for females, the elderly, and those with higher education were lower than their respective counterparts. Notably, females experienced significantly stronger effects from extreme cold and hot temperatures than males. Meanwhile, the mortality risks associated with both extreme hot and cold temperatures were higher for the elderly and those with low education levels. For instance, the results showed significant between-group differences for extreme hot effects, with RRs of 1.09 (95 %CI: 1.07, 1.11) and 1.04 (95 %CI: 1.00, 1.08) for the elderly and the younger group, respectively. Additionally, individuals with lower levels of education exhibited significantly heightened sensitivity to extreme cold temperatures, with RRs of 1.43 (95 %CI: 1.36, 1.52) and 1.19 (95 %CI: 1.02, 1.40) for the low and high education attainment groups, respectively.

The results of the sensitivity analyses indicated that the temperature-mortality associations remained robust after changing the maximum lag periods to 5 and 7 days, changing the percentiles of the knots at 10th, 75th, 90th and 25th, 50th, 75th, adjusting for six criteria air pollutants, air pressure and wind speed, or excluding relative humidity (Table S2).

4. Discussion

This is the largest single-city study systematically exploring the adverse effects of non-optimum temperature on cause-specific mortality. The results indicate that exposure to both hot and cold temperatures may increase mortality risk from various cardiopulmonary diseases, with a larger and longer impact observed in cold temperatures. Additionally, females, the elderly and individuals with lower level of education may be more susceptible to extreme cold and hot temperatures.

This study found that the MMT was 29.1℃ for the total mortality and varied across different regions and by specific causes. The discrepancy of MMT across causes of death may be attributed to the disparate pathogenesis of various diseases and the diverse temperature-related physiological mechanisms (Gasparrini et al., 2015). Notably, MMT in the northern subtropics typically ranges from 20℃ to 30℃ and increases with decreasing latitude, indicating the local long-term adaptation to the climate (Zafeiratou et al., 2021). Although some investigations have observed U- or V-shaped relationships between ambient temperature and mortality (Gasparrini et al., 2015; Psistaki et al., 2022), we found an inverse J-shaped curve in the temperature-mortality relationship, consistent with several prior studies (Dimitrova et al., 2021; Cao et al., 2021). Both cold and heat could pose a significant impact on total mortality, but the impact of cold temperatures was much greater than that of hot temperatures (Gasparrini et al., 2015; Zafeiratou et al., 2021).

Our findings indicated that extreme temperatures might have stronger effects on cardiorespiratory deaths than total deaths. These findings indicated the vulnerability of individuals with preexisting cardiorespiratory diseases, which is in line with prior researches (Fan et al., 2023; Cui et al., 2016). For instance, a recent systematic review revealed that an increase of 1℃ in temperature was positively associated with cardiovascular mortality, with a 2.1 % increase in the overall risk of cardiovascular mortality (Liu et al., 2022). A multicity investigation in China revealed a significant association between heat and elevated mortality risk for total, ischemic and hemorrhagic stroke, while the effect of hot temperature on mortality was more pronounced for ischemic stroke compared to hemorrhagic stroke (Zhou et al., 2017). However, a study investigating the impact of temperature on cerebrovascular mortality across five Chinese cities reported a non-significant heat effect (Zhang et al., 2014). These inconsistencies in findings may stem from variations in study designs, including study period, study population, time-series or case-crossover design, and statistical methods. Moreover, disparities in city-specific characteristics such as climate adaptation measures, socioeconomic development level, housing infrastructure, and air conditioner prevalence may also contribute to the discrepancies.

Consistent with previous investigations, hot temperatures have been found to have immediate and short-term effect (Liu et al., 2022). For example, Chen et al. conducted a nationwide study in 272 major cities and found that the heat effect persisted only 2–3 days in China (Chen et al., 2018). Yu et al. found similar effect of heat stress on non-accidental deaths in Shandong Province, China (Yu et al., 2023). In contrast, our study found that extreme cold had a marked effect that

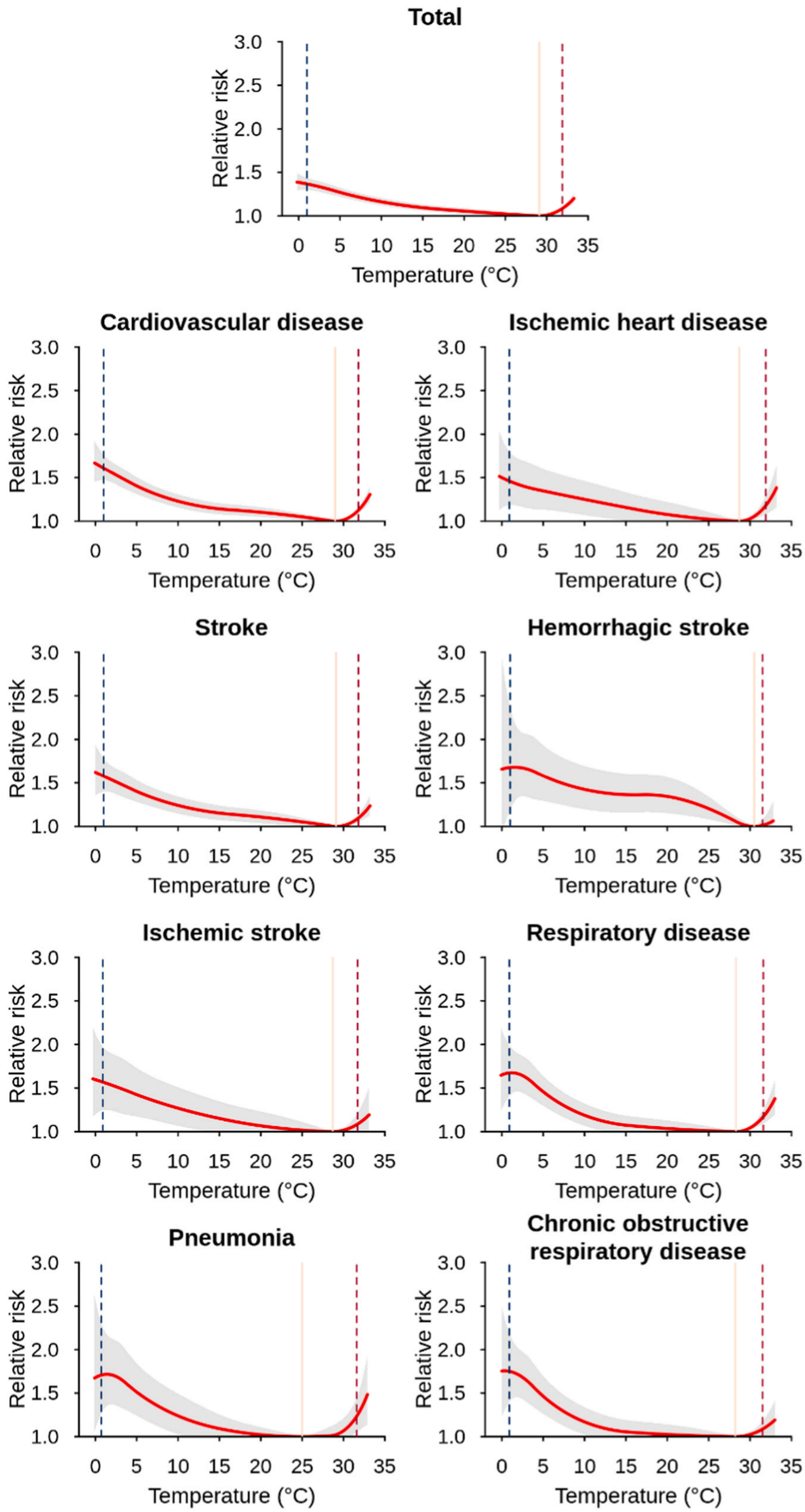

Fig. 1. Cumulative exposure-response associations of daily mean temperature with cause-specific mortality in Suzhou, China. Solid red lines = mean relative risks; gray areas = 95 % confidence intervals; dashed lines = 2.5th and 97.5th percentiles of temperature distributions; solid orange lines = minimum mortality temperature.

Table 2
Estimated relative risks and 95 % confidence intervals (CIs) of cause-specific mortality associated with ambient temperature in Suzhou, China.

Disease	MMT, °C	Extreme temperature, °C		Relative risk (95 % CI)		Between-group p-value	
		Extreme cold	Extreme hot	Extreme cold	Extreme hot	Extreme cold	Extreme hot
Total	29.1	1.0	31.9	1.37 (1.30, 1.44)	1.09 (1.07, 1.11)		
Cardiovascular disease	29.0	1.0	31.8	1.61 (1.47, 1.76)	1.12 (1.09, 1.16)	0.002	0.048
Ischemic heart disease	28.7	0.9	31.9	1.46 (1.19, 1.80)	1.18 (1.08, 1.29)	0.545	0.072
Stroke	29.1	1.0	31.8	1.58 (1.40, 1.78)	1.10 (1.05, 1.14)	0.032	0.690
Hemorrhagic stroke	30.5	1.0	31.5	1.68 (1.19, 2.36)	1.01 (0.95, 1.08)	0.246	0.038
Ischemic stroke	28.7	0.9	31.7	1.57 (1.25, 1.97)	1.09 (0.98, 1.21)	0.253	0.987
Respiratory disease	28.3	0.9	31.6	1.67 (1.41, 1.99)	1.17 (1.09, 1.25)	0.029	0.034
Pneumonia	25.0	0.7	31.6	1.71 (1.26, 2.31)	1.23 (1.05, 1.45)	0.156	0.114
COPD	28.2	0.9	31.5	1.75 (1.40, 2.19)	1.09 (1.00, 1.18)	0.035	0.982

Note: Extreme cold temperature was defined as the 2.5th percentile of temperature distributions; Extreme hot temperature was defined as the 97.5th percentile of temperature distributions; Z-tests were applied to assess the differences in effect estimates between total deaths and cause-specific deaths.
Abbreviation: MMT, minimum mortality temperature; CI, confidence interval; COPD, chronic obstructive respiratory disease.

lasted up to about two weeks, indicating a relatively long-lasting effect of cold. This duration is in line with that observed in previous studies, which typically lasted 1–3 weeks (Chen et al., 2018; Alahmad et al., 2023). The influenza epidemics indirectly induced by cold might explain the relatively stronger and prolonged mortality effects of extreme cold temperatures (Chen et al., 2022). It is important to note that this city does not have central heating as it lies south of the winter heating line. Generally, Suzhou residents may take effective and timely measures (e.g., drinking water, using air conditioners and fans, or reducing outdoor activity) to protect themselves from heat stress. However, they may not pay enough attention to the lagged and stronger health effects of extreme temperatures in winter, which might increase the cold-related mortality risk and disease burden. Therefore, public awareness and climate services should be improved to protect public health against the cold effects, even in the context of global warming.

Several potential mechanisms may be attributed to the temperature-related cardiopulmonary risks. Exposure to extreme heat may overwhelm the body's ability to regulate internal temperature (Ebi et al., 2021). On the other hand, the physiological thermoregulatory response to maintain body temperature triggers other types of physiological stress and may lead to cardiopulmonary events (The Lancet, 2021). Cold temperatures could increase the workload of the autonomic nervous system and circulatory system, leading to potential cardiovascular symptoms such as chest pain, arrhythmias, or elevated blood pressure (Ikäheimo et al., 2020). Moreover, cold temperatures may cause bronchoconstriction and dryness of the respiratory tract, which can result in respiratory symptoms, increase the risk of infection, and exacerbate the respiratory symptoms of chronic respiratory disease (D'Amato et al., 2018).

Our study found that females, the elderly and the less educated individuals are more sensitive to extreme temperature. Consistent with previous studies, extreme temperatures increase the risk of mortality with age (Liu et al., 2020; Wan et al., 2022). Compared to younger individuals, older adults may have a higher prevalence of underlying chronic conditions, such as hypertension, hyperglycemia, hyperlipidemia, and diminished lung function. Moreover, older adults may have a weakened capacity for thermoregulation, but they may not be sufficiently aware of the dangers of extreme temperatures to respond timely (Achebak et al., 2019). In line with other studies, individuals with lower levels of education are identified as vulnerable subgroup (Ellena et al., 2020). This may be due to lower socioeconomic status, limited access to healthcare, unhealthy behaviors, and increased exposure to extreme temperatures in their work environment (Linares et al., 2020). Finally, females were found to experience higher mortality risk for extreme temperatures (Petkova et al., 2021). The sex difference in temperature-related effect could stem from the differential physiological features, lifestyle, and behavioral factors (Yatim et al., 2021).

In the context of climate change, local governments should provide adaptation services to build resilience against the inevitable health impacts of non-optimal temperatures. Potential measures may include establishing long-term surveillance, early warning systems, and climate-resilient health systems, adapting the urban environment and surrounding landscape, and providing public health communication and education to enhance public awareness and engagement (Jay et al., 2021). Several low-cost, accessible, and sustainable individual-level protective measures are recommended, such as adjusting indoor temperature (e.g., using air conditioning for cooling or heating) and reducing outdoor activity to minimize exposure to extreme temperatures. Notably, more focus should be shifted towards implementing community-level preventive healthcare services for vulnerable subgroups. Furthermore, future public health plans are necessary to identify local priority actions (e.g., piloting central heating for Suzhou) to effectively mitigate the risks of climate change and extreme weather events.

Several limitations should be acknowledged. Firstly, this study relied on meteorological data from fixed-site monitoring stations closest to individual addresses instead of individual-level measurements, potentially introducing exposure measurement errors. However, this approach aligns with established practice in numerous epidemiological studies, and the exposure misclassification bias is more likely to be random and may underestimate the health effects (Guo et al., 2013). Secondly, our findings may not be fully generalizable to other regions because the current analyses were based on local data in Suzhou.

5. Conclusions

Our study provides local evidence of associations between non-optimal temperatures and increased risks of mortality from various causes in Suzhou, China. In addition to the immediate effect of heat, a more delayed and stronger effect of extreme cold temperatures was observed. To reduce the health risks associated with extreme temperatures, it is recommended that climate adaptation strategies be implemented at both community and individual levels.

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CRediT authorship contribution statement

Linchi Wang: Data curation. **Chunyan Huang:** Data curation. **Cong**

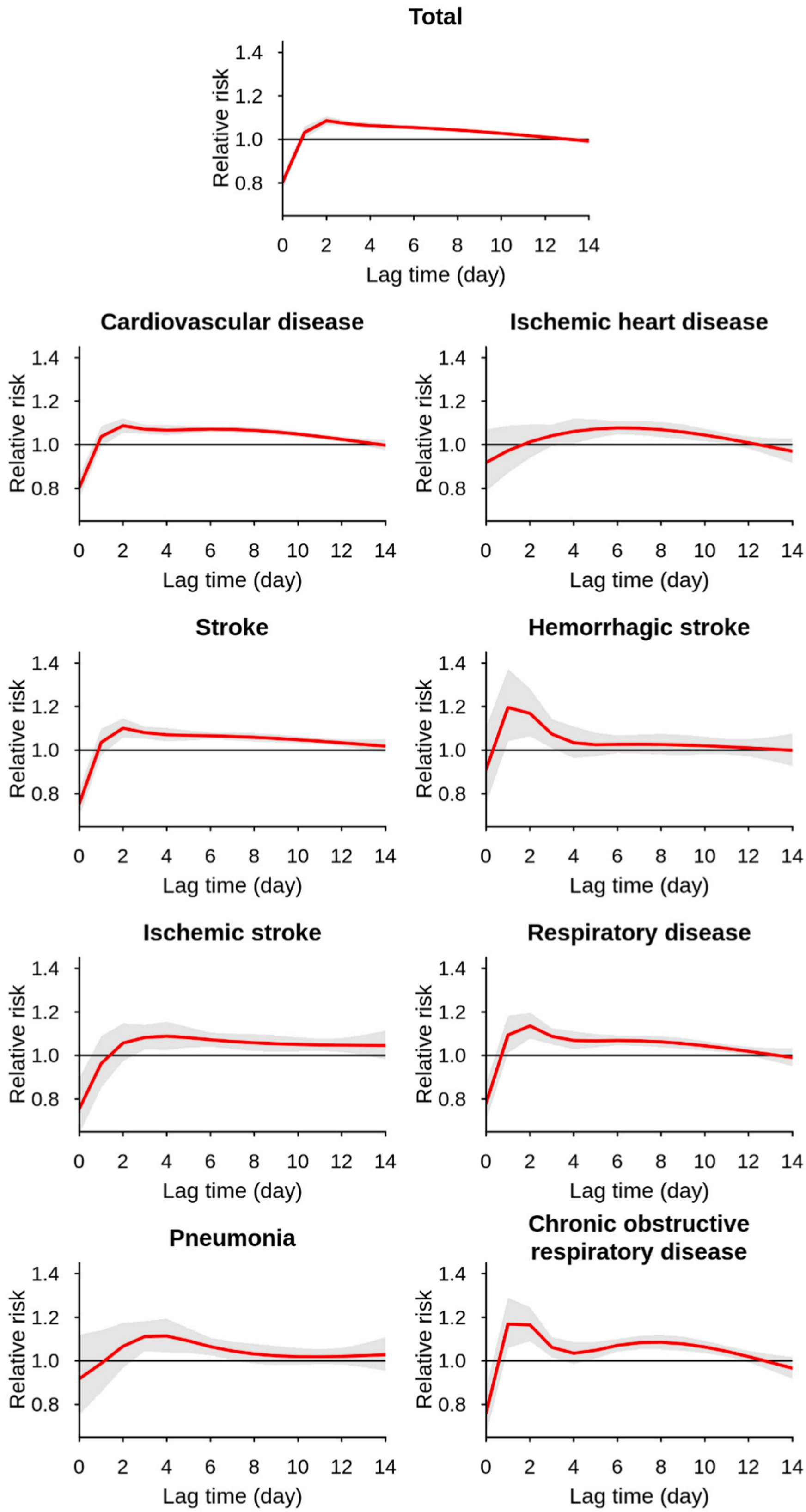

Fig. 2. Lagged associations of extreme cold effects on cause-specific mortality in Suzhou, China. Solid red lines = mean relative risks; gray areas = 95 % confidence intervals.

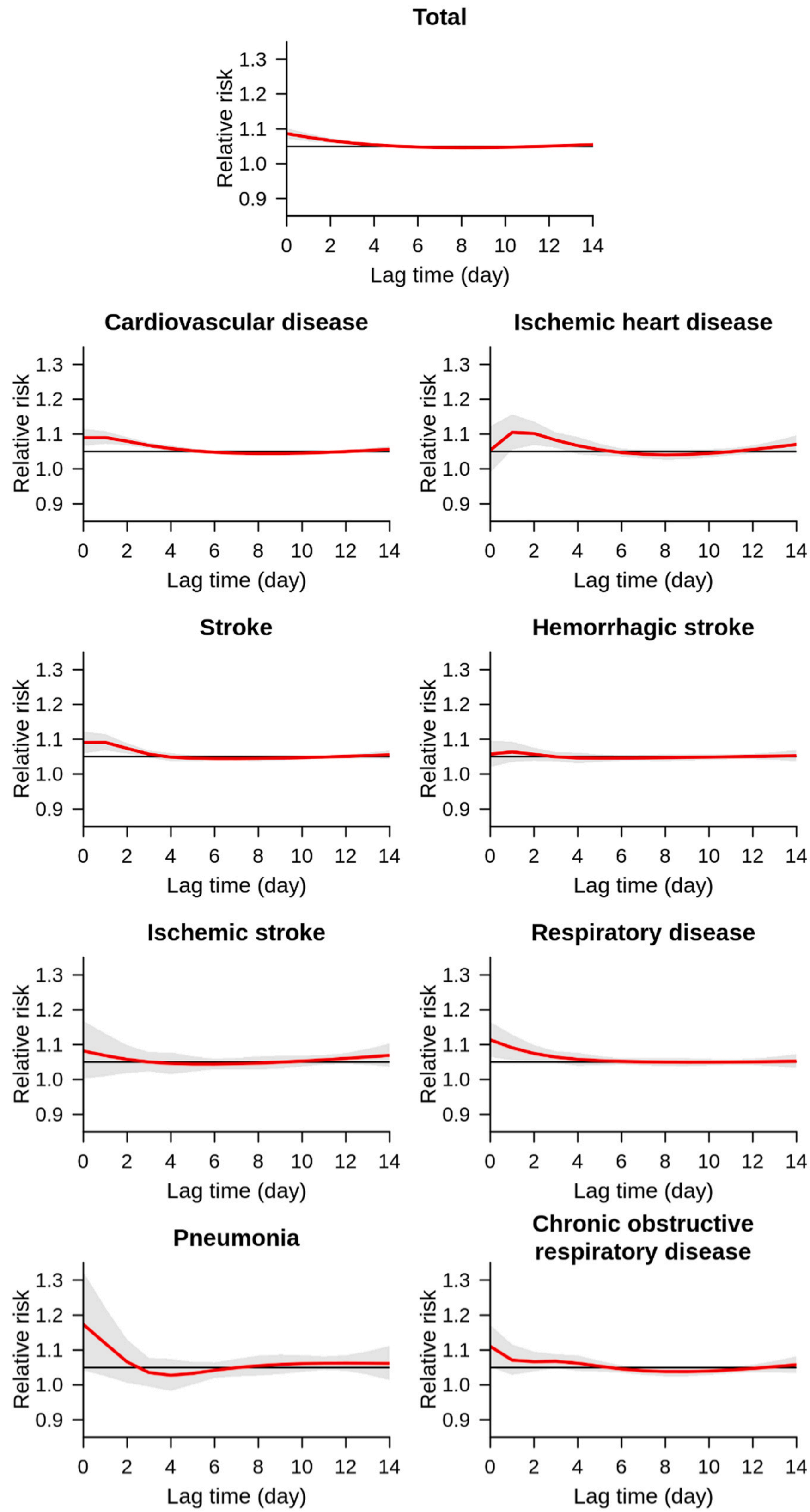

Fig. 3. Lagged associations of extreme hot effects on cause-specific mortality in Suzhou, China**.** Solid red lines = mean relative risks; gray areas = 95 % confidence intervals.

Liu: Writing – review & editing, Methodology. **Yan Lu:** Writing – review & editing, Supervision, Project administration, Funding acquisition. **Fang Liu:** Supervision, Project administration. **Haibing Yang:** Supervision, Project administration. **Yujie Hua:** Writing – original draft, Visualization, Formal analysis, Data curation. **Haitao Wang:** Writing – review & editing, Supervision, Project administration, Funding acquisition. **Haidong Kan:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. **Lu Zhou:** Writing – original draft, Visualization, Formal analysis, Data curation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Data availability

The data that has been used is confidential.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2024.116687.

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