Report

Ambient Temperature and Years of Life Lost: A National Study in China

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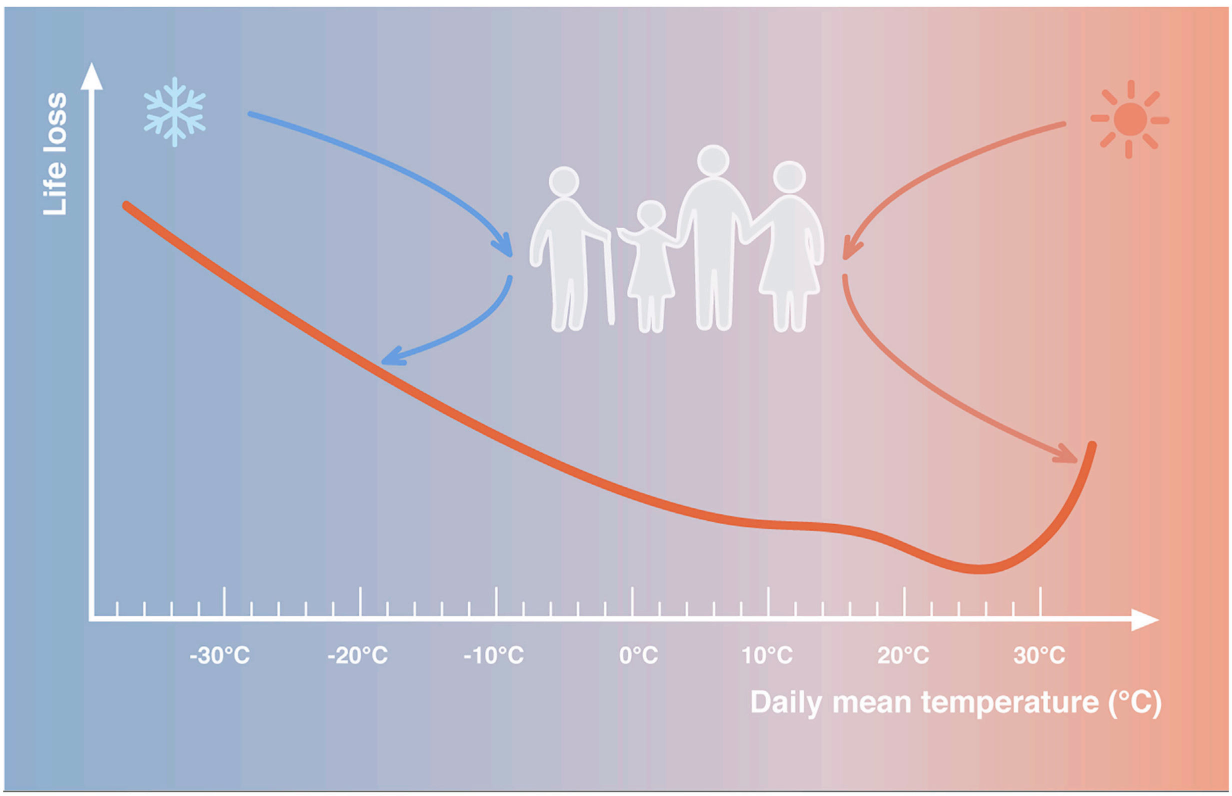
GRAPHICAL ABSTRACT



PUBLIC SUMMARY

- Years of life lost (YLL) is used to estimate the effects of temperature
- Both low and high temperatures can increase the YLLs
- Average 1.02 YLL per death is attributed to temperature exposure
- Temperature causes larger YLLs per death in males, younger people, and central China

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Although numerous studies have investigated premature deaths attributable to temperature, effects of temperature on years of life lost (YLL) remain unclear. We estimated the relationship between temperatures and YLL, and quantified the YLL per death caused by temperature in China. We collected daily meteorological and mortality data, and calculated the daily YLL values for 364 locations (2013–2017 in Yunnan, Guangdong, Hunan, Zhejiang, and Jilin provinces, and 2006–2011 in other locations) in China. A time-series design with a distributed lag nonlinear model was first employed to estimate the location-specific associations between temperature and YLL rates (YLL/100,000 population), and a multivariate meta-analysis model was used to pool location-specific associations. Then, YLL per death caused by temperatures was calculated. The temperature and YLL rates consistently showed U-shaped associations. A mean of 1.02 (95% confidence interval: 0.67, 1.37) YLL per death was attributable to temperature. Cold temperature caused 0.98 YLL per death with most from moderate cold (0.84). The mean YLL per death was higher in those with cardiovascular diseases (1.14), males (1.15), younger age categories (1.31 in people aged 65–74 years), and in central China (1.34) than in those with respiratory diseases (0.47), females (0.87), older people (0.85 in people ≥75 years old), and northern China (0.64) or southern China (1.19). The mortality burden was modified by annual temperature and temperature variability, relative humidity, latitude, longitude, altitude, education attainment, and central heating use. Temperatures caused substantial YLL per death in China, which was modified by demographic and regional characteristics.

KEYWORDS: TEMPERATURE; YEARS OF LIFE LOST; MORTALITY BURDEN; DISTRIBUTED LAG NONLINEAR MODEL; MULTIVARIATE META-ANALYSIS; CHINA

INTRODUCTION

In the 21st century, climate change presents a global public health concern.[1] In the context of climate change, the population around the world is becoming progressively more exposed to extreme temperatures.[2] Numerous epidemiological studies have demonstrated the associations between ambient temperature exposure and mortality and morbidity.[1,3–8] These studies have found that temperatures could increase the risks of mortality from cardiovascular, respiratory, cerebrovascular, and other causes.[9,10] However, most previous studies used death counts as a health outcome,[11] which may not adequately represent the actual mortality burden attributable to temperature, as it provides an equal weight to every death regardless of age. Although all lives are valuable, the loss of young lives results in a larger potential loss of social contributions.[12] Therefore, death counts may not capture the whole picture of mortality burden attributable to ambient temperature, which is not helpful for policy prioritization and decision making.

The years of life lost (YLL), an important component of disability-adjusted life years (DALYs), is an indicator of premature mortality. It considers the age at which a death occurs, and gives a greater weight to deaths at younger ages.[13] Some studies have argued that the YLL is better than the death count as an indicator when assessing the mortality burden attributed to ambient temperature.[14] However, few studies have estimated the exposure-response associations between temperature and YLL.[12,15–21] Moreover, most of these studies employed the daily overall YLL as a health outcome, and did not adjust for the offset effect of population size. As a result, the city- or community-specific association between temperature and YLL cannot be simply combined. Therefore, the extent to which temperature exposure reduces life expectancy needs more examination.

China is the world's most populous country with over 1.4 billion people. In the context of global warming, the annual average surface air temperature in China increased at a rate of 0.32°C per decade during the period from 1961 to 2017, which is higher than the global average (0.12°C/decade) from 1951 to 2010.[22,23] It is expected that the ambient temperature in China will continue to increase in the future.[23] Many previous studies have also estimated the exposure-response associations of temperatures with death counts in China.[9,24,25] However, the temperature-related mortality burden estimated using YLL has not been assessed in China.

In the current study, we employed a national dataset including 364 locations in China to examine the associations between temperature and YLL rates (YLL per 100,000 population) and to quantify the YLL per death

Table 1. General Characteristics of the Study Variables in 364 Locations across China

	Mean (SD)	Minimum	25th Centile	Median	75th Centile	Maximum
Daily nonaccidental YLL rate[a]						
Total	22.5 (23.4)	0.0	12.0	19.5	28.5	1,020.4
Cardiovascular disease	8.0 (12.5)	0.0	2.5	5.8	10.4	799.1
CED	3.9 (6.6)	0.0	0.0	2.3	5.3	324.3
Respiratory disease	2.2 (4.4)	0.0	0.0	1.0	3.0	620.4
Sex						
Male	26.6 (30.3)	0.0	11.6	21.9	35.0	1,826.0
Female	18.2 (24.6)	0.0	6.1	13.8	24.2	1,372.5
Age (years)						
0–64	13.9 (18.0)	0.0	4.2	10.8	19.2	994.7
65–74	69.7 (100.7)	0.0	0.0	54.0	97.2	4,824.5
$\geq$75	138.2 (142.3)	0.0	66.1	119.3	182.7	5,077.2
Region						
Northern	22.9 (15.9)	0.0	11.8	20.4	30.7	359.0
Central	24.7 (38.6)	0.0	11.9	19.2	28.0	1,020.4
Southern	21.6 (15.3)	0.0	12.1	19.4	28.3	928.5
Meteorological variable						
Daily mean temperature (°C)	15.9 (9.9)	−32.3	9.5	17.5	23.4	35.6
Daily maximum temperature (°C)	20.5 (10.0)	−27.2	14.1	22.3	28.1	41.2
Daily minimum temperature (°C)	11.8 (10.4)	−36.2	5.3	13.2	19.8	30.7
Temperature variability (°C)	9.3 (3.9)	0.3	6.3	9.4	12.3	23.2
Daily RH (%)	72.4 (15.6)	5.0	63.0	75.0	84.0	100.0
PM_{10} ($\mu g/m^3$)	81.6 (41.1)	8.3	51.4	76.7	103.0	767.3

[a]YLL rate was the average YLL per 100,000 population.

attributable to temperature. Our findings will provide deep understanding of the magnitude of adverse health effects caused by ambient temperature, which is important for risk communication and interventions to reduce the mortality burden due to temperatures because YLL is a better indicator than death count to estimate mortality burden attributed to ambient temperature.

RESULTS

General Characteristics of the Study Samples

Table 1 shows the general characteristics of the YLL rates (YLL per 100,000 population) and weather factors in the 364 study locations. The total YLL was 98.8 million, and the mean daily YLL rates for nonaccidental mortality, CVD-, cerebrovascular disease (CED)-, and RESP-related mortality were 22.5, 8.0, 3.9, and 2.2 per 100,000 per day, respectively. Geographically, the largest mean daily YLL rate was observed in central China (24.7), while the lowest was in southern China (21.6). The mean daily temperature, temperature variability, RH, and PM_{10} were 15.9°C, 9.3°C, 72.4%, and 81.6 $\mu g/m^3$, respectively. Daily temperature was significantly associated with daily temperature variability (r = −0.13, $p < 0.001$), RH (r = 0.24, $p < 0.001$), and PM_{10} (r = −0.32, $p < 0.001$) in all included locations. Other characteristics are shown in Table S1 and Figure S5.

Exposure-Response Associations of Temperatures with YLL Rates

Figure 1 shows a U-shaped cumulative exposure-response relationship between temperatures and YLL rates. The MYT was 27.4°C nationwide with a higher MYT in southern China and a lower MYT in northern China. Cold temperature had a larger impact than hot temperature on the overall YLL rates. The overall YLL rates attributable to cold were greater in low-latitude regions than in high-latitude regions, while reverse patterns were found for heat-related YLL rates. We observed similar association patterns between temperature and cause-specific YLL rates among different geographic regions of China. For instance, cold temperatures had greater effects on the YLL rate from CVD in southern China, and hot temperatures had bigger effects on YLL rates from CVD in northern China. Temperature had a greater impact on YLL rates in males, populations $\geq$65 years old, and people with CVD than on females, populations $\leq$65 years old, and those with respiratory disease. The effects of extreme cold were more pronounced and lasted longer than those of extreme heat (Figures S6 and S7).

Mortality Burden of Temperature Exposures

A mean of 1.02 (95% confidence interval [CI], 0.67–1.37) YLL per death was associated with temperature exposures nationwide, out of which 0.98 (95% CI, 0.65, 1.32) years were attributable to cold, particularly moderate cold (0.84; 95% CI, 0.52, 1.16). The mean YLL per death was higher in those with CED (1.37; 95% CI, 0.87, 1.87) or CVD (1.14; 95% CI; 0.77, 1.52) than in those with RESP (0.47; 95% CI, 0.26, 0.67), higher in the younger population (1.31 in people 65–74 years old; 95% CI, 0.75, 1.86) than in the oldest group (0.85 in people $\geq$75 years old; 95% CI, 0.64, 1.05), and higher in males (1.15; 95% CI, 0.71, 1.59) than in females (0.87; 95% CI, 0.43, 1.31) (Table 2 and S2). We found higher YLL per death in central China (1.34; 95% CI, 0.79, 1.89) than

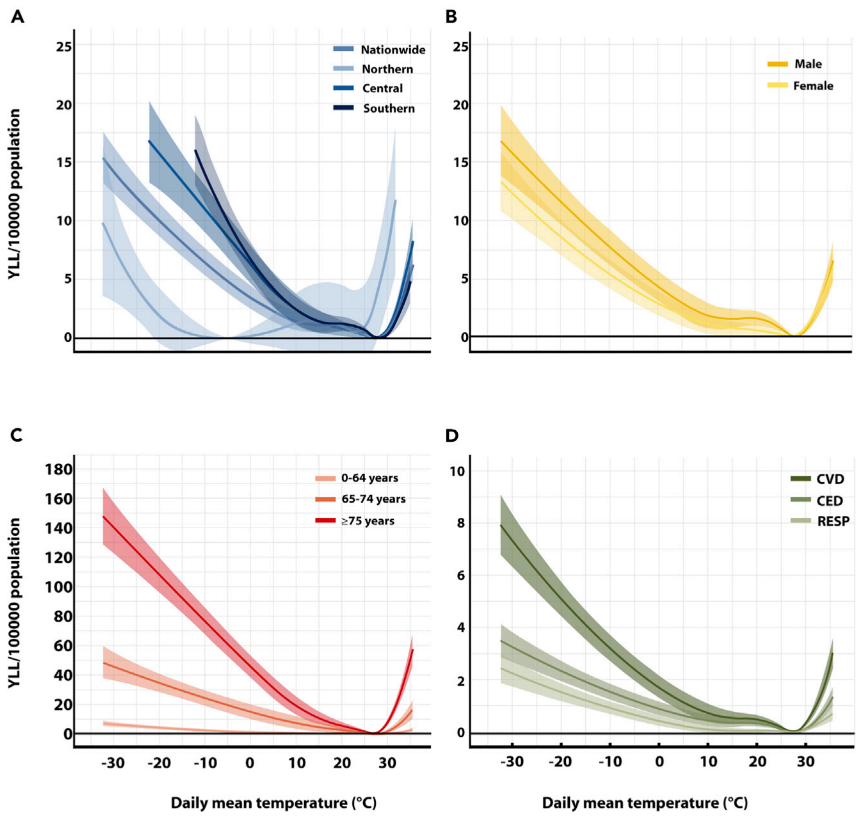

Figure 1. Pooled Cumulative Exposure-Response Relationships between Daily Mean Temperature and YLL Rate Over 0–21 Days lag in All 364 Locations and in Different Subgroups across China

in southern China (1.19; 95% CI, 0.70, 1.68) and northern China (0.64; 95% CI, −0.98, 2.26), which was consistent with the spatial distribution of annual mean YLL attributable to temperatures in China. The highest YLL values were found in Shandong Province (906,700), and the lowest burden was found in Hainan Province (21,100). At the city level, we found that Chongqing city had the largest mortality burden (217,800), and Sansha city in Hannan Province had the lowest mortality burden (20) (Figure 2).

Effect Modification Analysis

We observed an increase in YLL per death related to temperatures in locations with moderate annual temperatures, high annual temperature variability, low annual RH, moderate latitude, small longitude, high altitude, and a short central heating period. The urbanization rate, GDP per capita, and education level were found to have weak modification effects on the YLL per death (Figure S8).

Sensitivity Analyses

The associations of temperature with YLL per death were generally robust to the changes in df for seasonality. The cold-attributed YLL rate and MYT reduced with a smaller maximum lag day (Figure S9).

DISCUSSION

In this study, we found that temperatures were associated with an increased YLL rate, and a mean of 1.02 YLL per death was attributable to temperatures nationwide, with most from moderate cold. Higher YLL values per death caused by temperatures were found in individuals with CVD and CED than in individuals with RESP, in those from central China than in those from southern or northern China, in the group aged 65–74 years than in the group aged ≥75 years, and in males than in females. To the best of our knowledge, this is the first study involving a large number of locations and a large population size to estimate the temperature-related premature death indicated by YLL.

Although many studies have estimated the association between temperature and mortality rates,[9,25,26] few studies have assessed the relationship between temperature and YLL.[12,15–18] In this study, we used the YLL rate to quantify the association, and observed U-shaped relationships between ambient temperatures and YLL rates with higher cold effects, which is consistent with several previous studies using death counts.[27,28] Furthermore, we found higher MYTs and larger cold effects in southern China than in northern China, which also confirmed a similar pattern of minimum mortality temperature (MMT) in previous studies.[24,29,30] For example, Ma et al.[24] observed in 17 large Chinese cities that the MMT increased with decreasing latitude, with a Spearman correlation coefficient equal to 0.62. The spatial heterogeneity of cold effects is partially due to the differences in geography, adaptative capacity, and climatic characteristics among regions.[29,31] For example, people in northern China generally have central heating in the winter season.[32] The meta-regression results in this study also showed a lower mortality burden per death in locations with a central heating system than in other locations (Figure S8).

Our study first reported the mean YLL per death caused by temperature. We found that a mean of 1.02 YLL values per death was caused by exposure to temperature during the study period. We also analyzed YLL caused by different components of temperature, and found that cold temperatures, particularly moderate cold temperatures, were mainly responsible for the effects. Using mortality as the outcome, Chen et al.[9] also found that moderate cold contributed to the largest fraction (ranging from 64.55% to 80.57%) of total temperature effects with only a small fraction of mortality effects from extreme cold (5.8%–10.16%) or extreme heat (2.73%–4.90%). The large fraction of moderate cold effects is related to the high frequency of moderate cold temperatures and their prolonged lag effects. The results of YLL per death caused by temperatures increase the body of evidence for the public and policy makers to better understand the magnitude of the health effects from temperature exposures and which populations and where are most at risk.

Previous studies based on daily mortality rates have found that exposure to temperature has a greater effect on females than on males.[9,10] In contrast, we found a greater YLL per death in males than in females. This result indicates that the impact of temperatures on mortality burden was greater for males than for females.[10] The reasons for this sex difference are not totally

Table 2. YLL per Death (Years, 95% CI) Attributable to Temperatures in China

	MYT (°C)	Total	Cold	Heat
Causes of death				
Total mortality	27.4	1.02 (0.67, 1.37)	0.98 (0.65, 1.32)	0.04 (0.03, 0.05)
CVD	27.3	1.14 (0.77, 1.52)	1.1 (0.74, 1.46)	0.05 (0.03, 0.06)
CED	27.6	1.37 (0.87, 1.87)	1.33 (0.84, 1.82)	0.04 (0.02, 0.05)
RESP	26.8	0.47 (0.26, 0.67)	0.43 (0.24, 0.61)	0.04 (0.02, 0.06)
Geographic regions				
Northern	−5.2	0.64 (−0.98, 2.26)	0.56 (−0.83, 1.96)	0.07 (−0.15, 0.3)
Central	27.5	1.34 (0.79, 1.89)	1.28 (0.75, 1.82)	0.06 (0.04, 0.08)
Southern	28.1	1.19 (0.70, 1.68)	1.16 (0.69, 1.64)	0.02 (0.01, 0.04)
Age of death (years)				
0–64	27.9	1.08 (0.46, 1.71)	1.04 (0.44, 1.65)	0.04 (0.02, 0.07)
65–74	27.1	1.31 (0.75, 1.86)	1.27 (0.73, 1.81)	0.03 (0.02, 0.05)
≥75	26.8	0.85 (0.64, 1.05)	0.81 (0.62, 1.01)	0.03 (0.03, 0.04)
Sex				
Male	27.8	1.15 (0.71, 1.59)	1.12 (0.69, 1.55)	0.03 (0.02, 0.04)
Female	26.9	0.87 (0.43, 1.31)	0.82 (0.4, 1.24)	0.05 (0.03, 0.07)

clear. Compared with females, males are more likely to have poor diets and unhealthy lifestyles, more mental stress, and other aspects of exposure such as occupational exposure to hazardous substances.[33] Males therefore may be more susceptible to ambient temperature, and have a shorter life expectancy, which makes higher YLL values for males. In addition, it was suggested that females may have an innate enhanced potential to withstand immune challenges due to more highly activated innate immune pathways,[34] which may attenuate the effects of inflammation induced by temperatures.[35] Therefore, while using YLL per death as a measure, we should give more attention to males in planning public health interventions to mitigate the impact of temperature.

We also found some significant regional modifiers of YLL per death caused by temperatures, including annual mean temperature, temperature variability, and RH, latitude, longitude, altitude, level of education, and usage of central heating. These findings could not only help explain the spatial heterogeneous of temperature-related effects but also provide important information for policy makers to plan specifically tailored preventive actions to reduce the health impacts of temperatures.

This study also estimated the annual mean mortality burden attributable to temperatures at the province and city level in China, and observed substantial mortality burden caused by temperatures, particularly in central China. These findings have important implications for further understanding of the health impacts of temperatures. In the context of global warning, temperature-related deaths may increase in future in China.[36] In addition, the rapid urbanization and population aging process may increase the impacts of temperature on human health.[18,37] Therefore, efforts to adapt to climate change and reduce its health impacts are urgently needed in China. Chinese governments have conducted enormous health adaptation efforts to respond to climate change, including adaptation policies, health warning systems, risk communication, and the provision of healthcare and social services.[38] However, there remain challenges for adaptation to climate change in China. For example, the integration or better collaboration across multiple government departments and improved community participation are needed to advance adaptation to climate change, and more research on adaptation interventions and their benefits and negative impacts is needed.

Strength and Limitations

The present study has several strengths. First, this study employed a large database with good-quality data, which increases the generalizability of our findings. Second, we applied a population-adjusted YLL rate to estimate the associations of temperature with the YLL rate, which was used to combine temperature effects across locations. Third, we estimated the mean YLL per death resulting from temperature. These measures provide novel insights because they provide an intuitive understanding of the health impact of temperature.

This study also has several limitations. First, similar to many previous studies, it was inherently an ecological study. Our findings should thus be interpreted with caution. Second, more locations were selected in several southern provinces in China, which may lead to selection bias in the results, such as the MYT and meta-regression results, since these five provinces may have more weight than the other provinces. For example, the higher MYT found in this study than in previous studies may be related to the unbalanced selection of locations.[4,9] Third, climate change is a global public health concern. The present study included only locations in China (except for Hainan Province), which may limit the generalizability of our findings to other countries and regions. Fourth, we divided all study locations into three major zones based on their latitudes, which may potentially mask the difference in climate variability between provinces within the same zone. However, a meta-regression analysis was used to examine the effects of several location-level characteristics on the association of temperature with YLL rates. Fifth, we did not include the same study period in all locations due to the unavailability of mortality data. However, a study conducted in Shanghai indicated that both hot and cold effects on mortality did not substantially change during 2001–2012.[39] Sixth, cancer is ranked top in the cause-of-death spectrum across many countries in the world.[40] However, we did not estimate the association of temperature with cancer mortality in this study because daily cancer mortality data were not collected. Finally, the study locations were selected from both the DSPS and provincial mortality surveillance system. Although the provincial mortality surveillance system followed the DSPS standards, disparity between the two systems may potentially lead to bias.

Conclusions

Temperatures, especially moderate cold, have been found to be associated with substantial mortality burden of 1.02 YLL per death in China. The mortality effects of temperatures were modified by demographic and regional characteristics. Our findings add to the increasing body of knowledge to better inform policy making and adaptation intervention in the context of climate change.

MATERIALS AND METHODS

Study Location Selection

Study locations in Yunnan, Guangdong, Hunan, Zhejiang, and Jilin provinces during 2013–2017 were selected from provincial mortality surveillance systems. Locations in other provinces during 2006–2011 were obtained from China's Disease Surveillance Points System (DSPS) (see the Appendix).[25,41] The DSPS is administered by the Chinese Center for Disease Control and Prevention (China CDC), and the provincial mortality surveillance system was administered by the provincial CDC following the same protocol as that of DSPS. At each surveillance point, all deaths certified by clinical doctors or local CDC professionals are reported to the DSPS using an internet-based reporting system. The data from the DSPS have been widely applied in policy making and disease burden assessment.[9,25,42]

To ensure adequate statistical power, study locations from both provincial surveillance systems and DSPS were selected if they met either or both criteria: (1) a population size >200,000, and (2) an annual mortality rate >4‰.[25] We set these two criteria because time-series analyses depend on both good quality of mortality data and adequate daily number of deaths. A total of 364 locations were selected and categorized into three groups:[43] northern China (latitude ≥40°; 46 locations), central China (latitude ≥30° and <40°; 72 locations), and southern China (latitude <30°; 246 locations) (Figure S1). A total of 203.7 million people permanently live in the study locations.[42]

Data Collection

Daily nonaccidental mortality data during 2013–2017 were obtained from the corresponding provincial CDCs in the above five provinces. However, we only obtained the

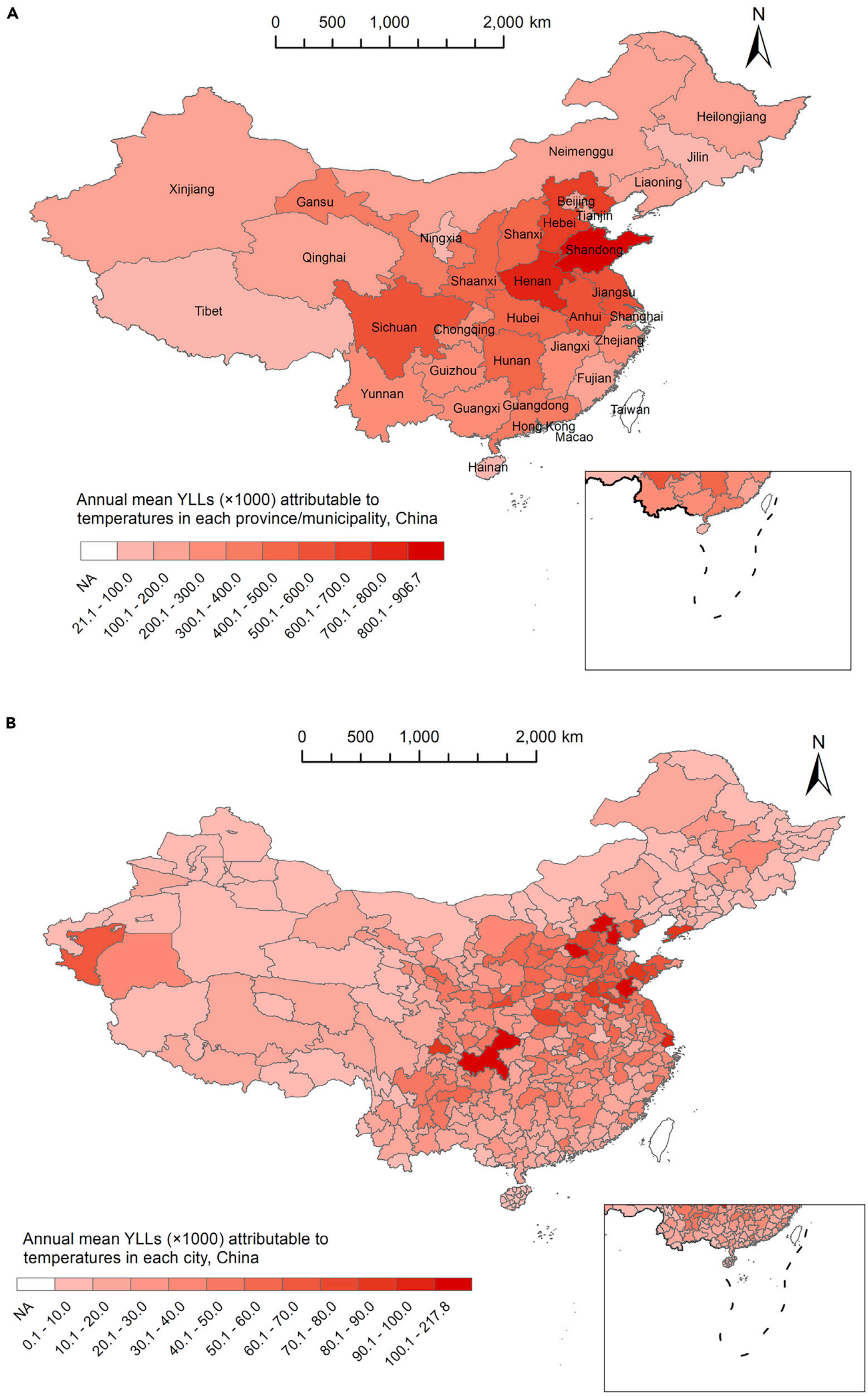

Figure 2. Spatial Distribution of Annual Mean YLL Attributable to Temperatures in China (A) At the provincial level. (B) At the city level.

daily mortality data during 2006–2011 in locations beyond the five provinces.[25] Therefore, there are two study periods in this study. The population and mortality data of all provinces were obtained from the 6th national population census conducted in 2010 (Census data: http://www.stats.gov.cn), which was used to calculate male and female life tables (<1 year, 1–4 years, and every 5 years from ages 5 to 100+ years) of each province using the methods provided by the World Health Organization.[44] We then calculated the individual YLL by matching the death age and sex of each individual record to the province-specific life table. All deaths were classified into groups according to the International Classification of Diseases, 10th revision (ICD-10) categories: non-accidental causes (codes: A00-R99), cardiovascular disease (CVD, codes I00-I99), respiratory disease (RESP, codes J00-J98), and cerebrovascular disease (RED, codes I60–I69). The daily total YLL for each cause was calculated by summing the YLL for all deaths on the same day. We also calculated the daily YLL by sex and age group (0–64 years, 65–74 years, and ≥75 years).

The annual mean population size during 2013–2017 for each study location in the five provinces was obtained from national or local statistical yearbooks, and population data for the other study locations were extracted from the 6th national population census, conducted in 2010 (Census data: http://www.stats.gov.cn). Based on these data, we calculated the daily YLL rate (YLL per 100,000 population) by dividing the daily recorded YLL by the corresponding population size of each location, which was used to estimate the association of temperature with YLL. Then, the association in every location was combined in a multivariate meta-analysis model. We also collected the annual mean population size during 2013–2017 for each city in China, which was used to estimate the total mortality burden in China.

Daily meteorological data including mean temperature and relative humidity (RH) from 698 weather stations across China were extracted from the China Meteorological Data Sharing Service System (Weather data: http://data.cma.cn/). We employed the Australian National University Splines (ANUSPLIN) thin plate smoothing software to interpolate the daily mean temperature, TMax, TMin, and RH at a $0.01^\circ \times 0.01^\circ$ resolution across China. The results of 10-fold cross-validation showed that the R^2 values of the daily mean temperature, TMax, TMin, and RH were 0.96, 0.94, 0.94, and 0.81, respectively, and the corresponding root mean squared errors (RMSEs) were 2.37°C, 2.8°C, 2.8°C, and 7.7%. These results suggest good prediction accuracy of the interpolation method (see the Appendix).[45] We obtained the daily mean temperature, TMax, TMin, and RH of the grids where each selected location overlapped. We then calculated the daily temperature variability by estimating the standard deviation of daily maximum and minimum temperatures ($TMax_{lag0}$, $TMax_{lag1}$, $TMin_{lag0}$, and $TMin_{lag1}$) of the preceding 2 days.[46] Here, we calculated the daily temperature variability as a potential cofounder of mean temperature, because previous studies showed that temperature variability was also an independent risk factor for mortality.[46,47]

The values of the daily mean particulate matter with an aerodynamic diameter of 10 μm or less (PM_{10}) during 2006–2017 were obtained from the China National Environmental Monitoring Center. Since some studied locations were not covered by the air quality monitoring system, we employed a land-use-regression model to assess the daily PM_{10} value at each location using the following predictors: daily mean temperature, daily RH, latitude, longitude, altitude, population density, road density, types of land use, and gross domestic product (GDP) per capita. The fitness results showed that the R^2 was 73.90%, and the RMSE was 16.49 $\mu g/m^3$. The method has been described in our previous study[48] (see the Appendix).

The GDP per capita in 2010 for each location was obtained from the Data Center for Resources and Environmental Sciences (GDP data: http://www.resdc.cn). Other 2010 city-level characteristics, including the urbanization rate, mean years of education, and use of central heating, were collected from national and provincial statistical yearbooks.

We collected the daily mean temperatures, population size, and its components in each city during 2013–2017, using the same methods mentioned above. Based on the regional exposure-response associations between temperatures and the YLL rate in 364 locations, we estimated the annual mean YLL attributable to temperatures in each city in China.

Statistical Analysis

We used a two-stage approach in our study. In the first stage, we used a distributed lag nonlinear model (DLNM) linked with a Gaussian distribution function to estimate the associations of temperature with the YLL rate in each location.[49] A cross-basis function was introduced to model the nonlinear and lag associations of temperature and temperature variability with the YLL rate, in which the temperature variability was adjusted for as a potential confounder. The DLNM can optimally adjust for other confounders, including those that change slowly over time expressed as seasonality, day of the week (DOW), other meteorological factors (e.g., RH), and air pollutants (e.g., PM_{10}). We employed a natural cubic B-spline (ns) of time with seven degrees of freedom (df) per year to control for the seasonal and long-term trends in mortality, a categorical variable to control for the DOW, and a linear model to control for the same day PM_{10} concentration. An ns was also employed to adjust for the potential confounding effect of the present day RH with three df in the ns function, which can estimate the nonlinear effects of the RH on the YLL rate in the same day.[9] We used 21 days as the maximum lag period for both mean temperature and temperature variability.[4,25,46,48,50]

In the second stage, we employed a multivariate meta-analysis to combine the location-specific cumulative associations of temperatures with the YLL rate at 21 lag days.[51] The MYT (minimum YLL temperature) was identified in the combined curves of the YLL rate with temperature (see the Appendix).

Based on the overall cumulative YLL rate of temperature devised from the combined curve, we estimated the mean YLL per death caused by temperature and its components. We divided daily mean temperatures into four components, namely extreme cold, moderate cold, moderate heat, and extreme heat (defined as ≤2.5th percentile, the 2.5th percentile to the MYT, MYT to the 97.5th percentile, and >97.5th percentile of temperature, respectively). Similarly, we applied regional cumulative exposure-response associations between temperature and YLL rate to the daily mean temperatures and population data in each city (see the Appendix).

A univariable meta-regression model was employed to explore the impacts of location-level characteristics on YLL per death caused by temperature. These location-level variables included were the urbanization rate, mean years of education, annual mean temperature, annual mean temperature variability, annual mean RH, latitude, longitude, altitude, GDP per capita, and central heating.

All analyses were performed using R software (version 3.5.0, R Foundation for Statistical Computing, Vienna, Austria). The dlnm and mvmeta packages were the primary packages used. Two-tailed p values < 0.05 were considered to be statistically significant. All codes are available at https://github.com/gztt2002/YLL-of-Tm-and-Tv.

Sensitivity Analyses

A series of sensitivity analyses were conducted to test the robustness of the estimates nationwide. We employed alternative maximum lag periods of 14 and 28 days, and changed the df of time from 6 to 8 per year.

WEB RESOURCES

The mortality data can only be applied for through a government data sharing portal (www.phsciencedata.cn/Share/edtShare.jsp) or from the provincial mortality surveillance system. Data on the environment and location characteristics are available on the government's statistic yearbooks or websites listed in the methods section. All codes were available in https://github.com/gztt2002/YLL-of-Tm-and-Tv.

ETHICAL APPROVAL

This study was approved by the Ethics Committee of Guangdong Provincial Center for Disease Control and Prevention (2019025). Data were analyzed at aggregate level and no participants were contacted.

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AUTHOR CONTRIBUTIONS

T.L., C.Z., H.Z., and B.H. are joint first authors. W.M. (mawj@gdiph.org.cn), M.Y., and M.Z. contributed equally to the correspondence work. W.M., M.Z., M.Y., C.Z., H.Z., and B.H. set up the collaborative network. T.L., C.Z., H.Z., and B.H. performed the statistical analysis and took the lead in drafting the manuscript and interpreting the results. T.L. provided substantial scientific insight into the interpretation of the results and drafting of the manuscript. Yanjun Xu, L.L., L.W., R.H., Z.H., Y. Xiao, J.L., X.X., D.J., M.Q., Q.Z., W.G., P.Y., Yiqing Xu, J.H., J.X., W.Z., X.L., S.C., L.G., Z.R., Y.Z., C.H., Y.D., S.R., and Y.G. provided the data and contributed to the interpretation of the results and the preparation of the submitted version of the manuscript. All authors contributed to the development of the manuscript and approved the final draft. W.M., M.Y., and M.Z. are study guarantors. The corresponding authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

DECLARATION OF INTERESTS

The authors declare no competing interests.

SUPPLEMENTAL INFORMATION

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Supplemental Information

Ambient Temperature and Years of Life Lost: A National Study in China

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Supplemental Information

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1.Supplementary text

1.1 China's Disease Surveillance Points system and study location selection

The China's Disease Surveillance Points System (DSPS) is administrated by the Chinese Center for Disease Control and Prevention (China CDC). This system selected county and district across China as surveillance points. Currently, the DSPS has included 605 districts and counties comprising 21.1% of all counties and districts in China, and covers a population of 323.8 million (24.3% of the total population). To ensure the representativeness of surveillance points, all selected counties and districts are evenly distributed across different geographical areas with different characteristics.[1] At each surveillance point, all deaths certified by clinical doctors or local CDC professionals are reported to the DSPS in real time using an internet-based reporting system. The data from the DSPS has been widely applied in policy making and disease burden assessment.[2]

Although the DSPS covers a wide range of China territory, and can well represent the Chinese population, many surveillance points especially in western China have small population sizes, and the quality of mortality data were relatively poor which could be indicated by recorded low mortality rate (<5‰). The time-series analyses depend on both good quality of mortality data and adequate daily number of deaths. The small number of daily deaths caused by poor quality of mortality data or small population size may lead to biased associations of temperatures with YLL rates. In the present study, we therefore added surveillance points with good quality of data, which were selected from several provincial mortality surveillance system (Yunnan, Guangdong, Hunan, Zhejiang, and Jilin provinces). To ensure adequate statistical power, surveillance points from both provincial surveillance system and the DSPS were selected if they met anyone or both criteria: a) a population size >200,000, and b) an annual mortality rate >4‰. Under these two criteria, the daily average death count was larger than three, which was consistent with a previous similar study conducted in China.[3]

1.2 Interpolation of daily meteorological factors

We employed the Australian National University Splines (ANUSPLIN) thin plate smoothing software to interpolate the daily nationwide mean temperatures in China. The model was as follows:

$$Temp_i = f(lat_i, lon_i) + b \times alt_i + e_i \qquad \text{(Equation 1)}$$

Where $Temp_i$ denotes the daily mean temperature at station i. $f()$ denotes the thin plate function. lat_i, lon_i and alt_i are the latitude, longitude, and altitude for station i. b denotes the coefficient for alt_i, and e_i denotes the error term at station i. Using this method, daily temperatures across China were obtained at a resolution of 0.01°×0.01°. The results of 10-fold cross-validation show good prediction accuracy of the interpolation method for daily mean temperature [R^2 = 0.96, root mean squared prediction error (RMSE) = 2.37°C]. In the process of 10-fold cross-validation on the model, we selected only the 15th day in the following months: January 2006, February 2007, March 2008, April 2009, May 2010, July 2011, June 2012, August 2013, September 2014, October 2015, November 2016, and December 2017; this was done as the inclusion of all study days during 2006-2017 would be time-consuming. We employed this method also to interpolate the daily nationwide relative humidity (RH), daily maximum temperatures (TMax) and daily minimum temperatures (TMin) in China. The results of fitting performance show that the R^2 of RH, TMax and TMin were 0.81, 0.94 and 0.94, respectively (Figure S2).

1.3 Daily PM_{10} estimation using a land-use-regression (LUR) model

We selected the PM_{10} as an agency of air quality during the entire study period (2006-2017), and adjusted for it in the DLNM assessing the associations of temperatures with YLL rates. PM_{10} is the only ambient air pollutant obtained during 2006-2012 in this study. Daily average PM_{10} during the 2013-2017 were obtained from the National Urban Air Quality Real-time Publishing Platform (http://106.37.208.233:20035/), which is administrated by the China National Environmental Monitoring Centre. The platform was put in operation since January 2013, and displays real-time concentrations of criteria air pollutants in all state-controlled monitoring stations. Daily average PM_{10} during 2006-2012 were obtained from the China National Environmental Monitoring Centre. The 24-h mean concentrations for PM_{10} were simply averaged from all valid monitoring sties in a city. Since some selected locations were not covered by the air quality monitoring system, we employed a random forest model to assess the daily PM_{10} at each location.

First, we extracted the latitude, longitude and altitude of each included air quality monitoring station across China, and extracted the daily mean temperature, and relative humidity at each monitoring station during the study period from the interpolated data in the appendix section 1.2. We also extracted the population density, length of road, types of land use (farm land, cropland, forest land, water area, and living land) and GDP per capital at each monitoring station using a radius of 1,300 meters, which was chosen based our previous studies.[4 5] The population density data in 2015 were obtained from GeoData Institute in University of Southampton (www.worldpop.org.uk), and the geographic information system (GIS) covariates (geographic map, road density, land use data and GDP per capita) were obtained from the Data Center for Resources and Environmental Sciences (http://www.resdc.cn). Then we established a LUR model implemented by a random forest model to input the above prepared predictors of all air quality monitoring stations and the daily PM_{10} data. One smooth temporal basis function was included in the model to fit the long-term and seasonal trend of PM_{10} concentrations (Figure S3). The results of fitness showed that the R^2 was 73.90%, and the RMSE (Root mean square error) was 16.49 µg/m^3 (Figure S4). We then extracted the daily mean temperature, relative humidity, latitude, longitude, altitude, population density, road density, land use data and GDP per capita at the center of each selected location, and put them into the established LUR model. Finally, we can obtain the daily mean PM_{10} concentrations during the study period at each location.

1.4 Estimation of the associations of temperatures and TVs with YLL rates

A two-stage approach was employed in our study. In the first stage, we employed a distributed lag nonlinear model (DLNM) to estimate the nonlinear and lag effects of mean temperature on daily YLL rates. The location specific association of temperate with daily YLL rates is entirely defined by a set of parameters namely regression coefficients in the function chosen for representing the associations. The model was as follows:

$$E(YLL_t) = \alpha + \beta_1 T_{1,t,l}(\mathrm{TM}) + \beta_2 T_{2,t,l}(\mathrm{TV}) + ns(\mathrm{RH, df}) + \beta_3 \mathrm{PM}_{10} + ns(\mathrm{time}_t, \mathrm{df}) + \eta\mathrm{DOW} + e \qquad \text{(Equation 2)}$$

Where t denotes the day of observation, YLL_t denotes the expected YLL rate on day t, which was calculated by dividing the daily observed YLL_t by the total population size (/100,000) in each included location. Therefore, the YLL rate included in the DLNM was the daily YLL in every 100,000 population (YLL/100,000); α denotes the intercept indicative of baseline risk; e denotes a Gaussian error. TM denotes the daily mean temperature. $T_{1,t,l}$ is a matrix obtained by applying the DLNM to mean temperature, and $T_{2,t,l}$ is a matrix obtained by applying the DLNM to TV that is adjusted for as a cofounding factor; β_1 and β_2 denotes the vector of coefficients for $T_{1,t,l}$ and $T_{2,t,l}$, respectively, and l denotes the number of lag days; β_3 denotes the coefficient of daily PM_{10} concentrations; e denotes the error term. To ensure that the meta-analysis can provide meaningful and interpretable results in the second stage, we employed the same function by placing the internal and boundary knots at the same temperatures in all location-specific models. In particular, a quadratic B-spline (*bs*) and natural cubic B-spline (*ns*) were employed to estimate the nonlinear and lagged effects of mean temperature and TV, respectively. In the *bs* function, three internal knots placed at the 10th, 50th and 90th centiles and boundary knots placed at the average minimum and maximum temperatures of location specific temperature distributions were used to model the association of nonlinear curves of mean temperature and TV with the YLL rate. In the *ns* function, an intercept and three internal knots placed at equally spaced values was used to model the lagged effects of temperature and TV. We used a maximum lag period of 21 days to capture the long-term delay of the impact of cold, and also excluded the impact of the harvesting effect. The nonlinear associations of mean temperature and TV with the YLL rate can be interpreted as the effect of the exposure versus a reference which is usually centered on a specific value.[6]

In all epidemiological studies, a basic issue is to control properly for potential confounding. The DLNM model can optimally adjust for confounders including those which change slowly over time (e.g. age, socioeconomic status) expressed as seasonality or long-time trends, day of week (DOW), other meteorological elements, and air pollutants.[7] Additionally, the time-series study design can control for the individual level risk factors such as smoking and alcohol consumption, because these factors at the population level do not vary from day to day, and hence will not influence the short-term effects of temperatures on mortality.[8] Consistent with previous studies,[9 10] we employed a *ns* of time with seven degrees of freedom (*dfs*) per year to control for the seasonal and long-term trends in mortality, a categorical variable to control for the day of the week (DOW), and a linear model to control for the same day PM_{10} concentration. DOW was a dummy variable representing the day of the week, and η was a vector of coefficients. It has been demonstrated that RH is an important contributor to heat stress.[11] We also employed a *ns* to adjust for the potential confounding effect of the present day RH with three *df*s in the *ns* function, which could estimate the nonlinear effects of RH on the YLL rate in the same day.[3] Three internal knots placed at equally spaced values was used to model the nonlinear effects of RH. The family function for DLNM had a Gaussian distribution.

In the second stage, we employed a multivariate meta-analysis method to combine the location-specific 0-21 days' lag in cumulative associations of temperature with the YLL rate.[12]

Multivariate meta-analysis is a method originally developed to pool multiple correlated outcomes in randomized controlled trials. Here it is used to combine the location-specific nonlinear exposure-response curves which are described with function defined by multiple parameters. The multiple parameters obtained from the first stage were used as outcomes for the multivariate meta-analysis, which aims to define an average exposure-response association across the locations, test and quantify the amount of heterogeneity, and further identify the sources of the heterogeneity. Here, in contrast to the original setting of randomized controlled trials, it is not necessary that the parameters are individually interpretable, and the associations is instead characterized through their joint distribution. The multivariate meta-analysis model can be written as follows:

$$\hat{\theta}_i \sim N_k(\theta, S_i + \psi) \qquad \text{(Equation 3)}$$

with $S_i + \psi = \Sigma_i$. The marginal model has independent within-location and between-location components. In the within-location component, the estimated $\hat{\theta}_i$ is assumed to be sampled with error from $N_k(\theta_i, S_i)$, a multivariate normal distribution of dimension k (k is 5 in the present study), where θ_i is the vector of true unknown outcome parameter for location *i*. In the between-location component, $\hat{\theta}_i$ is assumed to be sampled from $N_k(\theta, S_i)$, where ψ is the unknown between-location (co)variance matrix. θ here can be interpreted as the population-average outcome parameters, namely the coefficients of the function s defining the average exposure-response association. A restricted maximum likelihood (REML) method was used to combine the location specific exposure response associations.

The MYT (minimum YLL temperature) was re-centered based on the location-specific MYT identified in the first stage. We specified the combined exposure-response curves with three internal knots (the 10th, 50th and 90th centiles) and two boundary knots (the average minimum and maximum temperatures of location specific temperature distributions). This choice could generate the combined exposure-response curves with the uniform distribution of mean temperatures at national or regional levels. In order to reduce the heterogeneity between locations and uncertainty in the first-stage model, we used a best linear unbiased prediction (BLUP) model to generate the adjusted location-specific exposure-response curves.[12] The BLUP approach made use of a trade-off between the city specific association and the second stage pooled estimation, which could thus provide more precise estimations, especially in cities with small numbers of deaths. We also provided the lag patterns in YLL rates associated with the average extreme cold temperature (2.5th centile), and extreme hot temperature (97.5th centile).

1.5 Calculations of the YLL per death due to temperatures

The YLL per death (YLL*per*) caused by temperatures was calculated using the following two equations:[13]

$$YLL_{tem} = \sum_{i=TMin}^{I=TMax} YLL' \times Freq \qquad \text{(Equation 4)}$$

Where, YLL_{tem} denotes the total YLLs attributable to temperatures in every 100,000 population in a study location. *TMin* denotes the minimum daily temperature, and *TMax* denotes the maximum daily temperature in an included study location. *YLL'* denotes the YLL rate attributable to each temperature, which could be estimated by Equation 2. *Freq* denotes the frequency of each TM in an included study location.

$$YLL_{per} = YLL_{tem}/N \qquad \text{(Equation 5)}$$

Where YLL_{tem} is calculated in Equation 4, and *N* denotes the number of deaths in every 100,000 population in a study location.

1.6 Calculations of the annual mean YLL due to temperatures in China

The annual mean YLL (YLL_{city}) caused by temperatures in each city was calculated using the following equation.

$$YLL_{city} = YLL_{tem} \times Pop/5 \qquad \text{(Equation 6)}$$

Where YLL_{tem} denotes the total YLLs attributable to temperatures in every 100,000 population in a study location, which is calculated in Equation 4. Pop is the annual mean population size (/100000). The number of 5 is the number of years studies (2013-2017). Then we summed the annual mean YLLs attributable to temperatures in all cities, and obtained the annual mean YLLs across China. All codes were available in https://github.com/gztt2002/YLL-of-Tm-and-Tv.

2.Supplementary tables

Table S1. General characteristics of included 364 locations in China

	Mean (SD)	Minimum	25th centile	Median	75th centile	Maximum
Population size (×10,000)	56.9 (31.9)	2.3	33.7	49.2	74.1	207.2
Percentage of male (%)	51.1 (1.2)	48.4	50.4	51.0	51.7	56.8
Percentage of elderly (%)	10.4 (2.3)	3.5	8.8	10.4	11.7	18.7
GDP per capital (×1000 yuan)	3.3 (2.5)	0.4	1.6	2.7	4.2	21.5
Urbanization rate (%)	52.8 (24.4)	6.4	34.5	46.9	67.7	100.0
Average years of education	10.0 (1.5)	5.2	9.1	9.8	10.7	16.7

Table S2. YLL per death due to different components of temperature across 364 locations in China

	YLL per death (years, 95%CI)			
	Extreme cold	Moderate cold	Moderate heat	Extreme heat
Causes of death				
Total mortality	0.14 (0.12, 0.16)	0.84 (0.52, 1.16)	0.01 (0.01, 0.02)	0.03 (0.02, 0.03)
Cardiovascular disease	0.17 (0.15, 0.19)	0.93 (0.59, 1.27)	0.01 (0.01, 0.02)	0.03 (0.02, 0.04)
Cerebrovascular disease	0.17 (0.14, 0.20)	1.16 (0.70, 1.62)	0.01 (0.00, 0.02)	0.03 (0.02, 0.04)
Respiratory disease	0.14 (0.11, 0.18)	0.28 (0.13, 0.44)	0.01 (0.01, 0.02)	0.02 (0.01, 0.03)
Geographic regions				
Northern	0.05 (0.01, 0.10)	0.51 (-0.84, 1.86)	0.03 (-0.12, 0.19)	0.04 (-0.03, 0.11)
Central	0.15 (0.12, 0.17)	1.14 (0.64, 1.64)	0.02 (0.01, 0.03)	0.04 (0.03, 0.05)
Southern	0.12 (0.09, 0.14)	1.05 (0.59, 1.50)	0.01 (0.00, 0.01)	0.02 (0.01, 0.03)
Age of death (Years)				
0-64	0.2 (0.15, 0.25)	0.84 (0.29, 1.39)	0.01 (0.00, 0.01)	0.03 (0.02, 0.05)
65-74	0.16 (0.13, 0.2)	1.11 (0.60, 1.62)	0.01 (0.00, 0.02)	0.02 (0.01, 0.03)
≥75	0.12 (0.11, 0.14)	0.69 (0.51, 0.87)	0.01 (0.01, 0.02)	0.02 (0.02, 0.03)
Sex				
Male	0.15 (0.12, 0.17)	0.98 (0.57, 1.38)	0.01 (0.00, 0.01)	0.02 (0.02, 0.03)
Female	0.14 (0.12, 0.17)	0.68 (0.28, 1.07)	0.02 (0.01, 0.03)	0.03 (0.02, 0.04)

3.Supplementary figures

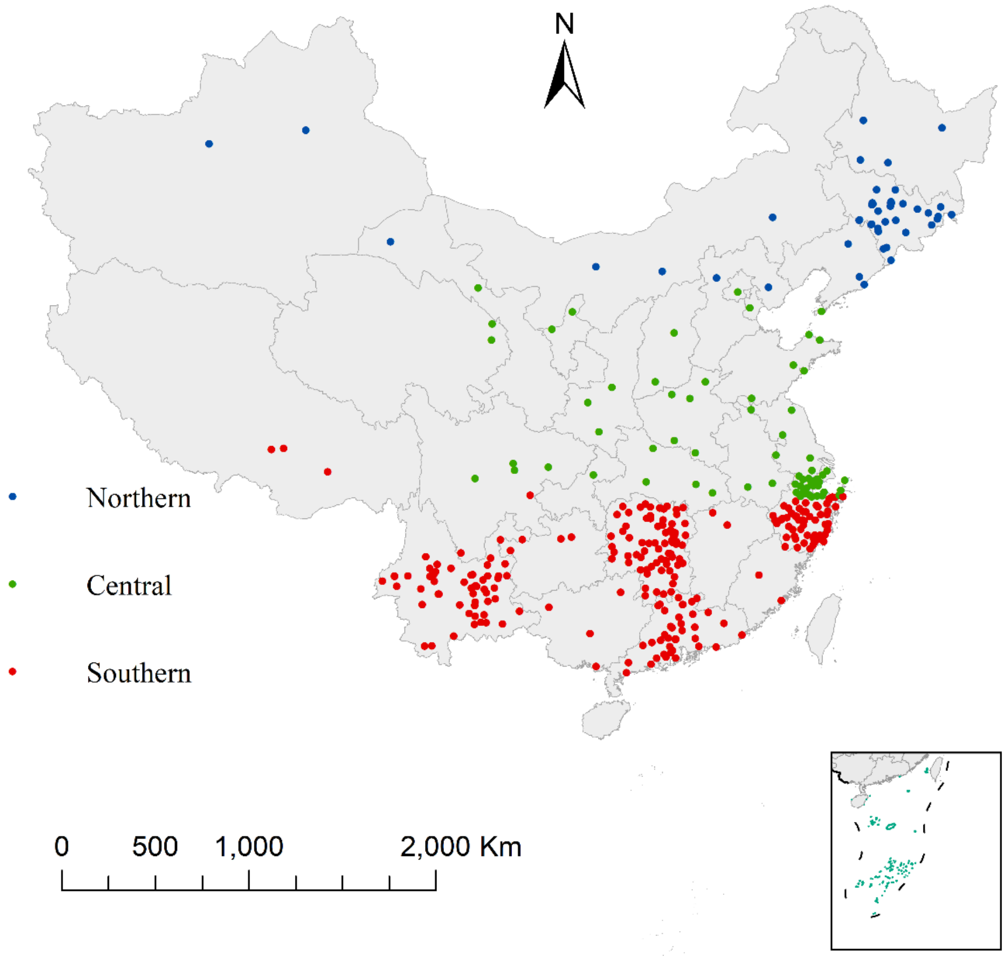

Figure S1. The geographic distribution of 364 locations in China

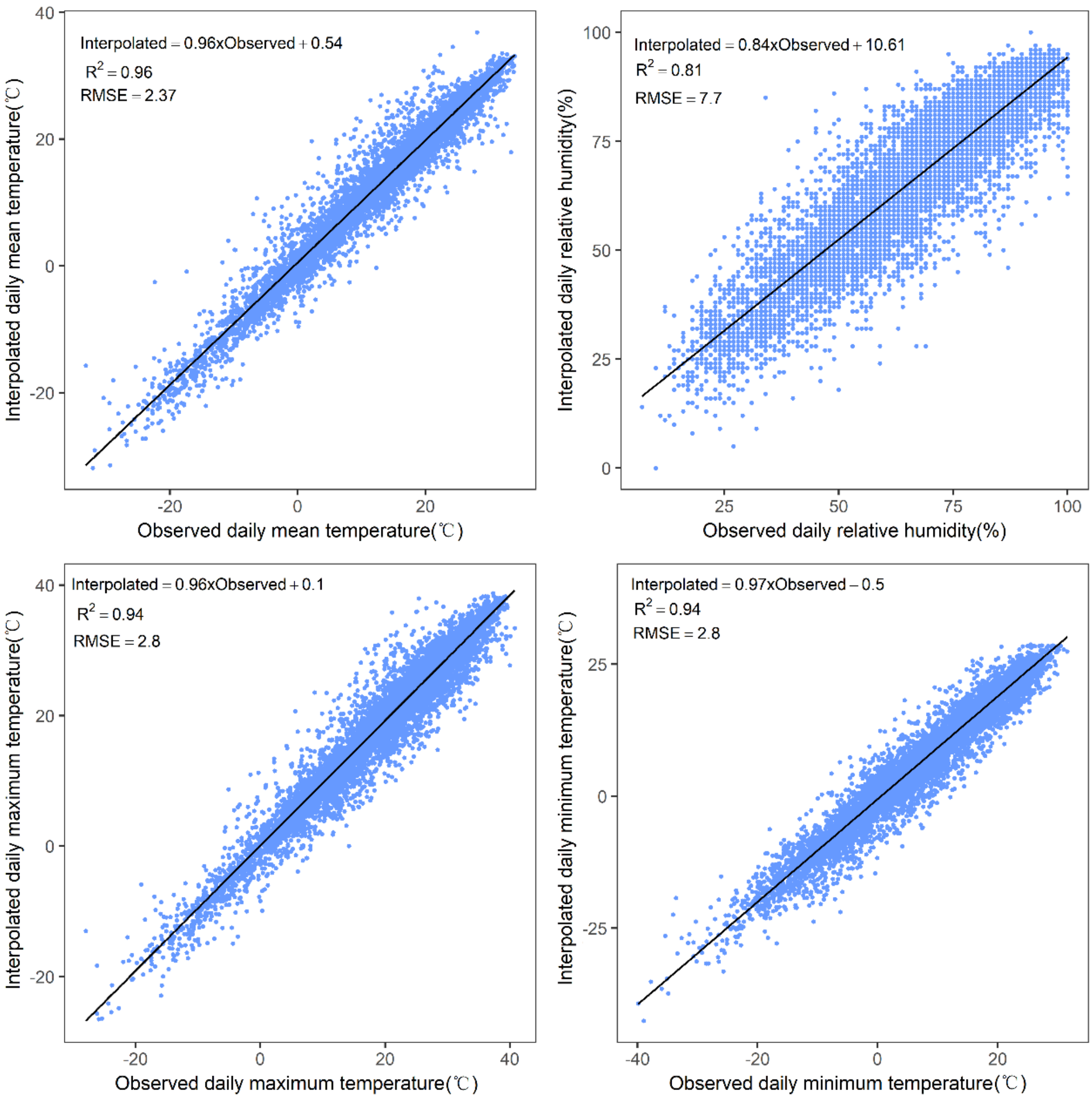

Figure S2. Scatter plot of 10-fold cross-validation of interpolated meteorological factors in 698 weather stations in China

Note: Since 10-fold cross-validation of all study days during 2006-2017 was time consuming, we only selected the 15th day in the following months to test the fitting performance of the model: January 2006, February 2007, March 2008, April 2009, May 2010, July 2011, June 2012, August 2013, September 2014, October 2015, November 2016, and December 2017.

RMSE: root mean squared prediction error (°C)

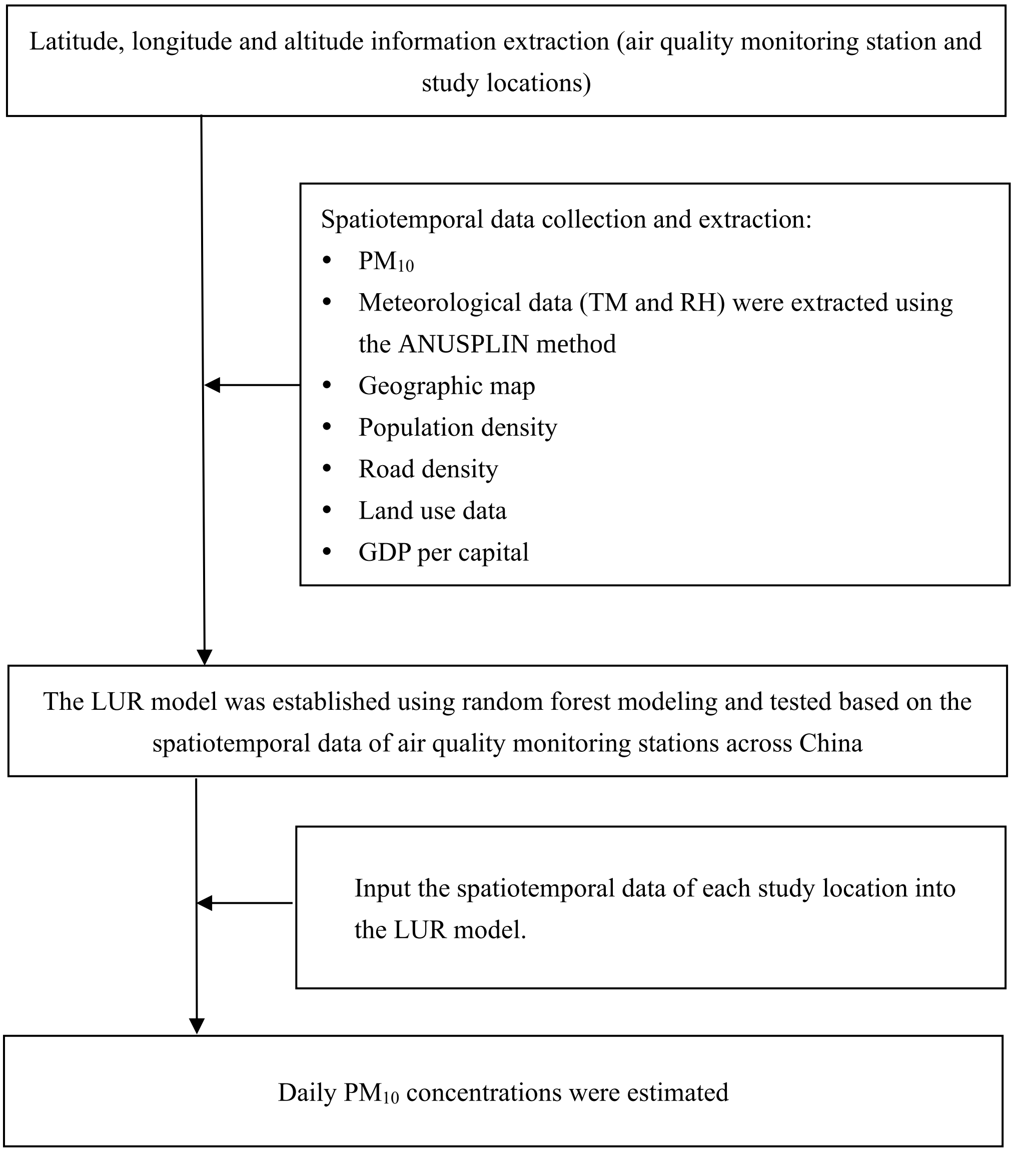

Figure S3. The process of daily PM_{10} concentration estimation

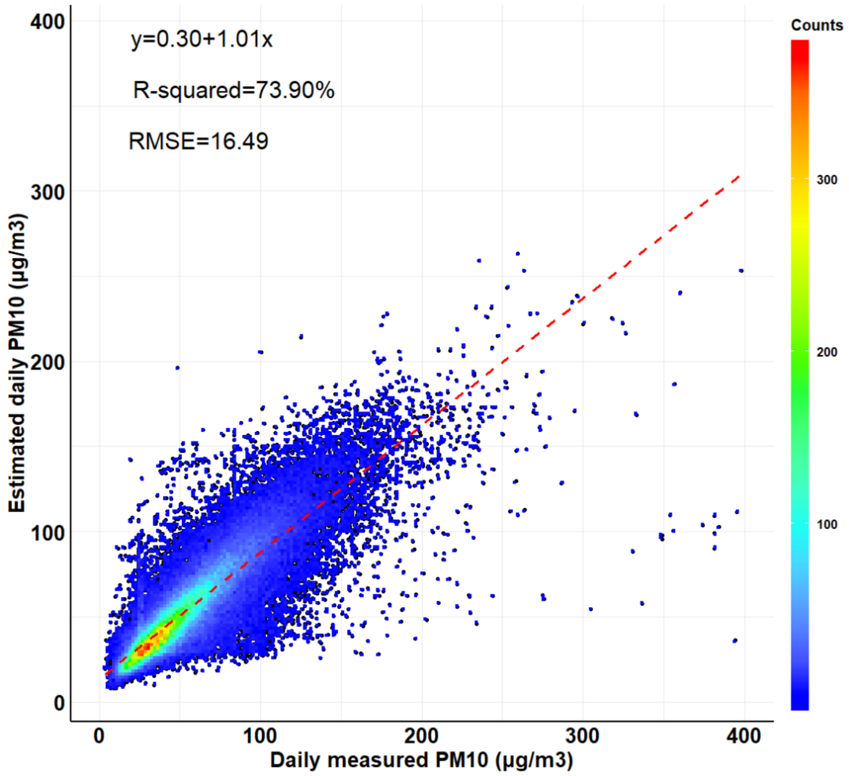

Figure S4. Performance and validation of estimating the daily PM_{10} concentration in China

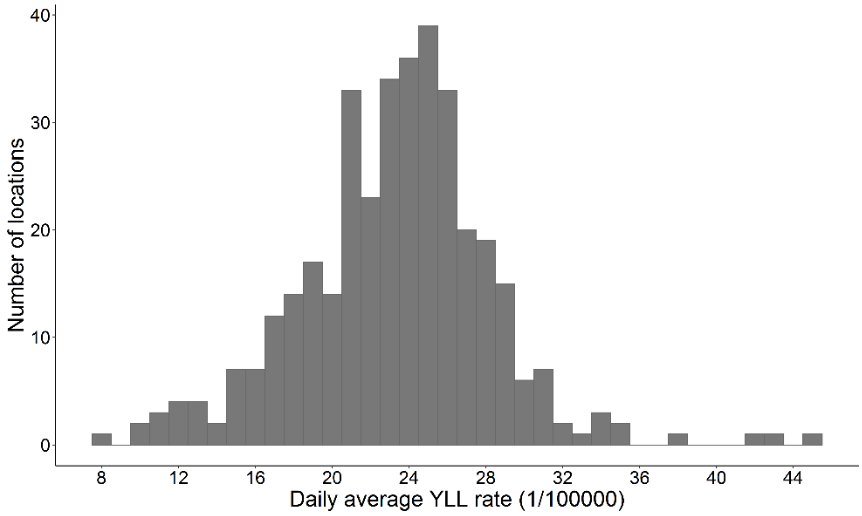

Figure S5. The distribution of daily average YLL rate (/100,000 population) in 364 locations in China

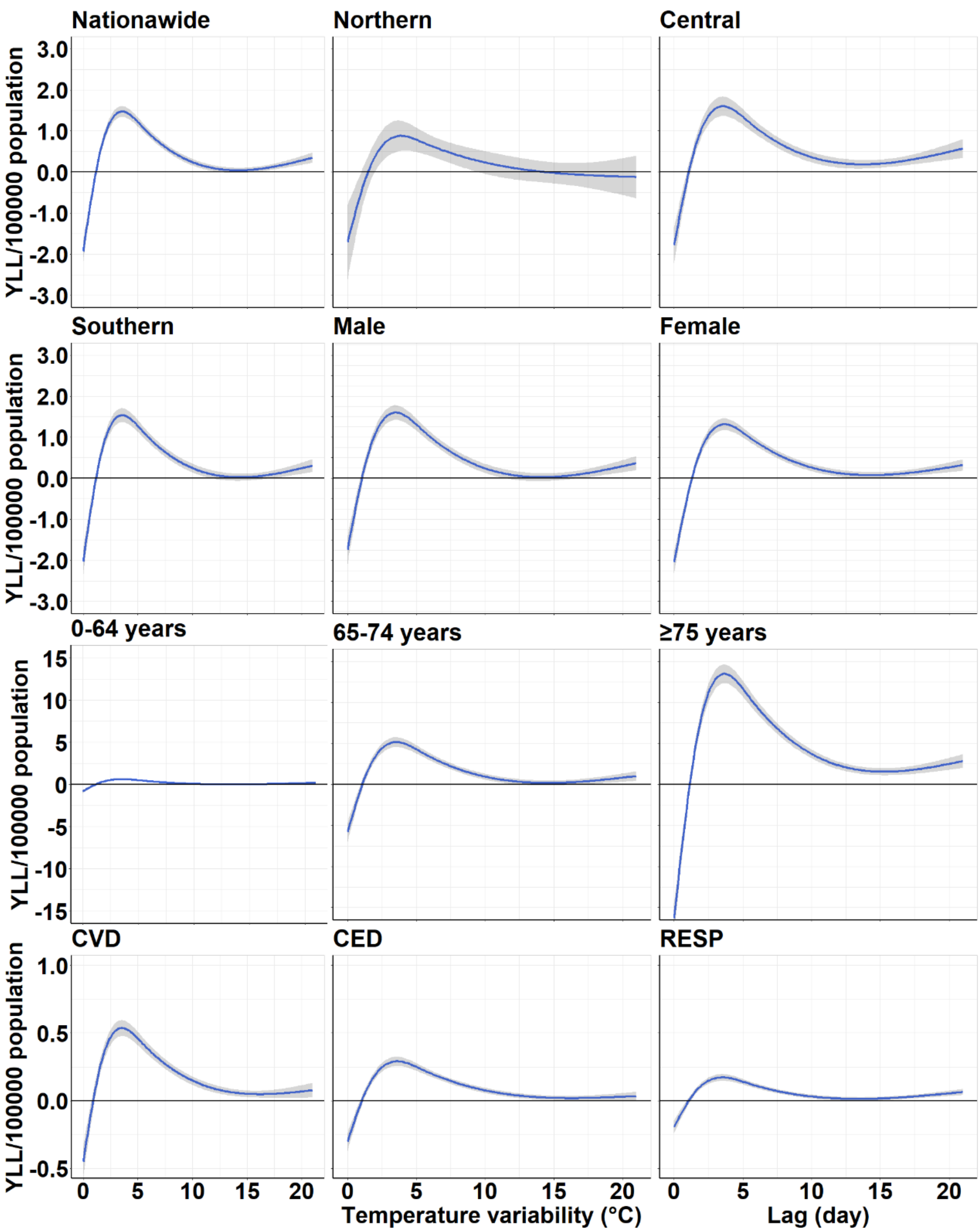

Figure S6. Overall lag structure in effects of extreme cold temperature on daily YLL rates in all 364 locations and in different subgroups in China

Effects were defined as the risks at the mean of the 2.5th centile of temperature distributions compared with the estimated MYT

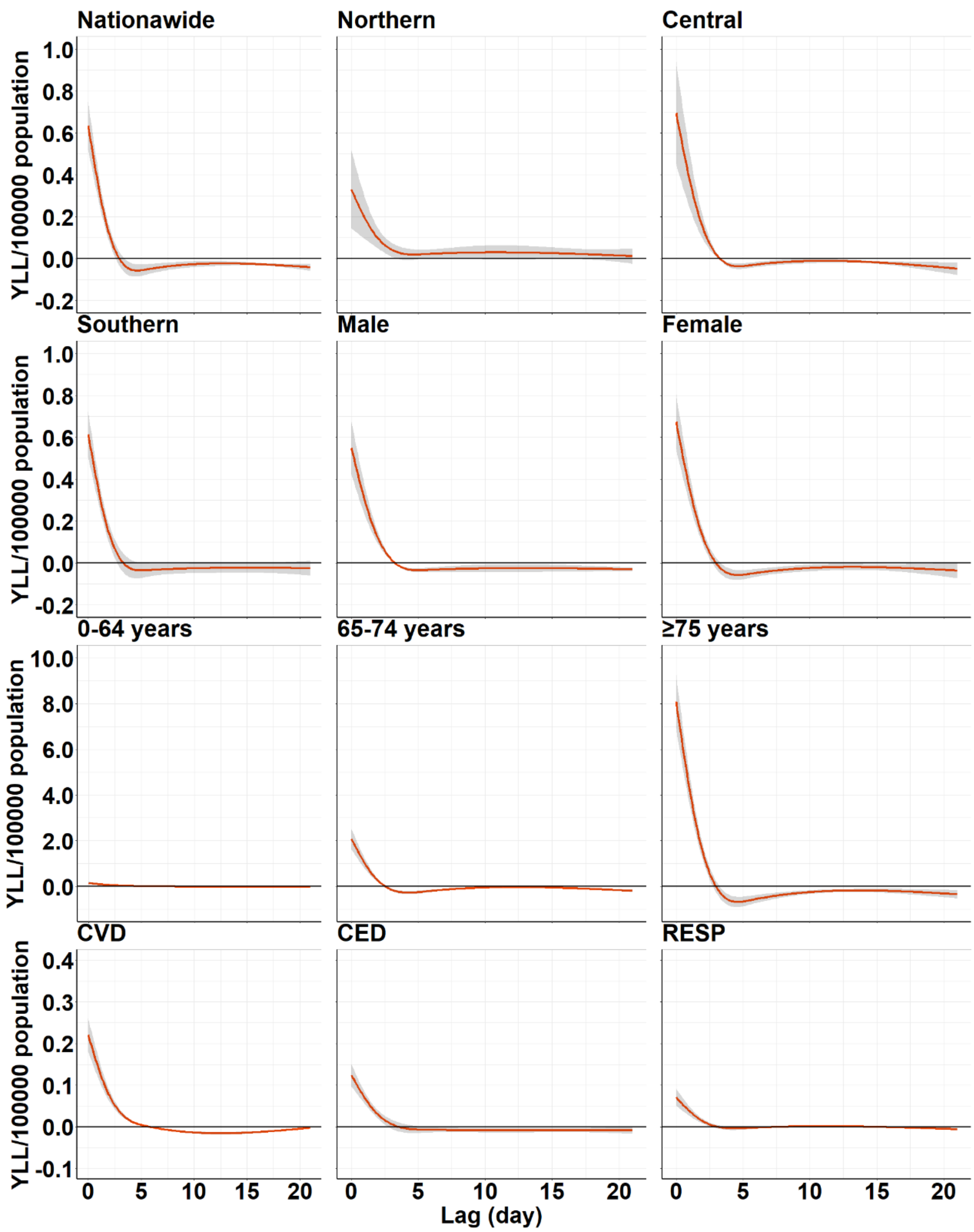

Figure S7. Overall lag structure in effects of extreme hot temperature on daily YLL rates in all 364 locations and in different subgroups in China

Effects were defined as the risks at the mean of the 97.5th centile of temperature distributions compared with the estimated MYT

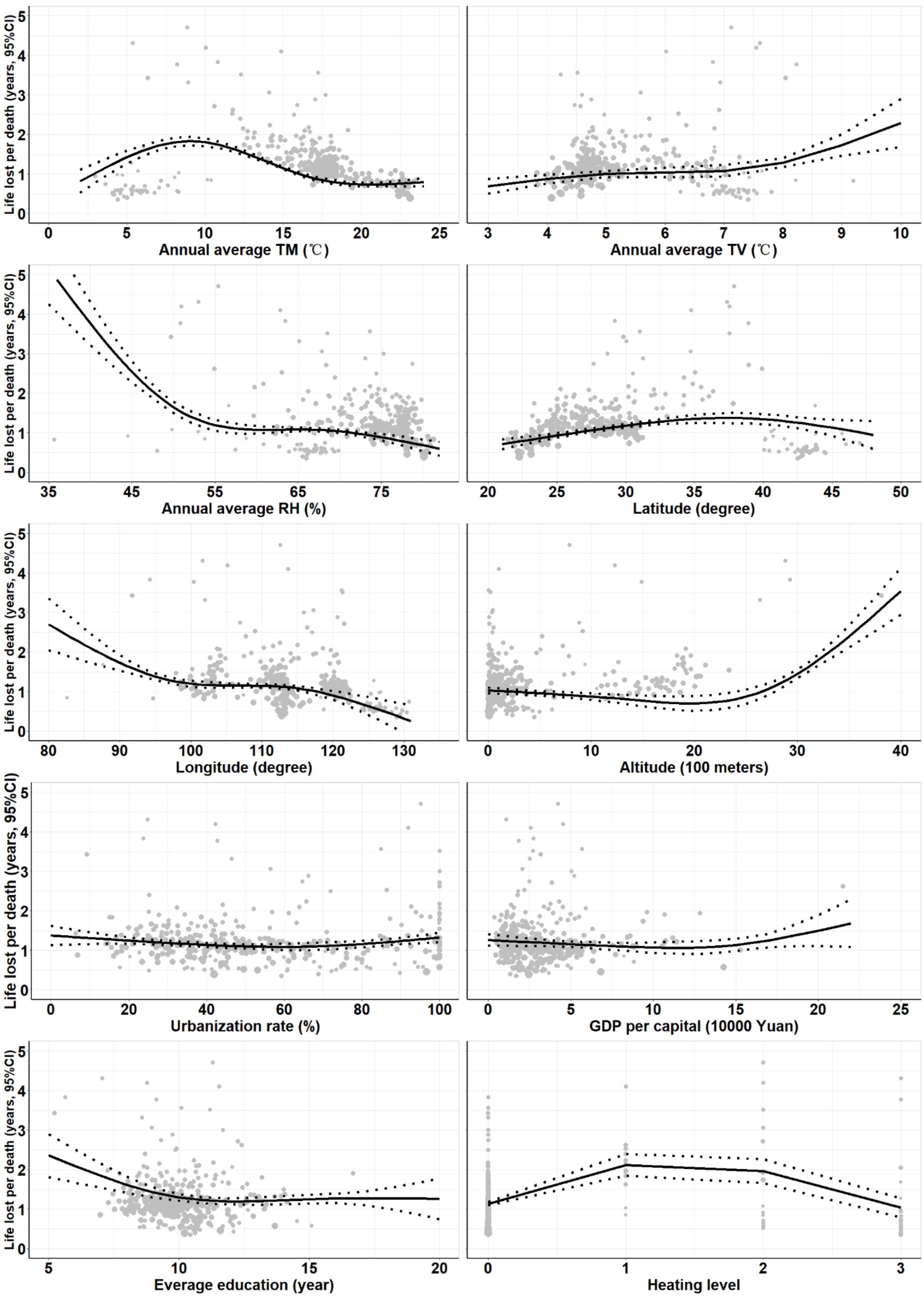

Figure S8. Univariable meta-regression results of the modification effects of city level characteristics on the YLL per death caused by temperatures in 364 locations in China

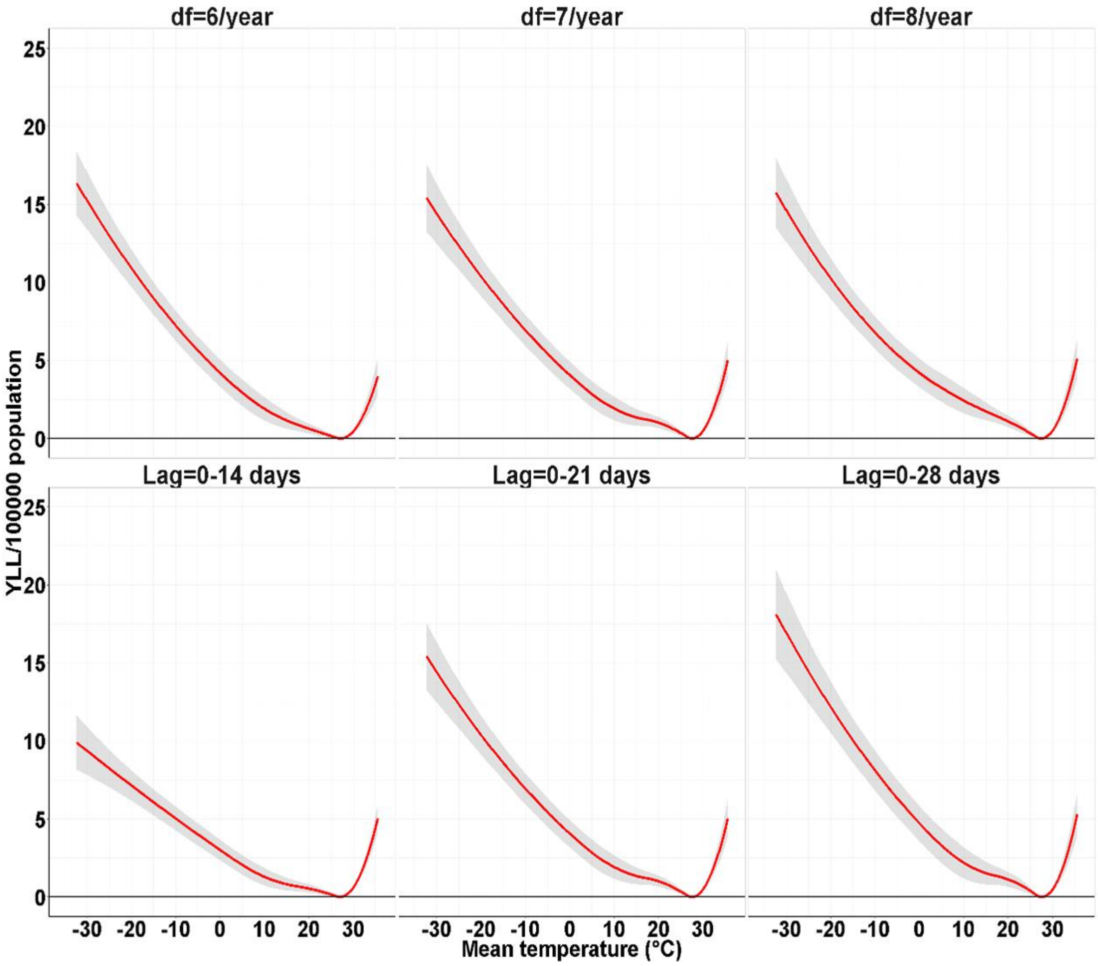

Figure S9. Sensitivity analyses on the impacts of lag days and df (/year) on the nationwide exposure-response relationship between temperature and YLL rate in China

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