Original article

Extremely cold and hot temperatures increase the risk of ischaemic heart disease mortality: epidemiological evidence from China

Yuming Guo,1,2 Shanshan Li,3 Yanshen Zhang,4 Ben Armstrong,5 Jouni J K Jaakkola,6 Shilu Tong,7 Xiaochuan Pan1

ABSTRACT

Objective To examine the effects of extremely cold and hot temperatures on ischaemic heart disease (IHD) mortality in five cities (Beijing, Tianjin, Shanghai, Wuhan and Guangzhou) in China; and to examine the time relationships between cold and hot temperatures and IHD mortality for each city.

Design A negative binomial regression model combined with a distributed lag non-linear model was used to examine city-specific temperature effects on IHD mortality up to 20 lag days. A meta-analysis was used to pool the cold effects and hot effects across the five cities.

Patients 16 559 IHD deaths were monitored by a sentinel surveillance system in five cities during 2004–2008.

Results The relationships between temperature and IHD mortality were non-linear in all five cities. The minimum-mortality temperatures in northern cities were lower than in southern cities. In Beijing, Tianjin and Guangzhou, the effects of extremely cold temperatures were delayed, while Shanghai and Wuhan had immediate cold effects. The effects of extremely hot temperatures appeared immediately in all the cities except Wuhan. Meta-analysis showed that IHD mortality increased 48% at the 1st percentile of temperature (extremely cold temperature) compared with the 10th percentile, while IHD mortality increased 18% at the 99th percentile of temperature (extremely hot temperature) compared with the 90th percentile.

Conclusions Results indicate that both extremely cold and hot temperatures increase IHD mortality in China. Each city has its characteristics of heat effects on IHD mortality. The policy for response to climate change should consider local climate—IHD mortality relationships.

INTRODUCTION

Extremely cold and hot temperatures are natural hazards for the human body. The adverse effects of extremely cold and hot temperatures may vary according to climatic types and population characteristics, because people may acclimatise to their local environmental conditions, through adaptation in physiology, behaviour and culture.1 The health impacts of extreme temperatures are likely to depend on local conditions, and may be modified by social, economic and demographic factors, and characteristics of infrastructure.2 Other factors such as income, education, social isolation, intensity of urban heat islands, housing characteristics, access to air conditioning and availability of health-care services can also modify the effects of extreme temperatures on human health.3 4 Therefore, there is a need to assess the effect of extreme temperatures on health in different regions.

Previous studies have provided evidence that extremely cold and hot temperatures have negative impacts on vulnerable people.5–7 The elderly and children are more vulnerable to extreme temperatures than youth.8 9 People with particular diseases such as cardiovascular and respiratory diseases, diabetes, chronic mental disorders or other pre-existing medical conditions are more susceptible to the health effects of extreme temperatures than healthy people.10–12

Ischaemic heart disease (IHD) is the leading cause of death worldwide13 and the incidence is increasing in China.14 IHD was ranked fifth for the causes of disability adjusted life years worldwide in 1990, and is projected be ranked first in 2020.15 Previous studies indicate a seasonal trend in IHD mortality, with the highest rate in winter.16 17 Studies have examined the effects of temperature on IHD mortality,18–20 but few studies have assessed the lag effects of heat on IHD mortality, especially in China.

Developing countries are anticipated to be susceptible to the impact of extreme temperatures, because they have more limited adaptive capacity and more vulnerable people than developed countries.7 People have the ability to adapt to their local climates, through physiological, behavioural and cultural adaptation. So we need to consider human capacity to adapt to varied climates and environments. In China, only a few studies have examined the impact of temperature on non-accidental, cardiovascular and respiratory mortality in Shanghai,21 22 Beijing23 and Tianjin.24 To date, no study has examined the impact of extreme temperatures on IHD death in multiple cities in China.

In this study, we aimed to assess the regional characteristics of the associations between ambient temperature and IHD mortality in five cities (Beijing, Tianjin, Shanghai, Wuhan and Guangzhou, from north to south) in China (figure 1); and to examine the lag effects of extremely cold and hot temperatures on IHD mortality for each city.

METHODS

Data collection

We collected data from five cities (Beijing, Tianjin, Shanghai, Wuhan and Guangzhou) in China (figure 1). Beijing and Tianjin are located in
northern China. They are adjacent, and have a similar climatic pattern (table 1). They have four clear seasons, with cold, windy, dry winters, and hot, humid summers. Shanghai is located in eastern China. Its weather is generally mild and moist, with a warm spring, a hot rainy summer, a cool autumn and an overcast cold winter. Wuhan is located in central China. It is a humid subtropical city, and has an oppressively humid summer. Guangzhou is located in southern China. It has a humid subtropical climate, with a long humid and scorching summer and short winter.

Daily data on IHD deaths were obtained from the China Information System for Death Register and Report of Chinese Centre for Disease Control and Prevention (China CDC) from 1 January 2004 to 31 December 2008. There was a sentinel surveillance system in these five cities. The system aimed to confirm and track the cause of death for each person by trained workers. IHD deaths were classified according to the International Classification of Diseases, 10th revision (ICD-10: I20–I25). This study was approved by the Ethics Committee of Peking University Health Science Centre.

There were three key reasons for choosing these five cities. First, there are sentinel surveillances for death data in these cities, so the data of IHD deaths are reliable. Second, they are the five largest cities in China. Third, they have different characteristics of climate and population.

Daily meteorological data on mean temperature and relative humidity were obtained from the China Meteorological Data Sharing Service System for each city. The meteorological stations are located in the urban district of each city. Daily air pollution data on particulate matter less than 10 μm aerodynamic diameter (PM$_{10}$) and nitrogen dioxide (NO$_2$) were obtained from the each city’s Environmental Monitoring

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IHD, ischaemic heart disease.
were changed.

To check our main effects at lag 0 (which corresponds to the lowest IHD death) in each city.

We used a distributed lag non-linear model (DLNM) to examine the non-linear and delayed heat effects on IHD mortality.²⁶²⁷ We chose maximum lag days, degree of freedom for temperature and lags by the minimum value of the sum of the Bayesian information criterion (BIC) values in all the five cities. Finally, we used 20 days as the maximum lag for temperature. A natural cubic spline with five degrees of freedom was used for temperature, while a natural cubic spline with four degrees of freedom was used for lag. We used a natural cubic spline with six degrees of freedom for time to control for season and long-term trend. We controlled for day of the week as a categorical variable. We controlled for relative humidity, PM₁₀ and NO₂ using natural cubic splines with three degrees of freedom.²⁴

We examined the city-specific non-linear temperature–IHD mortality relationship and summary measures of the cold- and hot-related portions of this relationship by effect estimates of relative temperature changes.²⁰²⁹ To quantify the effects of extremely cold temperatures on IHD mortality, we calculated the relative risks of IHD mortality at the 1st percentile of city-specific temperature distribution compared with the 10th percentile (cold effect); to quantify the effects of extremely hot temperatures on IHD mortality, we calculated the relative risks of IHD mortality at the 99th percentile of temperature compared with 90th percentile (hot effect). These effect estimates have the ability to reflect the effects of extremely cold and hot temperatures on IHD mortality, because they are extracted from a part of the true non-linear temperature–IHD mortality curves.

We used a meta-analysis to pool cold effects and hot effects across the five cities, based on restricted maximum likelihood. To examine the characteristics of the delayed effects of extremely cold and hot temperatures, the cold effects and hot effects at lag 0–2, lag 0–13 and lag 0–20 were pooled, separately.

For all the cities, our initial analysis found that the temperature–mortality relationships were non-linear, with a potential threshold value for cold and hot effects. To compare the characteristics of the temperature–IHD mortality relationship in the five cities, we examined the minimum-mortality temperature (which corresponds to the lowest IHD death) in each city.

We used BIC to compare model performance. We used the autocorrelation function to check if the residuals were independent over time. To check our main findings, sensitivity analyses were conducted by changing the maximum lag from 15 to 50 days, the degrees of freedom for temperature, relative humidity, air pollutants and lags (3–6) and degrees of freedom (6–10 per year) for time. As Beijing and Tianjin are neighbours and have similar climatic characteristics, we used a two-stage meta-analysis to confirm if the pooled cold and hot effects were changed.

The R software (V2.15.0) was used to fit all models. The dlnm package was used to simultaneously smooth temperature and lags using a natural cubic spline.²⁶²⁷ The ‘metafor’ package was used to perform meta-analysis.

RESULTS

Northern cities have lower average temperature and relative humidity than southern cities (table 1). Generally, Beijing, Tianjin and Wuhan had higher PM₁₀ concentration than Shanghai and Guangzhou. All cities had similar NO₂ pollution. On average, Tianjin had the highest IHD mortality among the five cities. There was a seasonal trend of IHD mortality in all five cities, with higher mortality in winter than summer (see online supplementary material, figure S1).

Figure 2 shows a three-dimensional graph of the estimated relative risk for IHD mortality according to temperature and along the lag days (up to 20 days). The estimated effects of temperature on IHD mortality were non-linear in all the cities, with increased mortality rates on days with hot and cold temperatures. The effects of hot temperature were short-term in all the cities. The effects of cold temperature appeared late in Beijing, Tianjin and Guangzhou, but without delay in Shanghai and Wuhan.

We plotted the cumulative relative risks of city-specific IHD mortality associated with temperature over the 20 lag days (figure 5). Generally, the associations between temperature and mortality were non-linear in all the cities. Both extremely cold and hot temperatures increased the risk of IHD mortality, with a threshold corresponding to the lowest mortality. The minimum-mortality temperatures were 0.8°C in Beijing, –0.3°C in Tianjin, 12.2°C in Shanghai, 28.3°C in Wuhan and 27.1°C in Guangzhou.

Figure 4 shows the lag structure for relative risk of IHD mortality associated with extremely cold temperature (1st percentile of temperature against 10th percentile) and extremely hot temperature (99th percentile of temperature against 90th percentile) according to the duration of lag time up to 20 days. The form of the curve indicates that the effects of extremely cold temperature were delayed in Beijing, Tianjin and Guangzhou, while the corresponding effects occur with a short time lag in Shanghai and Wuhan. The effects of extremely hot temperature appeared immediately in all the cities except Wuhan. The effects of extremely cold temperature on IHD mortality lasted longer than associations with extremely hot temperatures.

Table 2 shows the cumulative effects of extremely cold and hot temperatures on IHD mortality at lag 0–2, lag 0–13 and lag 0–20 in the five cities. In general, southern cities had higher cold effects than northern cities, while all five cities had similar hot effects except Shanghai. For lag 0–20, the effects of extremely cold temperatures were higher than extremely hot temperatures.

Table 2 shows the cumulative effects of extremely cold and hot temperatures on IHD mortality at lag 0–2, lag 0–13 and lag 0–20 in the five cities. In general, southern cities had higher cold effects than northern cities, while all five cities had similar hot effects except Shanghai. For lag 0–20, the effects of extremely cold temperatures were higher than extremely hot temperatures.

Figure 5 shows the pooled effect estimates for extremely cold and hot temperatures for lag 0–2, lag 0–13 and lag 0–20. The pooled effects of extremely cold temperature were delayed, while the pooled effects of extremely hot temperature appeared immediately. The pooled relative risk of IHD mortality associated with extremely cold temperatures (1st percentile of temperature compared with 10th percentile) was 1.40 (95% CI 1.31 to 1.66) at lag 0–20 (table 3). The pooled relative risk of IHD mortality associated with extremely hot temperatures (99th percentile of temperature compared with 90th percentile) was 1.18 (95% CI 1.00 to 1.36) at lag 0–20 (table 3).

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**Data analysis**

To accommodate the remaining over-dispersion that we found in the IHD death data (as indicated by the model dispersion parameters), we used a negative binomial regression model to examine the city-specific temperature–mortality relationship.²⁵

We plotted the cumulative relative risks of city-specific IHD mortality associated with temperature over the 20 lag days (figure 3). Generally, the associations between temperature and mortality were non-linear in all the cities. Both extremely cold and hot temperatures increased the risk of IHD mortality, with a threshold corresponding to the lowest mortality. The minimum-mortality temperatures were 0.8°C in Beijing, –0.3°C in Tianjin, 12.2°C in Shanghai, 28.3°C in Wuhan and 27.1°C in Guangzhou.

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**Epidemiology**

Centre. The pollution monitoring stations were distributed throughout each city (12 Beijing, 10 Tianjin, 17 Shanghai, 10 Wuhan and 10 Guangzhou). The city-wide daily mean concentration was averaged from the daily mean concentration at monitoring stations in each city. If there was missing data for certain monitoring stations, other monitoring stations were used to calculate the city-wide mean value.

We used a distributed lag non-linear model (DLNM) to examine the non-linear and delayed heat effects on IHD mortality.²⁶²⁷ We chose maximum lag days, degree of freedom for temperature and lags by the minimum value of the sum of the Bayesian information criterion (BIC) values in all the five cities. Finally, we used 20 days as the maximum lag for temperature. A natural cubic spline with five degrees of freedom was used for temperature, while a natural cubic spline with four degrees of freedom was used for lag. We used a natural cubic spline with six degrees of freedom for time to control for season and long-term trend. We controlled for day of the week as a categorical variable. We controlled for relative humidity, PM₁₀ and NO₂ using natural cubic splines with three degrees of freedom.²⁴

We examined the city-specific non-linear temperature–IHD mortality relationship and summary measures of the cold- and hot-related portions of this relationship by effect estimates of relative temperature changes.²⁰²⁹ To quantify the effects of extremely cold temperatures on IHD mortality, we calculated the relative risks of IHD mortality at the 1st percentile of city-specific temperature distribution compared with the 10th percentile (cold effect); to quantify the effects of extremely hot temperatures on IHD mortality, we calculated the relative risks of IHD mortality at the 99th percentile of city-specific temperature distribution compared with the 90th percentile (hot effect). These effect estimates have the ability to reflect the effects of extremely cold and hot temperatures on IHD mortality, because they are extracted from a part of the true non-linear temperature–IHD mortality curves.

We used a meta-analysis to pool cold effects and hot effects across the five cities, based on restricted maximum likelihood. To examine the characteristics of the delayed effects of extremely cold and hot temperatures, the cold effects and hot effects at lag 0–2, lag 0–13 and lag 0–20 were pooled, separately.

For all the cities, our initial analysis found that the temperature–mortality relationships were non-linear, with a potential threshold value for cold and hot effects. To compare the characteristics of the temperature–IHD mortality relationship in the five cities, we examined the minimum-mortality temperature (which corresponds to the lowest IHD death) in each city.

We used BIC to compare model performance. We used the autocorrelation function to check if the residuals were independent over time. To check our main findings, sensitivity analyses were conducted by changing the maximum lag from 15 to 50 days, the degrees of freedom for temperature, relative humidity, air pollutants and lags (3–6) and degrees of freedom (6–10 per year) for time. As Beijing and Tianjin are neighbours and have similar climatic characteristics, we used a two-stage meta-analysis to confirm if the pooled cold and hot effects were changed.

The R software (V2.15.0) was used to fit all models. The dlnm package was used to simultaneously smooth temperature and lags using a natural cubic spline.²⁶²⁷ The ‘metafor’ package was used to perform meta-analysis.
The residuals from the negative binomial regression models were adequately independent over time in all five cities (see online supplementary material, figure S2). Sensitivity analyses were performed to check our main findings. The effect estimates were stable when using six degrees of freedom or more than 6 degrees of freedom per year for time (see online supplementary material, figure S3). When we changed degrees of freedom of smooth (3, 4 and 6 df) for temperature and lags, the estimated relative risks of IHD mortality were not changed substantially (see online supplementary material, figure S4). We modified degrees of freedom of smooth (1, 2, 4 and 5 df) for PM$_{10}$ and NO$_2$, and the results were not changed substantially (see online supplementary material, figure S5). In addition, we changed the maximum lag to 15, 25, 27 and 30 days, which gave similar results (see online supplementary material, figure S6). When we used the two-stage meta-analysis, the pooled cold effects were changed slightly and pooled hot effects were not changed (see online supplementary material, table S1). Consequently, we believe that the models used in this study adequately captured the main effects of temperature on IHD mortality.

**DISCUSSION**

To our best knowledge, this is the first study to examine the relationship between temperature and IHD mortality in China. We found that the temperature–IHD mortality relationships were non-linear in all five cities. The minimum-mortality temperatures in northern cities (with low mean temperature) were lower than in southern cities (with high mean temperature). Each city has its characteristics for lagged cold and hot effects on IHD mortality. Beijing, Tianjin and Guangzhou had apparent delayed cold effects, while Shanghai and Wuhan had immediate cold effects. Hot effects appeared immediately in all the cities except Wuhan. The effects of extremely cold temperatures on IHD mortality generally lasted longer than those of extremely hot temperatures. Meta-analysis showed that both extreme cold and hot temperatures significantly increased the risk of IHD mortality in China.

Previous studies have estimated associations between temperature and IHD mortality, but most of them only focused on winter and did not consider the lag effects. Pan et al found that the temperature–IHD mortality relationship was U-shaped in Taiwan, and the minimum-mortality temperature was higher than that in countries with colder climates. All the studies focused on the current day’s temperature, which based on our results is likely to underestimate the effects of both cold and hot temperatures.

The present results indicate that the minimum-mortality temperatures in the north (Beijing and Tianjin, with low mean temperature) are lower than in the south (Shanghai, Wuhan...
and Guangzhou). Our results are consistent with the hypothesis that people in the north are more susceptible to the effects of hot temperatures and in the south to the effects of cold temperatures. This hypothesis is based on the idea of acclimatisation to local climatic conditions. Our findings suggest that when healthcare providers and public health authorities develop response plans to protect people with IHD from ambient temperatures, it is necessary to consider the local climate type and geographic location.

One interesting finding of this study is that the minimum-mortality temperatures varied greatly across the five cities if we considered city-specific percentiles of temperature distribution. Temperature thresholds were lower than the 25th percentile of temperature distribution in Beijing and Tianjin, while temperature thresholds were higher than the 75th percentile of temperature distribution in Wuhan and Guangzhou. Similar temperature–mortality relationships were reported in Montreal and Quebec City in Canada. These results were not consistent with most previous studies which reported temperature thresholds above the 50th percentile of temperature distribution. The reason might be that the temperature effects are modified by social, economic, demographic and infrastructural conditions.
factors, education, social isolation, intensity of urban heat islands, housing characteristics, access to air conditioning and availability of healthcare services. For example, people living in cities in cold climates are better adapted for cold weather by having heaters and warm clothes, but may not have air conditioning which is needed during warmer days. In China,
northern cities tend to have central heating in winter, while southern cities do not. In urban Beijing, 78% of houses have central heating, as do 83% in urban Tianjin. In Beijing and Tianjin, the central heating system runs from November to March.

It is important to investigate the lag effect of temperature on IHD mortality, when healthcare providers and public health authorities develop response plans for extremely cold and hot temperatures. We investigated the role of time lag over 20 days for the effects on IHD mortality. In general, cold effects lasted longer than hot effects. Similar results were previously reported on the relationship between temperature and cardiovascular disease mortality. These findings indicate that using short lags cannot completely capture the cold effect, and therefore longer lags are required to examine the cold impact. The hot effects were more acute and short-term. Studies have shown that hot temperatures induce an acute event in people with previous myocardial infarction or stroke, or the elderly.

The biological mechanisms provide support to our finding. Physiological regulation constantly adjusts the heat exchange between the human body and environmental temperature.

Table 2 The cumulative cold and hot effects of temperature on IHD mortality along the lag days, using 5 degrees of freedom natural cubic spline for temperature and 4 degrees of freedom natural cubic spline for lag

<table>
<thead>
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<th>Effect</th>
<th>Lag</th>
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<th>Tianjin</th>
<th>Shanghai</th>
<th>Wuhan</th>
<th>Guangzhou</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold*</td>
<td>0–2</td>
<td>0.94 (0.82, 1.08)</td>
<td>1.01 (0.92, 1.11)</td>
<td>1.36 (1.19, 1.56)</td>
<td>1.08 (0.90, 1.29)</td>
<td>1.09 (0.92, 1.28)</td>
</tr>
<tr>
<td></td>
<td>0–13</td>
<td>1.31 (1.09, 1.57)</td>
<td>1.22 (1.07, 1.39)</td>
<td>1.47 (1.15, 1.88)</td>
<td>1.32 (1.09, 1.60)</td>
<td>1.60 (1.29, 1.98)</td>
</tr>
<tr>
<td></td>
<td>0–20</td>
<td>1.42 (1.11, 1.81)</td>
<td>1.39 (1.18, 1.64)</td>
<td>1.65 (1.20, 2.28)</td>
<td>1.59 (1.25, 2.03)</td>
<td>1.89 (1.43, 2.50)</td>
</tr>
<tr>
<td>Hot†</td>
<td>0–2</td>
<td>1.15 (1.01, 1.30)</td>
<td>1.21 (1.08, 1.35)</td>
<td>1.04 (0.89, 1.22)</td>
<td>1.21 (1.02, 1.43)</td>
<td>1.26 (1.10, 1.44)</td>
</tr>
<tr>
<td></td>
<td>0–13</td>
<td>1.25 (1.00, 1.55)</td>
<td>1.32 (1.07, 1.62)</td>
<td>1.04 (0.83, 1.31)</td>
<td>1.59 (1.16, 2.18)</td>
<td>1.34 (1.06, 1.70)</td>
</tr>
<tr>
<td></td>
<td>0–20</td>
<td>1.22 (0.94, 1.60)</td>
<td>1.21 (0.94, 1.56)</td>
<td>1.06 (0.80, 1.40)</td>
<td>1.24 (0.84, 1.82)</td>
<td>1.24 (0.92, 1.67)</td>
</tr>
</tbody>
</table>

*1st percentile of temperature relative to 10th percentile of temperature. †99th percentile of temperature relative to 90th percentile of temperature; see table 1 for the percentiles of temperature.

IHD, ischaemic heart disease.

Figure 5 Meta-analysis for cold effects (left) and hot effects (right) on ischaemic heart disease mortality at lag 0–2 (top), lag 0–13 (middle) and lag 0–20 days (bottom). Cold effect is associated with 1st percentile of temperature relative to 10th percentile; hot effect is associated with 99th percentile of temperature relative to 90th percentile. See table 1 for the percentiles of temperature. This figure is only reproduced in colour in the online version.
Exposure to cold temperatures is associated with an increase in blood pressure, blood cholesterol levels, heart rate, plasma fibrinogen concentrations, platelet viscosity and peripheral vasoconstriction. Exposure to hot temperatures may cause dehydration, salt depletion and increased surface blood circulation, which can induce a failure of thermoregulation. Hot temperatures may also be associated with elevated blood viscosity, cholesterol levels and sweating thresholds.

This study has some advantages. It is the first study to examine the relationship between temperature and IHD mortality in China. We examined both lagged cold and hot effects. We used a meta-analysis to pool the effects, which can give strong evidence for a temperature effect on IHD mortality in China. We used death data from sentinel surveillance, so the death data are reliable. Our findings can be used to promote capacity building for the local response to climate change.

Some limitations need to be considered. The data are only from five cities, so it is difficult to generalise our results to rural areas. We used the data on temperature and air pollution from fixed sites rather than measuring individual exposure, and therefore some measurement error is inevitable, but it is likely to be random, that is, not related to the risk of IHD deaths.

We did not control for the impact of ozone, as data on ozone were unavailable. Previous studies reported that effects of hot temperatures were slightly reduced when ozone was controlled for, but effects of cold temperatures were not changed. Future studies need to investigate this issue.

**CONCLUSION**

In conclusion, the temperature–IHD mortality relationships were non-linear in five Chinese cities. Our results are consistent with the hypothesis that people in the north are more susceptible to the effects of hot temperatures and in the south to the effects of cold temperatures. Both cold and hot effects last more than 2 days. The effects of extremely cold temperatures were delayed in Beijing, Tianjin and Guangzhou, whereas in Shanghai and Wuhan the effects appeared immediately. The effects of extremely hot temperatures appeared immediately in all the five cities except Wuhan. The results of meta-analysis also suggest that both extremely cold and hot temperatures increase the risk of IHD mortality in China. Therefore, the climate change adaptation policy should be modified according to the needs based on local climate–IHD mortality relationships.

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**Contributors** YG designed the study and directed its implementation, including data analysis, writing the paper, and quality assurance and control. YZ helped prepare the database and conduct the data quality assurance. SL, BA, JJKJ, ST and KP helped conduct the quality assurance, and reviewed and edited the paper.

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**Ethics approval** Ethics Committee, Peking University Health Science Centre.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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Extremely cold and hot temperatures increase the risk of ischaemic heart disease mortality: epidemiological evidence from China

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