Seasonal variations of temperature-related mortality burden from cardiovascular disease and myocardial infarction in China

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Abstract

Incidence rate of cardiovascular disease (CVD) has significant seasonal trend, being higher in winter. However, the extent to which the seasonal variation of CVD deaths was caused by temperature remains unclear. We obtained daily data on temperature and CVD and myocardial infarction (MI) mortality from nine Chinese mega-cities during 2007-2013. Distributed lag non-linear models were applied to assess the city-specific temperature-related daily excess deaths across lag 0-21 days, using the minimum-mortality temperature as reference. Then, estimates of excess deaths in four seasons were separately aggregated from the daily series, and its ratio to the corresponding total deaths produced seasonal attributable fraction (AF). In total, 1,079,622 CVD and 201,897 MI deaths were recorded in the nine Chinese cities. Significant and non-linear associations between temperature and mortality were observed, with a total of 195,516 CVD and 50,658 MI deaths attributable to non-optimum temperatures. 103,439 (95% empirical CI: 54,475-141,537) CVD and 24,613 (5,891-36,279) MI deaths related to non-optimum temperature occurred in winter, compared with 15,923 (1,436-28,853) and 4,946 (-325-9,016) in summer. Temperature-related AFs were higher among MI than CVD, with AFs of 42% (9-62%) and 35% (19-48%) in winter, and 13% (-1-23%) and 8% (1-14%) in summer, respectively. This study may have important implications for developing effective targeted intervention measures on CVD events.

Capsule： Temperature-related mortality burden from cardiovascular disease and myocardial infarction has significant seasonal trend.

Keywords: Seasonal variation; Ambient temperature; Cardiovascular disease; Myocardial infarction; Attributable fraction

1. Introduction

Cardiovascular diseases (CVDs) are the leading cause of death and disability-adjusted life years lost globally, placing a major social and economic burden on public health systems (Lozano et al., 2012). Myocardial infarction (MI), a common presentation of coronary artery disease, with higher fatal rate, has contributed dramatically to the increased health burden in low-income countries. The well-known risk factors for CVD and MI are related to lifestyle habits such as smoking, binge drinking, physical inactivity, and unhealthy conditions such as high blood pressure and cholesterol, diabetes mellitus and obesity (Cosselman et al., 2015; Fares, 2013; Marti-Soler et al., 2014; Yang et al., 2015c). Furthermore, recent epidemiological investigations reported that environmental factors such as ambient extreme temperatures and air pollution also contribute to CVD onsets and mortality (Brook et al., 2004; Yang et al., 2012; Yang et al., 2015a; Yang et al., 2015b).

The mortality rates of CVD and MI showed a clear seasonal pattern, being higher in winter than in other seasons, which has been documented in many countries including China (Fares, 2013; Ou et al., 2013; Rumana et al., 2008; Spencer et al., 1998). This variation was linked with multiple risk factors, such as low ambient temperature, physical inactivity, air pollution, infections and insufficient nutrients (Fares, 2013). Previous investigations have mainly focused on the impact of risk factors in the whole year, with less evidence on seasonal differences in the association between weather stressors and CVD/MI. Additionally, it is unclear to what extent the seasonal variation of CVD and MI deaths is attributable to temperature in the whole population, which has been confirmed as one of the strongest CVD environmental risk factors ever (Yang et al., 2015b).

Thus, in this study, we aimed to examine the seasonal variation of temperature-related CVD and MI deaths in nine provincial capital cities of China.

2. Materials and methods

2.1. Study sites

This study included nine large cities from northern to southern China: Beijing, Tianjin, Nanjing, Shanghai, Hefei, Wuhan, Chengdu, Hangzhou and Guangzhou (Supplementary Fig. A1). Beijing and Tianjin are located in northern China, with temperate monsoon climate and cold winter. Nanjing, Shanghai and Hangzhou are located in eastern China, with a subtropical monsoon climate and four distinct seasons. Hefei and Wuhan are located in central China, and Chengdu in western China, all of which have subtropical monsoon humid climate, mild winter and hot summer. Guangzhou is located in southern China, with subtropical climate, warm winter and hot summer. The total population of these cities is 111.8 million according to the Sixth Population Census Report in China. The study period was from 2007 to 2013, depending on data availability.

2.2. Data collection

Death counts were collected from Chinese National Center for Chronic and Noncommunicable Disease Control and Prevention from 1 January 2007 to 31 December 2013. The causes of death were defined according to the International

Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10): CVD (I00-I99) and MI (I21-I22).

We obtained daily meteorological data from the China Meteorological Data Network (http://data.cma.cn) for the period of January 2007- December 2013. The data were recorded from a national basic meteorological station in each selected city, including daily minimum, maximum and mean temperatures, barometric pressure and relative humidity.

2.3. Statistical analysis

We used time-series regression models to examine the association between temperature and mortality using distributed lag non-linear models (DLNMs) within generalized linear models (GLMs) following a quasi-Poisson family. We selected the daily mean temperature since our previous work suggested that it was a better predictor of exposure over the whole day period than daily maximum or minimum temperature (Yang et al., 2012; Yang et al., 2016b). Besides, it represents the exposure throughout the 24-hour period and provides more easily interpreted information for policy and public health purposes. We applied a two-step analysis strategy to assess the seasonal temperature-related death burden in each city, as described below.

Firstly, a GLM model was used to estimate city-specific association between temperature and mortality, after controlling for the potential covariates. The bi-dimensional exposure-lag-response function defining the DLNM was specified using a natural cubic B-spline with 3 internal knots placed at the 10th, 75th and 90th percentiles of city-specific temperature distributions for the exposure-response function, and a natural cubic B-spline with 3 internal knots placed at equally-spaced values in the log scale with maximum lag of 21 days as the lag-response function. The covariates were adjusted as follows: a natural cubic spline function of time with 8 degrees of freedom (df) per year, as previous study reported that this model choice can well adjust for the underlying seasonal patterns in the death series (unrelated to ambient temperature) and any trends (Hajat and Gasparrini, 2016); indicator variables for day of the week and public holiday, and a spline function with 3 df of barometric pressure and relative humidity to control for their potential confounding effects. These specifications have been proven to be suitable for short-term variation investigations of temperature and health outcomes (Gasparrini et al., 2015; Yang et al., 2015b).

Secondly, to estimate the temperature-related mortality risk, we used the minimum-mortality temperature (MMT) at which the mortality risk was the lowest as the reference temperature. The city-specific cumulative relative risk over lag 0-21 days was used to compute the daily attributable deaths (AD) corresponding to each day's temperature (Gasparrini and Leone, 2014). The monthly or seasonal AD was then calculated by aggregating the monthly or seasonal contributions from the days of the series, and its ratio to the corresponding total number of deaths yielded monthly or seasonal attributable fraction (AF). Seasons were defined as the following 3-month periods: spring as March to May, summer as June to August, autumn as September to November and winter as December to February. We used the city-specific MMT of total CVD mortality as the baseline temperature for MI mortality to make the estimations comparable.

Several sensitivity analyses were conducted to check the robustness of our results. We changed the location of knots for temperature-mortality dimension and used 10-21 lag days for temperature, 4-10 df for time trend and 4-6 df for barometric pressure and relative humidity, respectively.

For all statistical tests, statistically significance were defined as two-tailed $P<0.05$. All models were conducted in R software (version 2.15.3, R Development Core Team 2013). Distributed lag non-linear model was fitted using “dlnm” package.

3. Results

Table 1 summarizes the daily mortality and mean temperature data in the nine cities. The daily mean mortality from CVD and MI deaths ranged from 7 to 100 and from 1 to 27, respectively, depending on the city. The annual mean temperature varied from 12.9 °C (range: -14.1-32.4 °C) in Tianjin to 21.6 °C (range: 5.1-30.8 °C) in Guangzhou.

Figure 1 shows the monthly distributions of mean temperature and mortality in the nine Chinese cities. Temperature ranges between cities varied greatly during cold months. The monthly death rates had a significant seasonal trend, which was much higher in cold months (January to March and October to December) than warm months (May to September).

The relationships between temperature and CVD mortality were U-, V- or reverse J-shaped across cities. Generally, the MMTs increased from the northern city to the southern city, with 24.7 °C in Tianjin and 30.0 °C in Hangzhou. In total, 195,516 CVD and 50,658 MI deaths were attributable to non-optimum temperatures (Supplementary Fig. A2).

Figure 2 shows the monthly distributions of mortality attributable to temperature for CVD and MI in the nine Chinese cities. Consistently, the attributable fractions were much higher in cold months than hot months in all cities, with the highest estimate in January or December and the lowest in May-August. However, there was also a small peak in July for Beijing, Tianjin and Guangzhou. Furthermore, higher attributable estimates were found for MI, compared with those for CVD, particularly for the southern cities, such as Wuhan, Chengdu and Guangzhou.

Table 2 and Supplementary Table A2 show the seasonal temperature-related AF and AD for mortality from CVD. The AFs varied greatly by cities, with negatively but non-significantly correlated with latitudes ($P>0.05$) (Supplementary Fig. A3). All cities displayed a peak number in winter and the lowest number in summer, except for Shanghai and Guangzhou. The highest combined estimate was 35% (95%CI: 19-48%) and 103,439 (54,475-141,537) deaths in winter, followed by 19% (5-31%) and 46,821 (12,057-74,949) in spring, 13% (1-22%) and 29,333 (1,963-52,304) in autumn, and 8% (1-14%) and 15,923 (1,436-28,853) in summer.

Table 3 and Supplementary Table A3 show the seasonal temperature-related AF and AD for MI mortality. The AFs varied greatly by cities, with negatively and significantly correlated with latitudes ($P<0.05$) (Supplementary Fig. A4). The highest combined estimate was 42% (9-62%) and 24,613 (5,891-36,279) deaths in winter, followed by 26% (-2-44%) and 12077 (-911-20433) in spring, 19% (-3-35%) and

9,022 (-1,683-16,389) in autumn, and 13% (-1-23%) and 4,946 (-325-9,016) in summer.

We conducted several sensitivity analyses to test the robustness of our main findings. For example, effect estimates were stable or slightly decreased, when using six or ten df per year for the spline of time trend. When we changed the location of knots for the association between temperature and mortality and the maximum lag for temperature, the results changed little (Supplementary Table A4 and A5).

4. Discussion

Here we quantified seasonal variations of temperature-related death burden from CVD and MI. Associations between ambient temperature and CVD/MI mortality were U- V- or reverse J-shaped across nine cities in China. 195,516 CVD and 50,658 MI deaths were attributable to non-optimal temperatures. The temperature impacts on CVD mortality appeared to be much higher during cold season than hot season, with 35% (19-48%) in winter and 8% (1-14%) in summer. This burden caused by ambient temperature was greater among patients with MI than those with CVD, particularly for southern cities.

Seasonal variations of CVD and MI mortality rate have been investigated over a large range of latitudes, and their death rates were generally higher in winter than other seasons (Fares, 2013; Healy, 2003; Khanjani and Bahrampour, 2013; Rumana et al., 2008; Spencer et al., 1998). However, the magnitudes of the seasonal variation varied greatly across regions, causes and populations. For example, Healy (Healy,

2003) reported that the seasonality of mortality accounts for 16% more deaths in winter than in summer in Europe, while a recent cohort study in China found 41% higher CVD death risk in winter than summer (Yang et al., 2015c). Most of these investigations focused on the conventional risk factors that contributed to increases in winter mortality. For instance, significant seasonal vitamin D level variations (Gouni-Berthold et al., 2009; Nemerovski et al., 2009), physical inactivity (Magnus et al., 1979; Pescatello et al., 2015) and outdoor air pollutants variation among seasons (Chen et al., 2013; Cosselman et al., 2015) were found to be associated with seasonal variations of CVD events.

Our recent study found that ambient temperature could explain one-tenth to nearly one-quarter of the variation in CVD deaths, making it one of the strongest CVD environmental stressors (Yang et al., 2015b). However, the quantitative evidence on the extent to which the seasonal variation of CVD and MI mortality could be explained by ambient temperature is unclear. The present study found that the winter temperature-induced CVD and MI deaths were over 5 times more than those relating to summer temperature. Additionally, the temperature-related death burdens were negatively correlated with latitudes, confirming with our previous study (Yang et al., 2016). These findings highlight a need to strengthen the awareness of winter (cold) temperature for the public health domain, particularly for the southern regions where people may have difficulty with acclimatization to extreme cold weather. Furthermore, as climate change is likely to enhance the frequency and intensity of extreme temperatures (e.g., heat waves and cold spells), public health adaptation policies should take both temperature rises and increased short-term (eg, interday or intraday variation) and long-term (eg, seasonal variation) weather variability into account while we prepare for more impacts from high temperature-related mortality burden on the society and public health systems (Gasparrini et al., 2015; Yang et al., 2015b; Yang et al., 2016).

The possible mechanisms that related to the seasonal pattern of CVD and MI deaths remain to be determined. In winter, the rapid decreased temperature would trigger the acute events of myocardial infarction, myocardial ischemia and sudden deaths. Exposure to cold environment was related to an increase in biomarkers of inflammation (CRP, sl CAM-1 and sVCAM1), blood cholesterol, platelet viscosity, plasma fibrinogen and peripheral vasoconstriction (Keatinge et al., 1984; Woodhouse et al., 1994). Moreover, cooling of skins would enhance systematic vascular resistance, heart rate and blood pressure (decreasing the ratio of oxygen supplied to the myocardium) (Kawahara et al., 1989). These acute body alterations may exacerbate the internal pressure on those with health problem on cardiovascular systems. As for the heat exposure, it may also relate to increases in red blood cell counts, platelet counts and blood viscosity, as well as increases in heart rate (Keatinge et al., 1986).

Our findings may have significant public health implications as CVD and MI are leading causes of death in many countries. Firstly, the winter peak in CVD and MI deaths was clearly associated with cold ambient temperature, which emphasizes that further research on the mechanisms underlying this phenomenon is warranted. Secondly, increased vigilance in winter is required for patients with CVD, particularly for those with MI, who suffered more from the temperature variation. Thirdly, early warning and proper intervention measures impending the extreme cold weather can make CVD death preventable. Fourthly, hospital emergency departments and medical centers should make sufficient preparedness with ample medical resources preceding extreme weather events. Finally, community education is vitally important to increase people's knowledge about risk factors of CVD/MI and promote health behaviors to cope with the impact of extreme weather events.

Our study has three key strengths. To the best of our knowledge, this is the first multicity study to quantify seasonal variations of temperature-related CVD and MI burden. The application of advanced statistical approaches, which allows for non-linear and lagged temperature effects at the same time, can flexibly examine effects of temperature on mortality. Furthermore, our main results were robust even after a series of sensitivity analyses were conducted.

This study also has several limitations. This study focused specifically on urban populations and its findings cannot be generalized to the rural areas, where temperature-related effects may be greater because of their limited access to central heating or air-conditioning household appliances. As data on air pollutants were unavailable, we couldn't adjust them in this study. However, previous studies have found that impacts of ambient temperature on health were independent of air pollution impacts (Guo et al., 2011; Yang et al., 2012). Finally, as in previous investigations, we used ambient temperature as a surrogate of individual exposure, which may have some measurement errors. However, such error is likely to be random and to lead to underestimates of cold effects (Rothman et al., 2008).

5. Conclusions

There were significant seasonal variations of temperature impacts on CVD and MI in the nine cities of China and cold or extreme cold temperatures significantly increased CVD/MI mortalities. The mortality fractions attributable to temperature were higher among patients with MI than those with CVD. As climate change will increase the frequency and intensity of extreme temperatures (e.g., heat wave and cold spell), public health adaptation policies should focus on the impacts from both temperature rises and increased weather variability.

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Conflict of interest:

The authors declare no conflict of interest.

Author Contributions

Q.L. and J.Y. initiated the study. Q.L., M.Z., and P.Y. collected the data. J.Y.

performed statistical analysis. J.Y. and C.Q.O. drafted the first version. ST provided significant intellectual advice and A.G. developed the statistical methods and software implementation. Other authors revised the manuscript. All authors read and approved the final manuscript.

Ethics approval

This study was approved by the Ethics Committee of Chinese Center for Disease Control and Prevention (No.201214).

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Table 1

Daily death counts from cardiovascular disease (CVD) and myocardial infarction (MI), and mean temperature (°C) in the nine Chinese cities during 2007–2013

City	Population (million)	CVD	MI	Study period	Daily mean temperature						
					Min	25th	50th	75th	Max	Mean	SD
Beijing	19.6	100	23	2007-2013	-12.5	2.5	14.9	24.0	34.5	13.2	11.3
Tianjin	12.9	95	27	2007-2013	-14.1	2.1	14.4	23.7	32.4	12.9	11.5
Shanghai	23.0	49	4	2007-2012	-3.4	9.4	18.3	25.0	35.7	17.4	9.1
Nanjing	8.0	42	5	2007-2013	-4.5	8.1	17.8	24.8	34.6	16.5	9.6
Hefei	5.7	42	6	2011-2013	-2.9	7.2	18.4	25.0	34.4	16.6	9.9
Chengdu	14.0	58	8	2008-2013	-0.5	9.5	17.4	22.9	29.3	16.3	7.5
Wuhan	9.8	13	3	2009-2012	-2.9	8.2	18.1	25.0	35.3	16.8	9.6
Hangzhou	8.7	7	1	2007-2013	-2.0	9.8	18.6	25.7	35.7	17.7	9.3
Guangzhou	12.7	45	9	2011-2013	5.1	16.6	23	27.0	30.8	21.6	6.3

Note. 25th, 50th and 75th represents the 25th, 50th and 75th percentiles of daily mean temperature, respectively.

Table 2

Seasonal variation of temperature-related attributable fraction (%, 95% empirical CI) for CVD mortality in the nine Chinese cities

City	Spring	Summer	Autumn	Winter
Beijing	20 (11-29)	11(7-14)	16 (9-23)	34 (22-45)
Tianjin	18(6-28)	7(3-10)	12(3-19)	30(13-44)
Nanjing	32 (20-42)	8(3-14)	19(8-28)	51 (39-61)
Shanghai	10(-4-21)	5(-1-10)	2 (-6-9)	19 (3-34)
Hefei	31(1-50)	11(-3-22)	16 (-9 -35)	53 (27-70)
Chengdu	9 (-11-26)	2(-14-15)	4 (-13-19)	30(8-45)
Wuhan	35(6-54)	11(-5-23)	30 (1-49)	52(22-69)
Hangzhou	22 (-9-45)	5(-9-16)	9(-16-26)	44 (13-65)
Guangzhou	27(9-41)	16(2-27)	14 (1-25)	51 (35-63)
Overall	19 (5-31)	8(1-14)	13(1-22)	35 (19-48)

Table 3

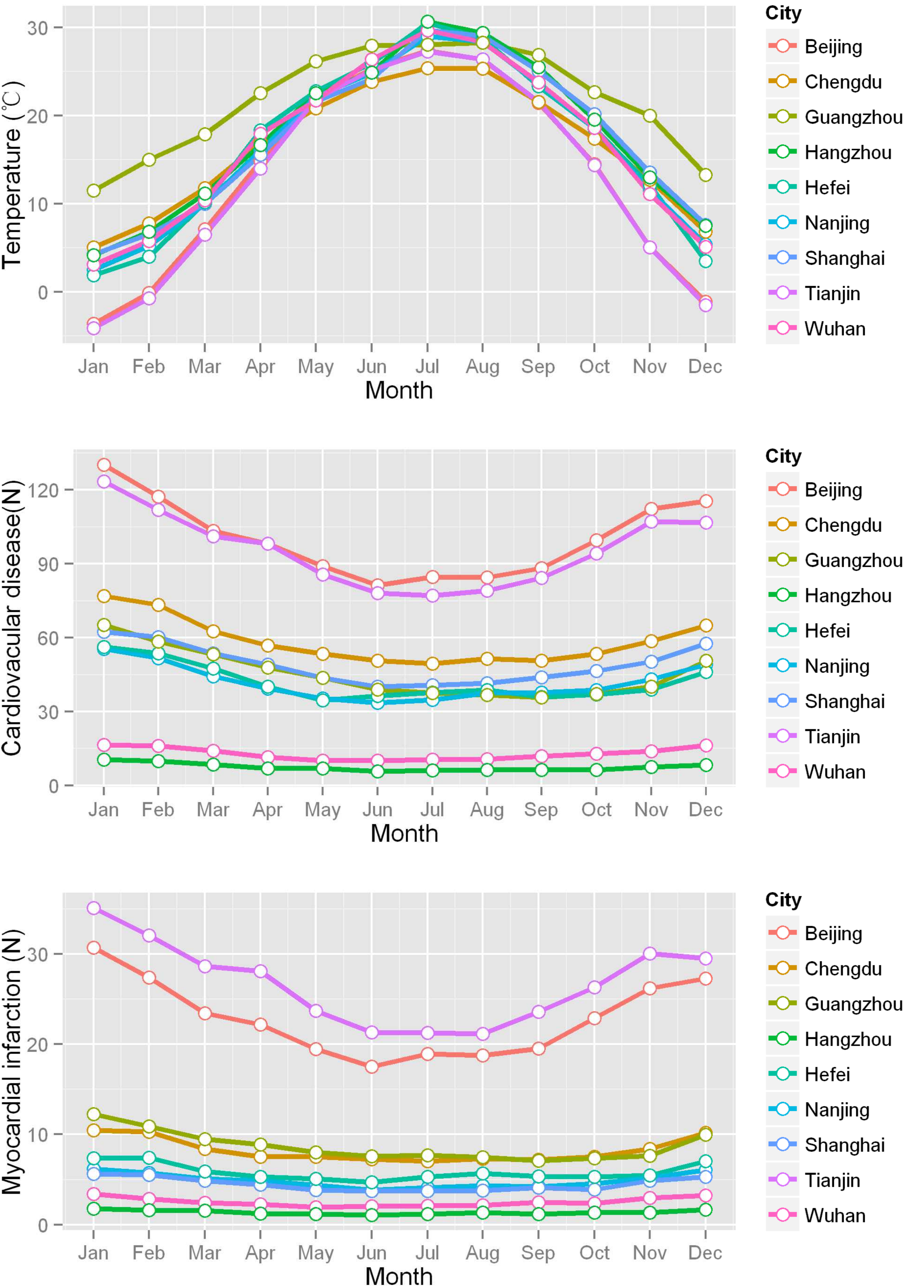
Seasonal variation of temperature-related attributable fraction (%, 95% empirical CI) for MI mortality in the nine Chinese cities

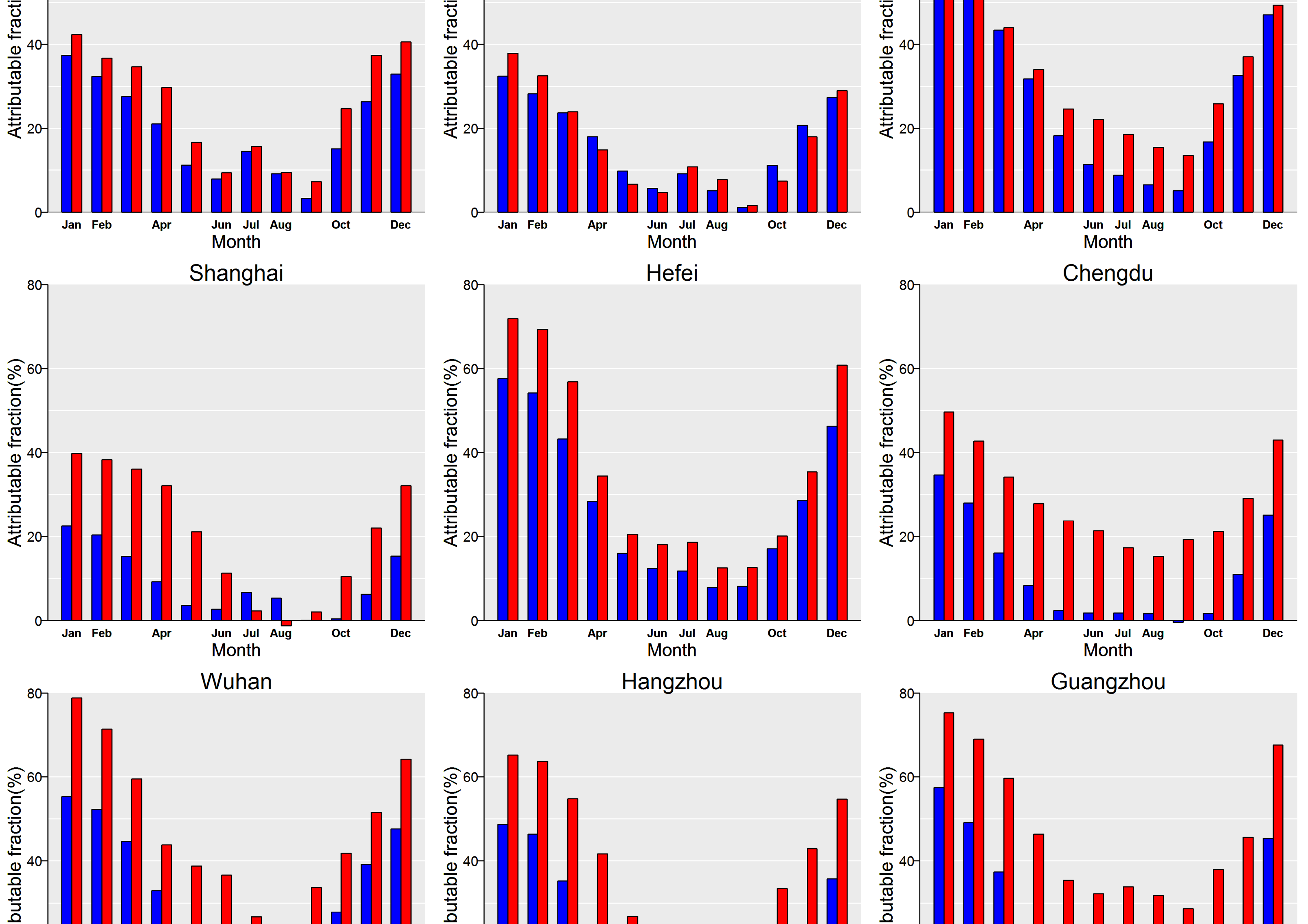
City	Spring	Summer	Autumn	Winter
Beijing	28(9-41)	12(5-18)	26(11-37)	40 (15-57)
Tianjin	16(-5-32)	8(1-14)	9 (-6-22)	33 (7-53)
Nanjing	35(-4-59)	19(4-30)	25 (-6-45)	54(14-75)
Shanghai	30 (-9-54)	4(-16-19)	12(-10-30)	37(-14-64)
Hefei	38 (-29-70)	16 (-17-38)	22 (-46-56)	67 (11-88)
Chengdu	29(-13-55)	18(-13-40)	23(-16-49)	45 (2-69)
Wuhan	48 (-20-77)	28(-3-48)	50(-25-82)	72(19-90)
Hangzhou	42 (-29-73)	13(-19-33)	31 (-23-60)	62(-14-86)
Guangzhou	48(17-67)	33(7-51)	31 (4-49)	71(48-84)
Overall	26(-2-44)	13(-1-23)	19 (-3-35)	42 (9-62)

Figure legends

Fig. 1. Monthly mean temperature (^oC) and averaged numbers of deaths from cardiovascular disease and myocardial infarction in the nine Chinese cities.

Fig. 2. Monthly temperature-related attributable mortality fractions for cardiovascular disease and myocardial infarction in the nine Chinese cities.


Temperature (℃)
30
20
10
0
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Month
City
Beijing
Chengdu
Guangzhou
Hangzhou
Hefei
Nanjing
Shanghai
Tianjin
Wuhan
Cardiovacular disease(N)
120
90
60
30
0
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Month
City
Beijing
Chengdu
Guangzhou
Hangzhou
Hefei
Nanjing
Shanghai
Tianjin
Wuhan
Myocardial infarction (N)
30
20
10
0
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Month
City
Beijing
Chengdu
Guangzhou
Hangzhou
Hefei
Nanjing
Shanghai
Tianjin
Wuhan



Shanghai
Hefei
Chengdu
Wuhan
Hangzhou
Guangzhou
Attributable fraction(%)
Month
Jan
Feb
Apr
Jun
Jul
Aug
Oct
Dec
0
20
40
60
80