

1 Cardiovascular mortality risk attributable to ambient
2 temperature in China

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1 **ABSTRACT**

2 **Objective** To examine cardiovascular disease (CVD) mortality burden attributable to
3 ambient temperature; to estimate effect modification of this burden by gender, age and
4 education level.

5 **Methods** We obtained daily data on temperature and CVD mortality from 15 Chinese
6 mega-cities during 2007-2013, including 1,936,116 CVD deaths. A quasi-Poisson
7 regression combined with distributed lag non-linear model was used to estimate the
8 temperature-mortality association for each city. Then, a multivariate meta-analysis
9 was used to derive the overall effect estimates of temperature at national level.
10 Attributable fraction of deaths were calculated for cold and heat (i.e. temperature
11 below and above minimum-mortality temperatures, MMT), respectively. The MMT
12 was defined as the specific temperature associated to the lowest mortality risk.

13 **Results** The MMT varied from 70th to 99th percentile of temperature in 15 cities,
14 centering at 78th at the national level. In total, 17.1% (95% empirical CI: 14.4-19.1%)
15 of CVD mortality (330,352 deaths) was attributable to ambient temperature, with
16 substantial differences among cities, from 10.1% in Shanghai to 23.7% in Guangzhou.
17 Most of the attributable deaths were due to cold, with a fraction of 15.8% (13.1-17.9%)
18 corresponding to 305,902 deaths, compared to 1.3% (1.0-1.6%) and 24,450 deaths for
19 heat.

20 **Conclusions** This study emphasizes how cold weather is responsible for most part of
21 the temperature-related CVD death burden. Our results may have important
22 implications for the development of policies to reduce CVD mortality from extreme

1 temperatures.

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3 **Key Words:** Cardiovascular disease, death, ambient temperature, attributable fraction,

4 China

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6 **Word count:** 2996

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1 **What is already known on this subject?**

2 Cardiovascular disease is the leading cause of mortality and particularly sensitive to
3 climate change. Extreme ambient temperatures are associated with an increased
4 relative risk of CVD mortality.

5

6 **What might this study add?**

7 Temperature was responsible for advancing 17.1% of CVD mortality. The majority of
8 CVD mortality burden of ambient temperature was caused by cold. The daily
9 attributable fraction due to temperature had a significant peak in the cold months
10 (November to February). CVD mortality burden of both cold and hot temperatures
11 were higher among the elderly and those with lower education level.

12

13 **How might this impact on clinical practice?**

14 Cold temperature plays an important role in the winter excess mortality of CVD.
15 Public health policies and adaptive measures should be extended to reduce the
16 temperature-related particularly cold-related CVD mortality, especially in the
17 developing countries. More attention should be paid to the vulnerable subpopulations.

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1 **INTRODUCTION**

2 In recent decades, reports have pointed out that extreme weathers (e.g., heatwaves and
3 cold spells) due to climate change is one of most serious challenge worldwide, with
4 direct (e.g., excess morbidity and mortality) impacts on human health.¹ The definition
5 and implementation of adaptation and mitigation strategies to extreme weathers
6 require a comprehensive and in-depth understanding and quantification of the effects
7 of weather factors on human health.

8

9 Cardiovascular diseases (CVD) are highly sensitive to weather variations.^{2 3} CVD
10 includes coronary heart disease, strokes and other heart diseases, and represents the
11 top cause of death globally. In the last decades, the prevalent rate have changed
12 differently between developed and developing countries, with a decline in many
13 high-income countries but a rapid increase in low- and middle-income countries.⁴
14 Based on economic development, population aging and changes in diet and physical
15 activity, annual CVD events are predicted to increase by an additional 23% and 7.7
16 million CVD deaths over 2010 to 2030 alone in China.⁵

17

18 Estimating how much temperatures affect CVD mortality is a very important for
19 development of health care system to reduce temperature-induced CVD events, for
20 example, clinics, hospitals, and nursing centers should add more staff and increase
21 their rotation during extreme cold and hot days. However, most of previous studies
22 examined the relation in terms of ratio measures, such as relative risk (RR) and odds

1 ratio (OR), providing estimates of the exposure-response relationship.⁶⁻¹⁰ These
2 indicators provided limited information on the excess burden due to the exposure,
3 comparing to relative attributable measures, such as attributable fraction and
4 attributable number, which are more suitable for estimating potential benefits of
5 preventive interventions.

6

7 To date, only few studies have reported estimates of the temperature-related mortality
8 using attributable risk, such as absolute excess (numbers) or relative excess (fraction)
9 of deaths.¹¹⁻¹³ These studies limited the analysis to one single city and applied
10 relatively simple statistical models unable to capture the non-linear and delayed
11 effects of temperatures. Moreover, less evidence was available on this topic from
12 developing countries. In this contribution, we aimed to provide figures of attributable
13 burden of CVD mortality due to temperatures, separating the contributions of cold
14 and heat effects from a national-scale analysis in China, and to assess the effect
15 modification of temperatures on CVD mortality by individual characteristics (e.g.,
16 gender, age group and education level).

17

18 **METHODS**

19 **Data collection**

20 We collected daily number of death data and meteorological data from 15 large cities
21 in China (Harbin, Changchun, Beijing, Shenyang, Tianjin, Shijiazhuang, Jinan,
22 Zhengzhou, Shanghai, Nanjing, Chengdu, Chongqing, Changsha, Kunming and

1 Guangzhou) during 2007-2013 (Figure 1). The latitudes varied from 23.2N of
2 Guangzhou to 45.4N of Harbin. Our study was restricted to the urban areas because
3 the Death Registry has not been well established in suburban and rural regions in
4 China.

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6 The daily counts of death data were obtained from the China Information System of
7 Death Register and Report of Chinese Center for Disease Control and Prevention
8 (China CDC) from 1 January 2007 to 31 December 2013. The causes of death were
9 coded by China CDC according to the International Classification of Diseases, Tenth
10 Revision (ICD-10): cardiovascular disease (ICD-10: I00-I99). In addition, we
11 stratified the data by different groups, including gender and age group (0-64, 65-74
12 and 75+ years), and education level (illiterate, primary education, and high school and
13 above).

14

15 The daily weather data were collected from China Meteorological Data Sharing
16 Service System (<http://cdc.nmic.cn/home.do>) from one weather monitoring station for
17 each city during the study period. Weather data include daily mean temperature,
18 maximum and minimum temperatures, relative humidity, and atmospheric pressure.
19 We used mean daily temperature to estimate the effects of temperature on CVD
20 mortality, as it represents the exposure throughout the entire day and night and
21 provides more easily interpretable results in a policy context.

22

1 **Statistical analysis**

2 We conducted a two-stage analysis to estimate the CVD mortality risk attributable to
3 cold and hot temperatures. At the first stage, individual-city data were analyzed and
4 city-specific effect estimates were extracted and subsequently used in a second-stage
5 meta-analysis to produce pooled estimates.

6

7 At the first stage, we adopted the distributed lag non-linear model (DLNM) combined
8 with a quasi-Poisson regression to examine city-specific non-linear and lag effects of
9 temperature on CVD mortality. The city-specific Poisson regression model is given as
10 following:

$$11 \text{Log}[E(Y_t)] = \alpha + \beta \text{Temp}_{t,l} + \text{NS}(\text{Time}, 8*7) + \text{NS}(\text{Hum}_t, 3) + \text{NS}(\text{Press}_t, 3) + \gamma \text{Dow}_t + \nu \text{Holiday}_t$$

12 where Y_t is the observed daily deaths at calendar day t ($t=1,2,3\dots 2557$); α is the
13 intercept; $\text{Temp}_{t,l}$ was the cross-basis matrix produced by DLNM.¹⁴ This matrix is
14 obtained by the combination of the exposure-response function with a natural cubic
15 spline with 3 internal knots placed at the 10th, 75th and 90th percentiles of
16 city-specific temperature distributions, and the lag-response function modelled with a
17 natural cubic spline with 3 internal knots placed at equally spaced values in the log
18 scale. The maximum lag was set up to 21 days, for effects of cold temperature
19 appeared only after some delay and lasted for several days, whereas effects of hot
20 temperature were immediate and possibly affected by mortality displacement.^{15 16}

21 NS(.) means a natural cubic spline; 8 df per year for time was used to control for the
22 long-term and seasonality;¹⁷ 3 df was used for relative humidity (Hum) and

1 atmospheric pressure (Press);⁹ Day of the week (Dow) and public holidays (Holiday)
2 were also included in the model as indicator variables.^{9 16}

3

4 At the second stage, a multivariate meta-analysis was applied to obtain the
5 nationally-pooled effect estimates, and then to produce the best linear unbiased
6 prediction (BLUP) for city-specific relationships, using a method recently
7 developed.¹⁵ Compared with previous meta-analysis method, this methodology offers
8 greater flexibility to capture the complex non-linear and delayed associations between
9 exposure and outcome from multiple locations. To pool the associations between
10 temperature and CVD mortality, we reduced the 16 estimated parameters of the
11 cross-basis, representing the bi-dimensional exposure-lag-response surface, to the 4
12 parameters of the one-dimensional overall cumulative exposure-response curve.
13 Heterogeneity was assessed through a multivariate extension of the I^2 statistics,¹⁸
14 which quantifies the percentage of variability due to the true differences across cities.

15

16 The minimum-mortality temperature (MMT) is derived by the lowest point of the
17 overall cumulative exposure-response curve, and it is interpreted as the optimal
18 temperature characterized by the lowest risk of CVD mortality. The MMT,
19 corresponding to a minimum mortality percentile (MMP) of temperature between the
20 1st and 99th, was selected from the city-specific cumulative overall
21 temperature-mortality association, which were re-centered on these values. The total
22 attributable number of deaths due to non-optimal temperatures is calculated by

1 summing the contributions from all the days of the series, using the MMT/MMP as
2 the reference. The ratio with the total number of deaths produces the total attributable
3 fraction. The components attributable to cold and hot temperature were computed by
4 summing the subsets corresponding to days with temperature below or above the
5 MMT, respectively. Empirical confidence intervals (eCI) were obtained by Monte
6 Carlo simulations assuming a multivariate normal distribution of the BLUPs of the
7 reduced coefficients.¹⁹

8

9 Significance tests on the effect modification of gender, age and education level were
10 performed in the second-stage meta-regression. The coefficients of all stratum-level
11 analyses were included in the same multivariate-meta regression estimated by
12 maximum likelihood, and the models with and without indicators for each
13 characteristic were compared through a likelihood ratio test to determine whether the
14 coefficients describing the temperature-mortality association change between the
15 groups.

16

17 Sensitivity analyses were performed to test the robustness of our results by changing
18 location of knots for exposure-response and using 14-28 lag days, 6-10 df for time
19 trend and 3-6 df for relative humidity and atmospheric pressure in the analyses,
20 respectively.

21

22 All data analyses were performed using the R software (version 3.0.3, R Development

1 Core Team 2010). The “dlnm” package was used to fit the distributed lag non-linear
2 model and the “mvmeta” package to conduct the multivariate meta-analysis. For all
3 statistical tests, two-tailed $P < 0.05$ were considered statistically significant.

4 5 **RESULTS**

6 Table 1 shows the descriptive data on population size, daily CVD mortality and mean
7 temperature in the 15 Chinese cities included in the analysis. This study included
8 more than 183.72 million permanent residents with daily mean CVD mortality counts
9 ranging from 30 to 100 in various cities. The annual mean temperature ranged from
10 5.3 °C in Harbin to 21.6 °C in Guangzhou. Temperature ranges between cities were
11 more varied during cold season (Table S1).

12
13 Figure 2 shows the overall cumulative exposure-response curves (best linear unbiased
14 predictions) in those cities, with the corresponding MMT and temperature distribution.
15 Generally, the temperature-mortality relationships were U-shaped at lag 0-21 days.
16 The histogram plots show that most daily mean temperatures are below the MMT.

17
18 Table 2 reveals that the median MMP was 78th, ranging between 70th and 99th
19 percentile of temperature. The I^2 statistics indicates a large and significant
20 between-city heterogeneity (86.6%, $P < 0.001$). In total, 17.1% (95% empirical CI:
21 14.4-19.1%) of CVD mortality, corresponding to 330,352 deaths, was attributed to
22 temperature, although it varies substantially across cities, with the highest estimate in

1 Guangzhou (23.7%) and the lowest estimate in Shanghai (10.1%). Cold temperature
2 accounted for most of the burden, with a fraction of 15.8% (13.1-17.9%),
3 corresponding to 305,902 deaths, while the burden due to hot temperature was
4 comparatively smaller, with a fraction of 1.3% (1.0-1.5%) , corresponding to 24,450
5 deaths (Figure 1 and Table S2).

6

7 The burden and heat /cold pattern was similar among males and females, while both
8 hot and cold attributable risks were higher among the elderly and those with low
9 education level, but the differences within these subgroups were not statistically
10 significant ($P>0.05$). The attributable fraction due to temperature were 16.4%
11 (13.6-18.8%), 16.9% (14.1-19.1%) and 17.3% (14.6-19.4%) for people with age less
12 than 65, 65-74 years and older than 75, respectively; figures of 18.1%(15.1-20.2%),
13 17.1%(14.1-19.1%) and 16.5%(13.9-18.7%) were estimated for the illiterate, people
14 with primary school and those with higher education level, respectively (Table 3).

15

16 The daily attributable fraction due to temperature generally had a significant seasonal
17 trend, with much higher in the cold months (November to February) than the hot
18 months (May to September). There was also a small peak in June or July (Figure S1).

19

20 Analyses were performed to test the sensitivity of our results to modelling choices.

21 The effect estimates were similar when we changed location of knots for the

22 exposure-response relationship and 4-6 df for relative humidity and air pressure in the

1 analyses; slightly smaller estimates were produced when using shorter maximum lag
2 days or changing df for the time trends (e.g. 6 or 10), respectively (Table S3).

3

4 **DISCUSSION**

5 To the best of our knowledge, this is the first study to examine CVD mortality
6 attributable to ambient temperature in developing countries and the first study to
7 explore effect modification of such risk by individual characteristics. The
8 minimum-mortality temperatures were generally distributed around 78th percentile of
9 temperature. The cold temperature was responsible for most of temperature-related
10 CVD mortality. The attributable burdens of both hot and cold temperatures were
11 higher among the elderly and those with lower education level.

12

13 The association between ambient temperature and CVD mortality has been well
14 documented in numerous epidemiological studies.^{3 6 7 9 10} However, most of these
15 studies measured the association using some ratio indicators, such as RR and OR.
16 There were very few studies examining the attributable burden, either as absolute
17 excess (attributable numbers) or relative excess (attributable fractions) of CVD
18 deaths.¹¹⁻¹³ Recently, an international study using similar design by Gasparrini and
19 colleagues estimated a 11.3% of all-cause deaths were attributable to ambient
20 temperatures in China,¹⁷ which was much smaller than our estimate of 17.1% of CVD
21 deaths. Carson and colleagues¹² also reported a much smaller attributable fraction
22 (4.6%) of CVD deaths due to cold but none to hot temperature in London. These

1 evidences confirmed that temperature-mortality association varied by regions,
2 populations and climates.

3

4 The mechanistic effects of ambient temperature on cardiovascular pathophysiology
5 are profound, which may be involved in the changes in vascular tone, autonomic
6 nervous system response, arrhythmia, and oxidative stress. The vascular tone change
7 was observed from repeated measurements on two consecutive days during colder
8 months (October-April) among 868 elderly individuals in Japan, a 1°C lower indoor
9 temperature was significantly associated with 0.22 mmHg higher daytime systolic
10 blood pressure and 0.34 mmHg higher sleep-trough morning blood pressure surge.²⁰

11 Another study of rats exposed in a cold room at 4 degree °C demonstrated attenuated
12 sympathetic nerve stimulation (NS)-induced overflow of noradrenaline in the
13 perfused mesenteric arterial bed.²¹ Cold exposure was also found to increase the
14 frequency of heart rate variability and ventricular ectopic beats.²² In addition,
15 exposure to cold caused significant increase of inflammatory cytokines and methane
16 dicarboxylic aldehyde (MDA) and decline of superoxide dismutase(SOD) and
17 glutathione peroxidase (GSH-Px) activity,²³ and the genes involved in the
18 hypoxia-inducible factor signaling pathway were activated in which oxidative
19 stress-associated genes were significantly upregulated, including superoxide
20 dismutase 2 (SOD2) and epoxide hydrolase 2 (EPHX2).²⁴ On the other hand,
21 exposure to hot weather may induce profound physiologic changes, such as increase
22 in blood viscosity and cardiac output leading to dehydration, hypotension, surface

1 blood circulation increase and even endothelial cell damage.²⁵ These responses may
2 overload the heart function and cause haemoconcentration, and induce a failure of
3 thermoregulation. Further mechanistic studies are warranted to disentangle these
4 complex relationships between CVD and ambient temperature.

5
6 Our results showed that cold effects accounted for over 90% percent of
7 temperature-related CVD mortality. These findings indicate that cold temperature
8 plays an important role in the winter excess mortality of CVD. The policymaker, local
9 community and the public should strengthen the awareness of preventing harmful
10 health effect of cold temperature, especially for people in southern areas, where
11 central heating was not available in winter. Moreover, attributable fraction of CVD
12 mortality due to temperature varies by cities, ranging from 10.1% to 23.7%. Generally,
13 the hot-related mortality fraction was higher in the north than in the south while there
14 was higher cold-related fraction in the south; the hot/cold-related mortality fraction
15 was moderately correlated with annual mean temperature [Spearman Correlation
16 Coefficient $r_s=-0.626$ for hot effect ($P=0.013$); $r_s=0.502$ for cold effect ($P=0.051$)].
17 Consistently, the MMT increased from the north to the south, which was strongly
18 correlated with annual mean temperature (Spearman Correlation Coefficient $r_s=0.772$;
19 $P=0.001$). This phenomenon indicates that people could acclimatize to their local
20 environmental conditions through physiological adaptation and individual behaviors.
21 Populations in northern regions are more vulnerable to heat, while people in southern
22 regions are more sensitive to cold weather. The popularity of air conditioning and

1 household heating appliances can be helpful to mitigate the health effects of hot and
2 cold temperatures, respectively.

3

4 Many epidemiological studies have provided evidence that susceptibility to cold and
5 hot temperatures is modified by age, gender and education level. For both hot and
6 cold temperatures, the effects were clearly larger in the elderly than in the youth.
7 Aging induces physiological changes in thermoregulation and homeostasis, together
8 with the prevalence of preexisting chronic conditions, limiting capacity to prevent CV
9 events, and use of medication, offering susceptibility to hot and cold stress.²⁶ Given
10 the increasing disease burden of CVD in China, it has been a significant challenge to
11 the government and the societal infrastructure that affects not only the economic
12 growth, but also the healthcare system. Age-appropriate primary care exacerbated by
13 user fees and social protection, and community-based measures should be targeted
14 particularly for the elderly, especially at time of hot and cold weathers.

15

16 Effect modification by gender varied among different regions and population. For
17 example, the impact of hot temperature was higher for women in Mexico, but higher
18 for men in Sao Paulo.²⁷ The differences in occupational exposure, physiology and
19 thermoregulatory may contribute to the temperature-related susceptibility between
20 genders.^{9 28 29} Education level is viewed as one of the most important indicators
21 relating to one's overall socioeconomic status. Previous investigations have reported
22 that those with low socioeconomic status have a greater vulnerability to

1 temperature-related mortality,^{9 27} which may be associated with poorer health status,
2 limited access to health care, poor housing conditions, lack of knowledge and
3 unhealthy behavior patterns such as smoking. These disadvantage factors may reduce
4 their capacity to take proper precautions in the heat or cold to prevent CV events.

5

6 This study has some limitations. Firstly, this study applies specifically to urban
7 populations and isn't necessarily able to be generalized to the rural areas in China
8 where cold and heat effects may be greater because of even less consistent access to
9 central heating or air conditioning. Similar with previous time-series investigations,
10 this study only assessed short-term effects of temperature on CVD mortality after
11 controlling for long-term trend and other covariates. While a large element of CVD
12 may be due to long-term pathology. Thirdly, the attributable fraction was calculated
13 assuming the causality between cold/hot temperatures and mortality, although the
14 evidence is still limited on this association. However, extensive epidemiological
15 studies have shown that the cold and hot temperatures have impacts on human
16 mortality^{2 3 8-11} and morbidity^{24 30}. Fourthly, the use of data on temperatures were from
17 fixed monitoring sites rather than measuring individual exposure, which may create to
18 some extent measurement errors in the exposure. However, these errors are likely to
19 be random. Meanwhile, we cannot ignore the misclassification bias since CV cause of
20 death was assigned according to ICD 10 code on death certificate. Fifthly, air
21 pollutants data were not controlled for in this study, because these data were not
22 available. However, previous studies have found that the effect of temperature on

1 mortality did not change when controlling for air pollution.^{9 16}

2

3 **CONCLUSIONS**

4 The cold temperature was responsible for most of temperature-related CVD mortality
5 in China. Our results may contribute significantly to the understanding of the adverse
6 health effects of cold and hot temperatures on CVD mortality. It may also have
7 important public health implications for policymakers and local communities with the
8 aim to protect vulnerable subpopulations from ambient extreme temperatures.

9

10 **Contributors**

11 J.Y. and Q.L. initiated the study. M.Z., Y.P. and Q.L. collected the data. J.Y., Y.L. and
12 G.L. cleaned the data. J.Y. performed statistical analysis. A.G. developed the statistical
13 methods and software implementation. J.Y. and C.Q.O. drafted the manuscript. Y.G.,
14 A.G., Y.Y., S.G., S.S., Q.S. and Q.L. revised the manuscript. All authors read and
15 approved the final manuscript.

16

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20

21 **Competing interests**

22 None.

1 **Ethics approval**

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

4

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1 **Table 1** Descriptive data on cardiovascular mortality (CVD) and daily mean
 2 temperature (°C) in 15 Chinese cities during 2007-2013

City	Population (million)	Daily CVD deaths	Study period	Daily mean temperature percentiles							
				Min	1st	25th	50th	75th	99th	Max	Mean
Harbin	10.6	82	2007-2013	-28.0	-24.0	-8.7	7.6	19.7	27.4	30.6	5.3
Changchun	7.7	30	2007-2013	-27.6	-22.0	-6.9	8.4	19.7	26.6	30.4	6.2
Shenyang	8.1	56	2007-2013	-24.0	-19.4	-3.3	9.9	20.7	27.0	29.0	8.0
Beijing	19.6	100	2007-2013	-12.5	-7.6	2.5	14.9	24.0	30.4	34.5	13.2
Tianjin	12.9	95	2007-2013	-14.1	-7.9	2.1	14.4	23.7	30.0	32.4	12.9
Shijiazhuang	10.2	36	2007-2013	-8.4	-5.7	4.1	15.7	24.3	31.5	34.3	14.3
Jinan	6.8	59	2011-2013	-9.4	-6.4	4.2	16.3	24.0	31.3	33.0	14.4
Zhengzhou	8.6	37	2011-2013	-4.4	-3.0	5.9	17.4	25.1	32.5	34.2	15.6
Shanghai	23.0	53	2007-2013	-3.4	0.2	9.4	18.3	25.0	33.3	35.7	17.4
Nanjing	8.0	42	2007-2013	-4.5	-1.7	8.1	17.8	24.8	32.5	34.6	16.5
Chengdu	14.0	55	2007-2013	-0.5	1.9	9.7	17.3	23.0	28.2	29.3	16.4
Chongqing	28.8	180	2011-2013	3.0	4.7	11.7	19.1	25.6	34.6	36.7	19.0
Changsha	6.1	48	2007-2013	-3.0	-0.2	10.2	19.1	26.5	33.8	35.8	18.4
Kunming	6.4	32	2007-2013	-0.9	4.5	12.2	16.9	20.0	23.3	24.6	16.0
Guangzhou	12.7	45	2011-2013	5.1	6.9	16.6	23.0	27.0	30.2	30.8	21.6

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1 **Table 2** Attributable cardiovascular mortality fraction by cities computed as total
 2 and as separated components for cold and hot temperatures in 15 Chinese cities

City	MMP (MMT)*	Attributable mortality fraction (% ,95%empiricalCI)		
		Total	Cold	Hot
Harbin	78(20.6)	15.2(4.3-24.1)	13.6(2.1-22.1)	1.7(0.3-2.8)
Changchun	78(20.6)	12.9(0.9-22.1)	11.1(-1.5-20.7)	1.8(0.4-3.0)
Shenyang	78(21.5)	16.2(6.8-23.8)	14.8(6.7-21.9)	1.4(0.1-2.6)
Beijing	79(24.9)	20.1(13.4-26)	18.3(11.0-24.3)	1.8(1.1-2.5)
Tianjin	78(24.5)	16.0(9.5-21.8)	14.8(7.5-21.1)	1.3(0.4-2.1)
Shijiazhuang	73(23.8)	16.1(10.3-21.3)	15.0 (7.9-20.7)	1.2(0.0-2.2)
Jinan	78(24.9)	16.7(8.5-23.1)	14.0 (5.4-21.0)	2.7(1.7-3.6)
Zhengzhou	79(25.9)	16.7(8.3-23.8)	15.2(5.0-22.6)	1.5(0.3-2.6)
Shanghai	73(24.5)	10.1(4.1-15.8)	8.8(2.2-14.7)	1.3(0.0-2.5)
Nanjing	88(27.9)	22.2(14.6-28.4)	21.5(14.2-28.6)	0.7(0.2-1.3)
Chengdu	81(24.1)	14.7(5.6-22.8)	14.5(4.9-22.5)	0.2(-1.4-1.5)
Chongqing	87(29.2)	18.1(8.0-26.7)	17.1(6.7-25.6)	1.0 (0.2-1.9)
Changsha	70(25.1)	18.1(12.3-22.5)	16.8(10.6-22.0)	1.3(-0.2-2.7)
Kunming	99(23.3)	23.0 (0.9-38.7)	23.0 (1.9-39.7)	0.0(-0.2-0.1)
Guangzhou	93(29.0)	23.7(10.6-33.8)	23.3(10.2-33.2)	0.5(-0.2-1.0)
Overall	78(-)	17.1(14.4-19.1)	15.8(13.1-17.9)	1.3(1.0-1.5)

3 * MMP: minimum mortality percentile of temperature (%); MMT: minimum mortality
 4 temperature (°C).

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1 **Table 3** The pooled attributable cardiovascular mortality fraction computed as total
 2 and as separated components for cold and hot temperatures, stratified by individual
 3 characteristics

Variables	Attributable mortality fraction (% , 95%empiricalCI)		
	Total	Cold	Hot
Gender*			
Male	17.0(14.4-19.1)	15.7(12.8-17.9)	1.3(1.0-1.5)
Female	17.2(14.5-19.2)	15.9(13.3-18.1)	1.3(0.9-1.5)
Age- years*			
0-64	16.4(13.6-18.8)	15.1(12.1-17.4)	1.3(1.0-1.6)
65-74	16.9(14.1-19.1)	15.7(12.8-17.8)	1.3(0.9-1.6)
75+	17.3(14.6-19.4)	16.1(13.5-18.4)	1.2(0.9-1.5)
Education attainment*			
Illiterate	18.1(15.1-20.2)	16.9(14.2-19.2)	1.2(0.9-1.4)
Primary school	17.1(14.1-19.1)	15.8(13.0-18.1)	1.3(0.9-1.6)
High school and above	16.5(13.9-18.7)	15.2(12.6-17.6)	1.3(1.0-1.6)

4 * Differences within gender, age group and education attainment were not
 5 statistically significant (P>0.05).

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1 **Figure legends**

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3 **Figure 1** The locations of 15 Chinese cities in this study, with attributable
4 cardiovascular mortality fraction computed as total and as separated components for
5 cold and hot temperatures.

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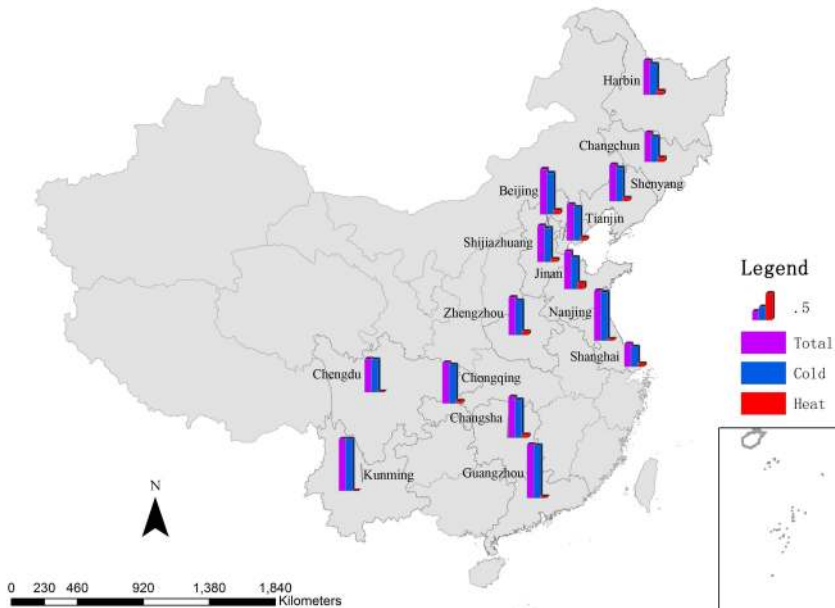
7 **Figure 2** Overall cumulative relative risk (RR) across lag 0-21 days (with 95%
8 empirical CI, shaded grey) in 15 Chinese cities, with histogram of daily temperature
9 distribution. The dashed grey lines are minimum-mortality temperatures. The blue and
10 red lines represent the exposure-response below (cold) and above (hot) the
11 minimum-mortality temperatures.

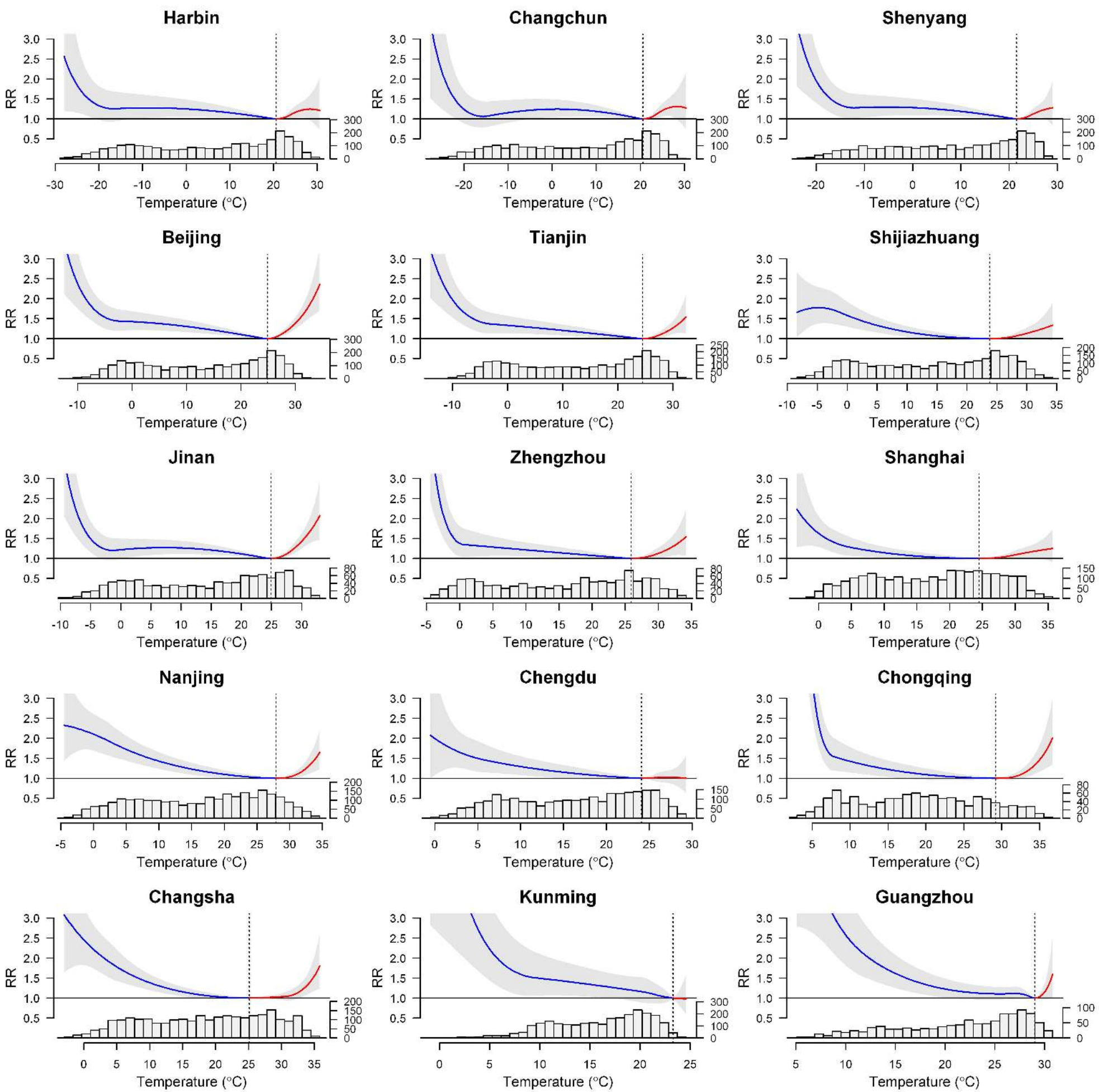
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Supplemental Materials

Cardiovascular mortality risk attributable to ambient temperature in China

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Table of contents

Title	Page
Table S1 The monthly median temperature (°C) in 15 Chinese cities.	3
Table S2 Attributable cardiovascular deaths by cities computed as total and as separated components for cold and hot temperatures in 15 Chinese cities.	4
Table S3 Sensitivity analyses of calculating the fraction (%) attributable to temperature by changing location of knots of exposure-response- maximum lag for mean temperature and degrees of freedom (df) for covariates.	5
Figure S1 Daily attributable fraction (%) for cardiovascular mortality due to temperature in 15 Chinese cities during 2007-2013.	6

Table S1 The monthly median temperature (°C) in 15 Chinese cities.

City	Jan.	Feb.	Mar.	Apr.	May.	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.
Harbin	-17.7	-12.6	-3.8	7.0	15.6	22.0	23.8	22.4	16.5	7.5	-4.8	-14.7
Changchun	-15.5	-10.4	-2.3	7.3	16.3	21.9	23.7	22.4	16.9	8.4	-3.0	-12.7
Shenyang	-13.7	-7.2	0.6	9.1	17.8	22.3	24.6	23.6	18.0	10.1	-0.4	-9.6
Beijing	-3.6	-0.1	7.1	14.8	22.1	25.4	27.4	26.4	21.4	14.5	5.0	-1.1
Tianjin	-4.1	-0.7	6.5	14.0	21.9	25.2	27.3	26.4	21.6	14.4	5.0	-1.5
Shijiazhuang	-2.3	1.4	8.6	16.1	22.8	26.6	28.2	26.6	21.6	15.6	6.5	0.2
Jinan	-1.9	1.8	8.2	16.2	22.7	27.1	27.8	25.9	21.1	16.5	8.0	0.1
Zhengzhou	-0.3	3.1	10.0	18.4	23.3	28.0	28.9	27.3	21.3	16.8	9.2	1.9
Shanghai	4.2	6.5	10.0	15.5	21.7	24.2	30.2	29.3	25.2	20.2	13.7	7.3
Nanjing	2.5	5.2	10.0	16.1	22.2	24.9	29.0	28.4	23.6	18.5	11.5	5.4
Chengdu	5.1	8.2	11.8	17.1	21.3	23.8	25.4	25.4	21.6	17.3	12.8	7.2
Chongqing	6.8	9.6	15.0	19.9	22.5	25.9	30.1	30.5	22.5	18.5	15.1	8.8
Changsha	4.3	7.7	12.7	18.2	23.5	27.1	31.4	29.5	24.6	19.7	13.7	7.8
Kunming	9.7	12.9	15.4	17.9	20.1	21.0	20.9	20.3	19.0	16.5	12.2	9.9
Guangzhou	11.5	15	17.9	22.6	26.2	27.9	28.1	28.3	26.9	22.7	20.0	13.3

Table S2 Attributable cardiovascular deaths by cities computed as total and as separated components for cold and hot temperatures in 15 Chinese cities

City	MMP (MMT)*	Attributable mortality number (n, 95%eCI)		
		Total	Cold	Hot
Harbin	78(20.6)	31804(8912-50288)	28349(4493-46251)	3455(545-5899)
Changchun	78(20.6)	9806(711-16719)	8414(-1141-15690)	1391(330-2310)
Shenyang	78(21.5)	22934(9543-33694)	20907(9435-31022)	2027(174-3634)
Beijing	79(24.9)	50936(33982-66060)	46374(28055-61753)	4563(2789-6362)
Tianjin	78(24.5)	38758(22882-52645)	35711(18163-51018)	3047(1040-5021)
Shijiazhuang	73(23.8)	14234(9049-18804)	13189(6963-18302)	1045(24-1977)
Jinan	78(24.9)	10621(5398-14733)	8930(3423-13369)	1692(1114-2275)
Zhengzhou	79(25.9)	6608(3280-9425)	6029(1995-8965)	579(101-1020)
Shanghai	73(24.5)	13613(5448-21140)	11874(2886-19729)	1739(67-3345)
Nanjing	88(27.9)	23443(15384-30011)	22664(14966-30197)	780(168-1339)
Chengdu	81(24.1)	20329(7679-31488)	20048(6761-31181)	280(-1868-2014)
Chongqing	87(29.2)	35015(15450-51727)	33001(13044-49498)	2014(380-3606)
Changsha	70(25.1)	21895(14863-27258)	20280(12852-26631)	1615(-288-3294)
Kunming	99(23.3)	18865(778-31678)	18872(1518-32569)	-7(-156-93)
Guangzhou	93(29.0)	11490(5111-16354)	11259(4930-16047)	231(-74-496)
Overall	78(-)	330352(278504-369304)	305902(253081-347504)	24450(18528-29629)

* MMP: minimum mortality percentile of temperature (%); MMT: minimum mortality temperature (°C).

Table S3 Sensitivity analyses of calculating the fraction (% , 95%empiricalCI) attributable to temperature by changing location of knots of exposure-response-maximum lag for mean temperature and degrees of freedom (df) for covariates

Model choices	Total	Cold	Hot
Knots for exposure-response: 10 th , 50 th and 75 th	17.5(14.8-19.5)	16.3(13.7-18.3)	1.2(0.9-1.5)
Knots for exposure-response: 25 th , 75 th and 90 th	17.2(14.1-19.5)	15.9(12.8-18.4)	1.3(0.9-1.6)
Lag period: 14 days	14.1(12.2-15.8)	12.5(10.6-14.2)	1.5(1.2-1.8)
Lag period: 28 days	17.1(12.9-20.2)	15.6(11.6-18.4)	1.6(0.4-2.4)
Df for year:6	14.1(11.7-16.0)	12.4(9.9-14.4)	1.7(0.9-2.5)
Df for year: 10	13.9(10.9-16.2)	12.6(9.5-14.7)	1.4(0.9-1.7)
Df for relative humidity: 4	17.0 (14.3-18.9)	15.7(13.2-17.9)	1.3(0.9-1.5)
Df for relative humidity: 6	17.0 (14.4-19.2)	15.7(13.1-17.9)	1.3(0.9-1.5)
Df for air pressure: 4	17.1(14.4-19.3)	15.9(13.1-18)	1.3(0.9-1.5)
Df for air pressure: 6	17.1(14.5-19.2)	15.9(13.3-18)	1.3(0.9-1.5)

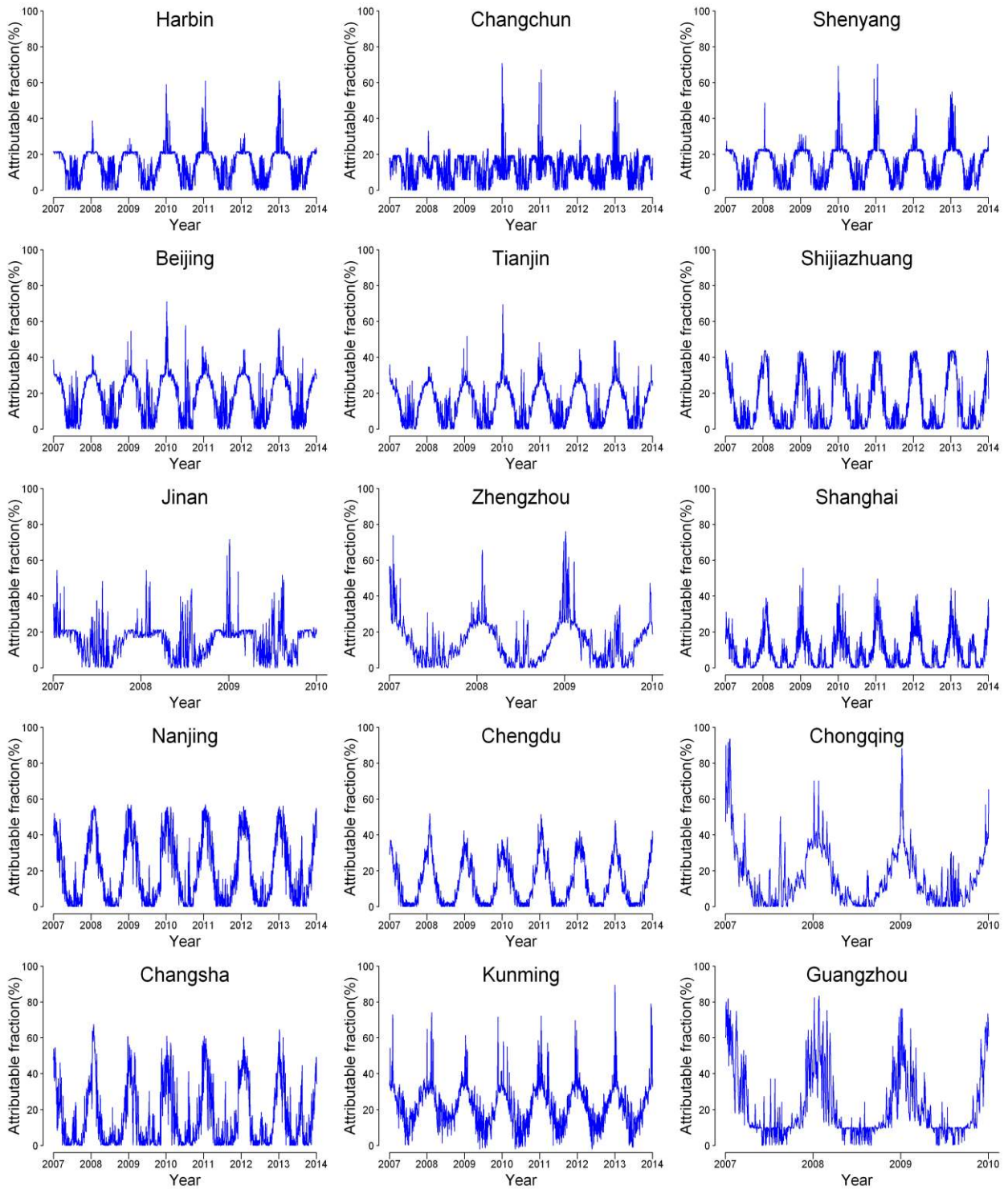


Figure S1 Daily attributable cardiovascular mortality fraction (%) due to temperature in 15 Chinese cities during 2007-2013.