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Association of Heat Exposure and Emergency Ambulance Calls: A Multi-city Study†

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Abstract: *Background* Evidence of the impacts of ambient temperatures on emergency ambulance calls (EACs) in developing countries is rare. This study aimed to examine the impacts and burden of heat on EACs in China, quantify the contributions of regional modifiers and identify the vulnerable populations. *Methods* A semi-parametric generalized additive model with a Poisson distribution was used to analyze the city-specific impacts of the daily maximum temperature (Tmax) on EACs during June to August in 2014-2017. Stratified analyses by sex and age were performed to identify vulnerable sub-populations. Meta-analysis was undertaken to illustrate the pooled associations. Further subgroup analysis stratified by climate, latitude and per capita disposable income (PCDI) and meta-regression analysis were conducted to explore the regional heterogeneity and quantify the contributions of possible modifiers. City- and region-specific attributable fractions (AF) of EACs attributable to heat were calculated. *Results* Strong associations between daily Tmax and total EACs were observed in all cities. 11.7% (95% CI: 11.2%–12.3%) of EACs were attributed to high temperature in the ten Chinese cities, and the central region with lower PCDI had the highest AF of 17.8% (95% CI: 17.2%–18.4%). People living in the central region with lower PCDI, the people aged 18-44 years and 0-6years were identified to be more vulnerable to heat than others. The combined effects of PCDI, temperature and latitude contributed 88.56% to the regional heterogeneity. *Conclusions* Our results complement the understanding of the burden of EACs attributable to heat in developing countries and the quantitative contribution of regional modifiers. *Highlights:* 1. This study covered multi-cities with different climatic zones in China. 2. 11.7% of emergency ambulance calls were attributed to heat in summer. 3. People living in the central region with lower economic level were more vulnerable. 4. Economy, temperature and latitude contributed 88.56% to regional heterogeneity. 5. People aged 18-44 years and 0-6 years were more susceptible to heat in this study.

Keywords: Attributable fraction; Emergency ambulance calls; High temperature; Regional modifiers; Risk assessment

1. Introduction

The health impact of climate change is the most serious health threat of the 21st century. Numerous epidemiological studies have reported the negative impacts of climate variability and change on mortality (Chen et al. 2018; Zhang et al. 2018) and morbidity

(Chen et al. 2018; Xu et al. 2019; Zhao et al. 2019). As an emergency health indicator, more and more attention have been paid to the emergency ambulance calls (EACs) among heat effects studies.

Epidemiological studies had discovered the association between heat and emergency ambulance dispatches in various parts of the world. For instance, a study in Italy found that the risk of ambulance dispatches for non-traumatic diseases would increase 1.45% (95% CI: 0.95, 1.95) with every 1°C increase in the mean apparent temperature between 25 and 30°C(Alessandrini et al. 2011). In Japan, the emergency transportation cases due to heat-related illness increased by 2.4–8.9 times when the daily maximum temperature was approximately 1.5°C above the mean daily maximum temperature(Ito et al. 2018). In Sydney, Australia, all-cause ambulance calls increased by 14% (95% CI 1.11-1.16) during heat wave (Schaffer et al. 2012). In Washington, USA, the emergency medical services calls increased 8 % (95 % CI: 6–9 %) for basic life support and 14 % (95 % CI: 9–20 %) for advanced life support on a heat day versus a non-heat day (Calkins et al. 2016).

The identification of vulnerable groups is of great significance to the implementation of public health policies and health services. However, there were no consistent results on vulnerable populations among the previous studies on heat and emergency ambulance calls. For example, a study in Fukuoka in Japan discovered that the groups aged 20–39 and 40–59 had higher relative risks of heat-related ambulance dispatches than other age groups (Kotani et al. 2018). Another study including 47 prefectural capital cities in Japan reported that the elderly (≥65 years) and children (7-18 years) were two high-risk groups for heat-related ambulance dispatches(Ito et al. 2018). The research conducted in Emilia-Romagna region in Italy demonstrated that the emergency ambulance dispatches risks increased with age (Alessandrini et al. 2011). While the analysis on associations between heat and ambulance calls in Brisbane Australia (Guo 2017) concluded no significant modification effect by age.

Several multi-city studies found the region-specific risks for emergency transport during periods of extreme heat (DeVine et al. 2017; Hartz et al. 2013; Murakami et al. 2012; Onozuka and Hagihara 2016), and identified that the region-specific risks were significantly modified by the percent of poverty(DeVine et al. 2017). While some analysis on associations between temperature and mortality indicated that the region-specific risks would be modified by regional socioeconomic level, geographic location, climate characteristics (Chen et al. 2018; DeVine et al. 2017; Huang et al. 2015; Yang et al. 2019; Zhang et al. 2019), etc. However, no study had provided the exact contributions of each modifier in explaining the regional variation of temperature-EACs associations.

In the mainland of China, numerous epidemiological studies have reported the associations between temperature and mortality and morbidity. But just limited studies involved in the impacts of temperature on emergency ambulance calls in several single cities, including Shanghai(Sun et al. 2014), Huainan(Cheng et al. 2016) and Shenzhen(Zhan et al. 2018), etc. All the studies discovered that high temperature increased the risk of emergency ambulance calls. In addition, the youth and middle-aged people suffered more from high temperature in Shenzhen. The study in Huainan found that temperature rise between neighboring days could acutely increase the ambulance dispatches, and the effect differed by season. However, no multi-city or national study on temperature and emergency ambulance calls had yet been reported in China.

Therefore, this study aimed to assess the impacts and attributable burden of high temperatures on EACs in ten cities with different latitudes and climatic conditions in China, to identify vulnerable populations and quantify the contribution of possible regional effect modifiers in explaining the regional variation of temperature-EACs associations. The results were expected to provide evidence for developing and implementing national and regional coordinated policies and guidelines against heat.

2. Methods

2.1. Study area and climatic characteristics

This study was based on a national project from Ministry of Science and Technology on Scientific Investigation on Regional Climate-sensitive Diseases in China. In this project, two sites were selected as the pilot sites in each meteorological geographic region in China. There are a total of 22 pilot sites that were selected in the 11 meteorological geographic regions for this project. Due to the availability and quality of the local data during the data analysis periods, 10 cities were included in this study (Figure 1). The 10 study cites are located in different geographical locations and climatic zones in China. Harbin and Liaoyang are located in the northeast of China and have a temperate continental monsoon climate and temperate humid monsoon climate, respectively. Xining is located in the northwest of China and belongs to the plateau temperate climatic zone. Yancheng Wuxi and Ningbo locate in the southeast of China and belong to a subtropical monsoon climate. Chengdu locates in the southwest of China and has a subtropical monsoon humid climate. Yichang locates in the central region and has a subtropical monsoon humid climate. Shenzhen and Mengzi are located in the southern China and have a subtropical monsoon climate.

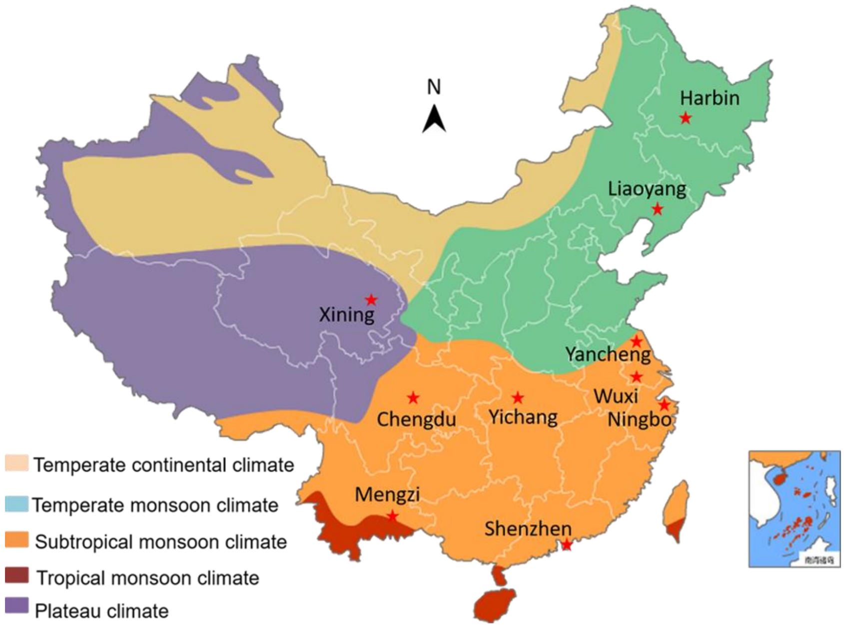

Figure 1 Locations and climates of ten study cities in China

2.2. Meteorological and air pollution data

The meteorological data from 2014 to 2017 were provided by the China Meteorological Administration, including daily maximum, mean and minimum temperatures (°C), mean relative humidity (%), atmospheric pressure (hPa) and wind speed (m/s).

The daily air pollutants data from 2014 to 2017 were obtained from the local Environmental Protection Bureaus. The variables included particulate matter of mass median aerodynamic diameter less than 10μm (PM10, 24 hour mean in μg/m3), PM2.5 (24 hour mean in μg/m3), nitrogen dioxide (NO2, 24 hour mean in μg/m3), sulfur dioxide (SO2, 24 hour mean in μg/m3), carbon monoxide (CO, 24 hour mean in mg/m3) and ozone (O3, 1 hour mean and 8 hour mean in μg/m3).

Per capita disposable income (PCDI) data were collected from the local statistical yearbook in each study city.

2.3. Emergency ambulance calls data

The individual emergency ambulance calls (EACs) data from 2014 to 2017 were collected from the local Emergency Medical Centers, who dispatched the ambulances timely to provide pre-hospital first aid on the spot, transport and in-transit care for the emergency and critically ill patients. Only emergency calls were included in the data analyses, while non-emergency services, such as transferring patients from hospitals to home, were excluded.

2.4. Statistical analysis

As an approximately linear correlation between daily maximum temperature (Tmax) and EACs during summer (i.e., June - August, the hottest three months in China) was detected in almost all ten cities (Supplementary file: Fig. A.1), we restricted the analyses to summer, so that the association between high temperatures and EACs could be quantified as the previous studies (Xu et al. 2019; Zhao et al. 2019).

A semi-parametric generalized additive model (GAM) with a Poisson distribution was performed to analyze the city-specific associations between daily Tmax and total EACs, as well as age- and age-specific EACs.

The relative humidity, long-term trends, day of week, wind speed, air pressure and air pollutants such as PM2.5, NO2 and O3 were considered as potential confounders(Wang et al. 2020; Yang et al. 2019). DOW was used as a dummy variable, and natural spline smoothed functions were used for other variables. The long-term trends were modeled with 7 degrees of freedom (df) per year. Air pollutants and the other meteorological factors were modeled with 4 df. The effect of temperature was evaluated as the percent increase in daily emergency ambulance calls in relation to a 1°C increase in the daily maximum temperature (Tmax). Wherever possible, effect estimates were calculated based on the relative risk (RR) and 95% confidence intervals (CI). The temperature term on the same day and moving average values up to 7 days before were considered to capture the lag effects of temperature (Sun et al. 2014).

A random-effect meta-analysis was undertaken to estimate the pooled associations of ten cities. Subgroup analyses firstly stratified by climate, geographic region and then by per capita disposable income (PCDI) were performed to explore the regional differences of high temperature-EACs relationships by heterogeneity test. Meta-regression analysis was conducted to further evaluate the possible modifiers for the regional differences and to quantify how much these modifiers contributed to the region-specific associations. Models with different heterogeneity factors, including latitude, Tmax and PCDI, were tested in the meta-regression analysis. The PCDI was divided into three levels according to its first (Q1) and third quartiles (Q3) among the ten study cities, i.e., low level when PCDI≤Q1, medium level when Q1< PCDI ≤ Q3 and high level when PCDI > Q3. Q1 and Q3 was 22.81 and 41.04 (1,000 Chinese Yuan/person), respectively.

Heterogeneity test was conducted by Cochrane Q test and I2 test. Generally, if I2 >50% or P < 0.05 (Q-test), the heterogeneity was thought to exist (Lu et al. 2019).

The statistical significance of differences between estimates of females and males and between different regions were tested by calculating the 95% confidence interval as formula (1)

$$\left(\hat{Q}_1 - \hat{Q}_2\right) \pm 1.96\sqrt{S\hat{E}_1^2 + S\hat{E}_2^2} \tag{1}$$

Where $\hat{Q}_1$ and $\hat{Q}_2$ are the estimates for males and females, and $S\hat{E}_1$ and $S\hat{E}_2$ are their respective standard errors (Chen et al. 2012; Zeka et al. 2006).

Given that the attributable fraction (AF) is used for quantifying the fraction of diseased or deceased ascribable to a given exposure or risk factor (Eide 2008), we calculated the city- and region-specific attributable fractions (AF) of EACs associated with heat in summer according to the formula (2) (Chen et al. 2018; Eide 2008)

$$AF = \frac{\sum_{i=1}^{n} N_i \frac{RR_i - 1}{RR_i}}{\sum_{i=1}^{n} N_i} \quad (2)$$

where i means the day with high temperature, that is the daily Tmax is higher than the minimum daily Tmax during the June to August in a city; n is the number of days with high temperature; N indicates daily number of EACs on the day i; RRi represents relative risk for the day i, which is calculated by comparing the daily Tmax on day i to the minimum daily Tmax during June to August. For 95% CI, standard errors and confidence intervals are obtained by transforming them from the RR-scale (Eide 2008).

2.5. Sensitivity analysis

Sensitive analysis was performed to evaluate the stability of the GAM models by comparing the results with and without controlling for the air pollutants and by changing df for long-time trends (5, 6 and 7) and air pollutants (3, 4 and 5) for total emergency ambulance calls (the results are shown in supplementary file: Table A.1).

GAM analysis was undertaken using SAS 9.1 (SAS Institute Inc., Cary, NC, USA) and meta-analysis and meta-regression analysis were conducted using the R software (version 3.5.1) with 'metafor' package. All statistical analyses were two-sided and significance was set at $P < 0.05$.

Ethical approval for this study was granted by the National Institute of Environmental Health, Chinese Center for Disease Control and Prevention.

3. Results

3.1. Descriptive statistics

A total of 1,499,721 emergency ambulance calls were enrolled during the study period. Totally, the group aged 0-17, 18-44, 45-59, 60-74, 75-89 and above 90 years accounted for 6.2%, 43.3%, 19.3%, 14.4%, 11.3% and 1.8%, respectively. The proportion for male and female was 59.6% and 40.4%, respectively.

Table 1 summarizes the numbers of EACs per 100,000 populations and daily EACs, the information of temperatures, relative humidity, and air pollutants for the ten study cities in China. In these study cities, the average number of daily EACs varied from 5.78 in Liaoyang (with 472 thousand population) to 463 in Chengdu (with 15,918 thousand population) during June to August. While, the number of EACs per 100,000 populations was from 120.1 in Yancheng to 1189.3 in Shenzhen. The average daily Tmax was from 24.5℃ in Xining to 32.3℃ in Shenzhen. The northern cities, such as Xining, Harbin and Liaoyang, have higher diurnal range of temperature and higher range of the daily maximum temperature during June to August than southern cities, such as Chengdu and Mengzi, etc.

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Table 1 Descriptive statistics of daily emergency ambulance calls, populations, meteorological parameters and air pollutants of 10 cities in China during June to August (Mean±SD)

Indicators	Xining	Harbin	Liaoyang	Yancheng	Wuxi	Yichang	Ningbo	Chengdu	Shenzhen	Mengzi
Emergency ambulance calls per 100,000 populations	725.9	717.3	447.0	120.1	564.6	404.8	212.7	1061.7	1189.3	1017.5
Daily emergency ambulance calls	46.4±9.34	182±16.8	5.78±2.70	23.8±20.3	101±14.9	45.8±11.1	45.9±8.06	463±42.4	388±51.1	12.6±9.76
Maximum temp. (℃)	24.5±4.33	27.6±3.05	29.8±3.04	30.6±3.79	30.7±4.13	30.5±4.07	30.8±4.02	30.1±3.44	32.3±1.84	28.4±2.25
Mean relative humidity (%)	63.2±13.2	72.5±10.6	66.2±12.2	81.4±11.1	78.8±11.6	81.9±10.2	82.4±8.44	83.5±6.82	79.8±8.49	73.6±9.29
Temperature range (℃)	22	17	20.9	20	18.3	19.2	18.3	17	10	11
Diurnal range of temperature (℃)	13.81±5.26	9.22±2.81	9.48±2.69	7.2±2.69	6.9±2.48	8.14±2.94	7.39±2.91	8.88±2.57	5.65±1.44	7.64±1.98
$PM_{2.5}$ (μg/m^3)	35.0±13.6	30.7±19.9	NA	30.3±18.3	44.6±20.3	40.8±22.6	27.4±12.6	43.2±17.2	17.4±10.7	24.4±15.6
NO_2 (μg/m^3)	27.3±6.73	34.5±8.70	NA	16.6±4.96	32.6±8.31	29.4±6.37	26.9±9.43	42.1±9.74	31.3±10.0	11.4±4.94
O_3 (μg/m^3)	113±29.5	94.3±31.3	NA	97.5±39.7	135±52.6	96.2±36.8	104±39.2	130±48.1	79.6±46.7	74.8±30.6
Periods of data	2014-2016	2014-2016	2014-2017	2015-2017	2014-2016	2014-2017	2014-2016	2014-2016	2014-2017	2014-2017

"NA" means the lack of data. Temperature range means the range of the daily maximum temperatures during June to August.

3.2. City-specific and pooled associations between daily maximum temperature and emergency ambulance calls

The city-specific and pooled associations between the daily Tmax and the EACs of different population groups were displayed in Table 2.

Significant associations between the daily Tmax and EACs were observed for all ten cities. An increase of 1℃ in the daily Tmax brought approximately 0.6% (95% CI: 0.2%–1.1%) increase in Wuxi to 2.7% (95% CI: 2.0%–3.5%) in Yancheng in daily total EACs in different study cities, with the pooled increment of 1.5% (95% CI: 1.0%–2.0%) for 1℃ increase in the daily Tmax.

The pooled RR for males (1.018, 95% CI: 1.011–1.025) across ten-cities was slightly higher than that for females (1.011, 95% CI: 1.006–1.016). But only in Chengdu, southwestern China, the significant difference between males and females was observed.

Meta-analysis results showed that EACs for the populations aged between 18 and 74 years were significantly associated with the daily Tmax, as well as the children aged less than 6 years (Table 2). Besides, the RRs were 1.033 (95% CI: 1.000–1.067) and 1.182 (95% CI: 1.132–1.234) for the groups aged 7–17 years in Chengdu, southwestern China, and in Shenzhen, southern China, respectively, suggesting other groups were also vulnerable to heat. However, the negative association was observed for the population aged 75–89 years in Yancheng, eastern China, with RR of 0.966 (95%CI: 0.946–0.986). This might be due to the small sample for these group of cases.

Table 2 City-specific and pooled associations between daily maximum temperature and emergency ambulance calls (EA calls) of 10 cities in China (the statistically significant results are bolded)

	Xining		Harbin		Liaoyang		Wuxi		Yancheng		Yichang	
	RR	**95%CI**	**RR**	**95%CI**	**RR**	**95%CI**	**RR**	**95%CI**	**RR**	**95%CI**	**RR**	**95%CI**
Total EA calls	**1.011**	**(1.006,1.017)**	**1.009**	**(1.005,1.014)**	**1.021**	**(1.006,1.036)**	**1.006**	**(1.002,1.011)**	**1.027**	**(1.020,1.035)**	**1.026**	**(1.019,1.032)**
Male	**1.009**	**(1.002,1.017)**	**1.010**	**(1.004,1.016)**	**1.027**	**(1.007,1.047)**	**1.007**	**(1.001,1.013)**	**1.019**	**(1.010,1.028)**	**1.028**	**(1.020,1.036)**
Female	**1.014**	**(1.006,1.023)**	**1.009**	**(1.003,1.016)**	1.003	(0.981,1.025)	1.006	(0.999,1.012)	**1.024**	**(1.011,1.038)**	**1.022**	**(1.013,1.032)**
Age group (years)												
0~6	**1.016**	**(1.000,1.031)**	1.021	(0.986,1.057)	NA	NA	1.018	(0.986,1.051)	0.999	(0.970,1.028)	1.000	(0.972,1.029)
7~17	0.993	(0.959,1.028)	1.000	(0.965,1.036)	NA	NA	1.022	(0.989,1.056)	1.005	(0.960,1.052)	0.980	(0.941,1.021)
18~44	**1.018**	**(1.009,1.028)**	**1.011**	**(1.003,1.020)**	**1.052**	**(1.022,1.084)**	**1.009**	**(1.000,1.017)**	**1.030**	**(1.016,1.044)**	**1.019**	**(1.008,1.030)**
45~59	1.010	(0.999,1.022)	**1.011**	**(1.002,1.020)**	1.017	(0.989,1.045)	**1.014**	**(1.003,1.024)**	1.004	(0.989,1.018)	**1.035**	**(1.022,1.049)**
60~74	0.998	(0.984,1.013)	1.000	(0.991,1.009)	1.000	(0.972,1.028)	1.002	(0.992,1.012)	**1.023**	**(1.006,1.040)**	**1.037**	**(1.023,1.050)**
75~89	1.010	(0.997,1.023)	**1.013**	**(1.004,1.023)**	NA	NA	0.980	(0.946,1.015)	**0.966**	**(0.946,0.986)**	**1.021**	**(1.006,1.036)**
≥ 90	0.990	(0.949,1.034)	1.001	(0.970,1.033)	NA	NA	1.021	(0.999,1.042)	0.988	(0.917,1.063)	1.023	(0.975,1.073)
Lag days[#]	7		1		1		7		7		7	

Note: "NA" means no analysis due to lack of data or too small samples; [#] means the moving average days for temperature.

3.3. Regional associations and possible causes for regional differences

The value of I^2 was 83.30% and the P value was <0.0001 (Fig. 2 (a)) for total EACs analysis, indicating that the results in ten cities were heterogeneous. Therefore, subgroup analysis stratified by climate zone were performed and the results were demonstrated in Figure 2 (b). The pooled RRs for Temperate zone (north of China) and subtropical zone were 1.011(95% CI: 1.007-1.014) and 1.016 (95% CI: 1.010-1.023), suggesting that the relative risks in subtropical region seemed higher than those in temperate region.

Given the value of I^2 was 86.30% and the P value was <0.0001 for the pooled results of subtropical region, indicating that there was still heterogeneity among these cities, the subtropical cities were classified into two subgroups by latitude and the results were shown in Figure 2 (c). Similarly, as the I^2 was 93.49% and the P value was <0.0001 for the pooled results of central region, which means high heterogeneity, the central region cities were classified into two subgroups by PCDI and the results were shown in Figure 2 (d). It demonstrates that I^2 <50% and P>0.05 for both two subgroups. The significantly highest pooled RR (1.024, 95% CI: 1.020-1.029) was observed in the group 1 cities including Yancheng, Yichang and Chengdu, which owned relatively lower PCDI than group 2 cities including Wuxi and Ningbo. The results indicated that the central region cities with lower PCDI had the highest risk of EACs associated with high temperature.

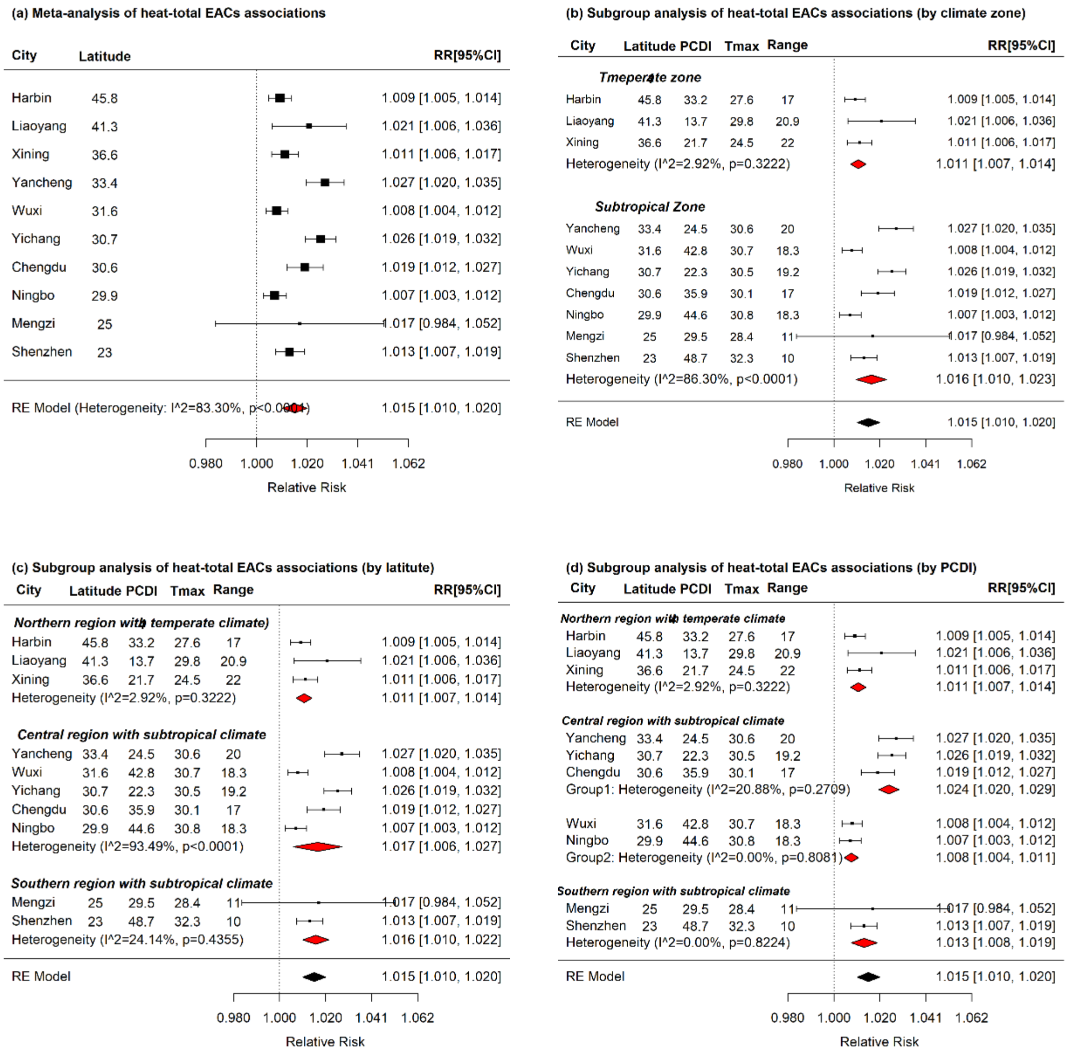

Figure 2 Meta-analysis (a) and subgroup analysis grouped by climate zone (b), latitude (b) and per capita disposable income (PCDI) for central region cities (d) of associations between high temperature and total emergency ambulance calls (EACs) from June to August during 2014-2017

Further, meta-regression results in Table 3 showed the contributions of temperature, PCDI and latitude to the regional heterogeneity of heat-related EACs risk. The contribution of PCDI, Tmax and latitude to the city heterogeneity was 32.18%, 12.11% and 15.25%, respectively. Furthermore, any two joint effects were greater than a separated effect. The joint contributions of PCDI, Tmax and latitude were up to 88.56%. It indicates that the regional heat-EACs associations might be due to the combined effects of geographical location, climatic characteristics and economic conditions.

Table 3 Meta-regression analysis of different models with different heterogeneous factors

Model	Heterogeneous factors	Estimate			P-value			Interpretable heterogeneity (%)
		Tmax	PCDI	Latitude	Tmax	PCDI	Latitude	
M1	Latitute	..	..	-0.0002	..	..	0.7817	15.25
M2	Tmax	0.0007	..	..	0.5468	..	..	12.11
M3	PCDI	..	-0.0004	..	..	**0.0447**	..	32.18
M4	Tmax+Latitude	0.0009	..	0.0001	0.5997	..	0.8959	28.22
M5	**PCDI+Latitude**	..	-0.0006	-0.0007	..	**0.0020**	**0.0437**	58.13
M6	**Tmax+PCDI**	0.0026	-0.0008	..	**<0.0001**	**<0.0001**	..	83.04
M7	**Tmax+PCDI**+Latitude	0.0022	-0.0008	-0.0002	**0.0019**	**<0.0001**	0.3468	88.56

Note: Tmax: daily maximum temperature (°C); PCDI: per capita disposable income (1,000 Chinese Yuan/person).

3.4 City- and region-specific attributable fractions of EACs associated with high temperatures

Table 4 shows that high temperatures were associated with the city- and region-specific attributable fractions (AF) of EACs. Totally, for the ten cities, 11.7% (95% CI: 11.2%-12.3%) of EACs in summer could be attributed to high temperature. The central region with lower level of PCDI had the highest EAC burden attributable to high temperature with AF of 17.8% (95% CI: 17.2%-18.4%), and followed by the northern region with AF of 7.32% (95% CI: 6.87%-7.78%). The central region with higher level of PCDI showed the lowest AF (6.98, 95%CI: 6.56, 7.40).

Table 4 City- and region-specific attributable fractions (AF) of emergency ambulance call-outs associated with high temperature.

Region	**City**	**AF (95%CI) (%)**
Northern region with temperate climate		**7.32 (6.87, 7.78)**
	Harbin	6.37 (5.96, 6.78)
	Liaoyang	16.8 (15.6, 18.0)
	Xining	8.95 (8.47, 9.44)
Central region with subtropical climate		
with lower PCDI		**17.8 (17.2, 18.4)**
	Yancheng	21.2 (20.6, 21.8)
	Yichang	15.5 (14.9, 16.0)
	Chengdu	17.9 (17.3, 18.5)
with higher PCDI		**6.98 (6.56, 7.40)**
	Wuxi	5.25 (4.84, 5.65)
	Ningbo	7.47 (7.05, 7.90)
Southern region with subtropical climate		**7.11 (6.54, 7.66)**
	Mengzi	23.7 (21.6, 25.8)
	Shenzhen	6.79 (6.25, 7.32)
Total		**11.7 (11.2, 12.3)**

3.5. Sensitivity analysis

Table S1 shows generally similar effect estimates with and without controlling for the air pollutants, as well as using different *dfs* for long-time trends (5, 6 and 7) and air pollutants (4, 5 and 6), suggesting robust results of this analysis.

4. Discussion

We assessed the impacts of high temperatures on EACs in summer across ten cities located in different latitudes and climate zones in China. Overall, the results demonstrate significant associations between daily Tmax and EACs after adjustment for potential confounders in all the study cities. Moreover, people living in central cities with lower PCDI and the young population were identified to be more vulnerable to heat, when using EACs as a health indicator. We found that 11.7% of EACs in summer could be attributed to high temperatures in the ten study cities in China, and the central cities with lower PCDI had the highest attributable fraction of 17.8%. In addition, we, for the first time, quantified the combined effects of local altitude, temperatures and economic status to the heat-EACs associations, with the joint contributions up to 88.56%.

Our results of time-series analysis indicate that the risk of EACs increased by 1.53% (95%CI: 1.04%-2.02%) for each 1°C increase in daily maximum temperature. This result was consistent with other studies in China, such as in Shanghai, eastern China, with the ambulance dispatches increasing by 1.25% (95%CI: 0.97%-1.53%) for each 1°C rise in temperature (Sun et al. 2014), and 2% (95%CI: 1%-3%) in Huainan, eastern China (Cheng et al. 2016).

The current studies about age effects on associations between temperature and emergency outcomes were inconsistent. Guo et al. examined the hourly associations between heat and ambulance calls in Brisbane, Australia and found that there were no significant modification effects by age (Guo 2017). However, studies in Japan (Fujitani et al. 2019; Ito et al. 2018), Sydney (Schaffer et al. 2012) and Brisbane (Turner et al. 2013) in Australia found that elderly people and children were particularly vulnerable to heat stress when using EACs as health indicator.

The results on emergency ambulance calls in Adelaide, Australia (Nitschke et al. 2011), King County, Washington (Calkins et al. 2016), Fukuoka, Japan (Kotani et al. 2018) and the results of other studies conducted in Shenzhen (Zhan et al. 2018) and Guangzhou (Yang et al. 2016), China showed that the strongest associations were discovered for the young population. While, our results found the robust associations between Tmax and EACs for children and the elderly people, as well the young people with the highest relative risk. It might be because the young people have more chances to work or stay outdoors even during hot days. Exposure to high temperatures can result in heat-related illness and increase the chance of being injured because of loss concentrations, fatigue, fogged-up safety glasses, or dizziness. For children, immature physiological and cognitive functions and unwilling to stay at home for a long while increase the vulnerability to heat. Our study even found negative associations for the very elderly in Yancheng, which might be related to the less time to go out on hot days even with decreased thermoregulation function for the elderly or relevant small sample size included in the analyses. Therefore, relevant adaptive actions should be taken accordingly to decrease extreme heat exposure to the most vulnerable groups, not only for the elderly, but also the young working population and children, especially outdoor workers.

The different categorization for age groups might be one of the reasons for these inconsistent results among different researches, such as, in some studies of Japan (Fujitani et al. 2019; Ito et al. 2018), age was categorized into groups of <18 (or 7-17) years, 18-64 years and ≥65 years, while study in Sydney, Australia classified populations into two groups (<75 years and ≥75 years) (Schaffer et al. 2012). In our study, the population was classified into seven groups according to the new age classification from the World Health Organization. We highlighted that consistent age classification should be implemented in future studies.

We found that males had slightly higher risk than females during hot days, but with no significant difference, which was consistent with the other studies (Bai et al. 2014; Guo 2017). However, most of the researches on mortality indicate that females were more sensitive to heat than males (Chen et al. 2018; Hu et al. 2019; Yang et al. 2019; Yin et al. 2018). It implies that the modification effect by age might be different with health outcomes. More research on different outcomes stratified by age should be further explored.

Our study found that the heat-EACs associations were modified by latitude, temperature and economic conditions, which is similar to other studies (Chen et al. 2018; DeVine et al. 2017; Huang et al. 2015; Yang et al. 2019; Zhang et al. 2019). However, these studies only identified these factors could affect the region-specific climate- or temperature-health associations, but rarely had quantified the contribution of the effect modifiers. We, for the first time, quantified both the individual and the joint contribution of the latitude, temperature and economic conditions to the city heterogeneity of heat-EACs associations, and found that the joint effects of latitude, temperature and economic conditions were much higher than individual effects. While temperature and latitude decide the climatic characteristics and the population heat exposure level, economic conditions determine residents' adaptive capability such as the usage of air-conditioners and access to health care infrastructure and services, as well as population's perception and behavior to take self-protective measurements and government decision-making capacity (Raya Muttarak and Lutz 2014; Sellers et al. 2019; Victoria van der Land and Hummel 2013). The quantitative evaluation of the modifiers' contributions to the heat-EACs association in our study will push the national and regional health risk assessment or projection of climate change in a more objective way. The results will also provide evidence for health resource allocation and profound adaptation policies and measures development, especially for vulnerable regions.

In addition, we also explored the national and regional attributable fraction (AF) of EACs associated with high temperature in summer. AF represents the fraction of the disease or adverse outcomes that could be attributed to a given exposure or risk factor, or would be eliminated the disease burden if the risk factor were removed (Deng et al. 2019; Gasparrini and Leone 2014; Gasparrini et al. 2015; Tian et al. 2016; Yang et al. 2017), which has important implications to policymaking and potential benefits of public health interventions (Deng et al. 2019; Tian et al. 2016). To the best of our knowledge, there has been no study that evaluates the burden of both national and regional EACs attributable to high temperature in the literature. Our results indicate that 11.7% of total EACs would be avoided by reducing heat exposure in summer in China, and even up to 17.8% of total EACs would be preventable in summer in central regions with higher summer temperature and lower economic conditions. The results would provide important scientific evidence and implications for benefits of developing heat-exposure intervention policies and the potential impacts of public health interventions and resource allocation, especially for vulnerable regions.

The strengthens of this study include the assessment of the national and regional AFs of EACs ascribed to high temperatures and the quantification of the contribution of potential modifiers to the city heterogeneity of the heat-EACs association through the multicity analysis, which contributes to an understanding of the impact and burden of heat on an emergency morbidity indicator in China. The results may have important implications for policymaking and public health interventions.

Meanwhile, some limitations should be noted. Firstly, the personal air temperature and pollutants exposure data were not available as in all other time series studies. We used the fixed station monitoring data as the temperature and pollutants exposure data, which might lead to exposure measurement error. Secondly, due to the lack of exact disease diagnosis in a large number of individual EACs data, we did not analyze the disease specific association between EACs and high temperature. Finally, the small number of study sites with intra-regional variation in climatic characteristics might have relatively poor representativeness for regional risk analysis. However, our results warrant further such research with more representative cities and a large number of cases for each region or climate zones.

5. Conclusions

Our study complements the understanding of the burden of both national and regional EACs attributable to high temperature in a developing country, as well as the quantitative contribution of regional modifiers. The findings on vulnerable population, attributable disease burden and quantitative contribution of modifiers from 10 Chinese cities may help local health authorities, ambulance services and hospital emergency departments to improve public health policies and practices, medical emergency management and response protocol for resource allocation, frontline staff capacity building to reduce disease burden associated with current and future abnormal weather with high temperature, especially within the context of climate change. The knowledge advancement in this field might also be helpful for other developing countries with similar climatic and geographic conditions.

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