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# Mortality risk and burden associated with temperature variability in China, United Kingdom and United States: Comparative analysis of daily and hourly exposure metrics



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# ABSTRACT

*Background:* Temperature variability (TV) is closely associated with climate change, but there is no unified TV definition worldwide. Two novel composite TV indexes were developed recently by calculating the standard deviations of several days' daily maximum and minimum temperatures ( $TV_{daily}$ ), or hourly mean temperatures ( $TV_{hourly}$ ).

*Objectives:* This study aimed to compare the mortality risks and burden associated with  $TV_{daily}$  and  $TV_{hourly}$  using large time-series datasets collected from multiple locations in China, United Kingdom and United States.

*Methods*: We collected daily mortality and hourly temperature data through 1987 to 2012 from 63 locations in China (8 communities, 2006–2012), United Kingdom (10 regions, 1990–2012), and USA (45 cities, 1987–2000). TV-mortality associations were investigated using a three-stage analytic approach separately for China, UK, and USA. First, we applied a time-series regression for each location to derive location-specific TV-mortality curves. A second-stage meta-analysis was then performed to pool these estimated associations for each country. Finally, we calculated mortality fraction attributable to TV based on above-described location-specific and pooled estimates.

*Results*: Our dataset totally consisted of 23, 089, 328 all-cause death cases, including 93, 750 from China, 7,573,716 from UK and 15, 421, 862 from USA, respectively. In despite of a relatively wide uncertainty in China, approximately linear relationships were consistently identified for  $TV_{daily}$  and  $TV_{hourly}$ . In the three countries, generally similar lag patterns of TV effects were consistently observed for  $TV_{daily}$  and  $TV_{hourly}$ . A 1 °C rise in  $TV_{daily}$  and  $TV_{hourly}$  at lag 0–7 days was associated with mortality increases of 0.93% (95% confidence interval [CI]: 0.12, 1.74) and 0.97% (0.18, 1.77) in China, 0.33% (0.15, 0.51) and 0.41% (0.21, 0.60) in UK, and 0.55% (0.41, 0.70) and 0.51% (0.35, 0.66) in USA, respectively. Larger attributable fractions were estimated using  $TV_{daily}$  than those using  $TV_{hourly}$ , with estimates at 0–10 days of 3.69% (0.51, 6.75) vs. 2.59% (0.10, 5.01) in China, 1.14% (0.54, 1.74) vs. 0.98% (0.55, 1.42) in UK, and 2.57% (1.97, 3.16) vs. 1.67% (1.15, 2.18) in USA, respectively. Our meta-regression analyses indicated higher vulnerability to TV-induced mortality risks in warmer locations.

*Conclusions:* Our study added multi-country evidence for increased mortality risk associated with short-term exposure to large temperature variability. Daily and hourly TV exposure metrics produced generally comparable risk effects, but the attributable mortality burden tended to be higher using  $TV_{daily}$  instead of  $TV_{hourly}$ .

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### 1. Introduction

Climate change, a significant global environmental problem, has been widely regarded as the greatest public health threat across the globe in the 21st century (Huang et al., 2013; Watts et al., 2015). Shortterm links between temperature extremes and morbidity/mortality, for instance, have been extensively demonstrated at regional and national scales over the past decades (Cheng et al., 2019a; Song et al., 2017; Ye et al., 2012). As shown by global epidemiologic evidence, temperaturemortality relationships generally exhibit U, V, or J patterns in various climate zones (Gasparrini et al., 2015; Guo et al., 2014), indicating increased mortality burden arising from both low and high temperatures (Gasparrini et al., 2015; Hajat et al., 2010; Zhang et al., 2019).

In addition to cold and heat, temperature variability (TV) has also been increasingly identified as a significant potential trigger for extra mortality risks (Guo et al., 2016). Diurnal temperature range (DTR), defined as the difference of maximum and minimum temperature within a day, was previously adopted to assess mortality impacts associated with short-term temperature variability (Lim et al., 2015; Yang et al., 2018b; Zhang et al., 2018a). In recent years, there is emerging epidemiologic evidence showing that temperature change between neighboring days (TCN) may also play an independent role in influencing daily mortality (Lin et al., 2013; Zhan et al., 2017). These growing epidemiologic findings provide some evidence guiding TV-related health assessment by considering both intra-day and inter-day temperature variability (Vicedo-Cabrera et al., 2016). However, models that simultaneously include both intraday and interday TV variables may potentially lead to invalid effect estimates because there might be strong collinearity between intraday and interday TV, particularly when considering lag effects (Guo et al., 2016).

Recently, two novel composite TV indexes were consequently developed by calculating the standard deviations of several days' daily maximum and minimum temperatures ( $TV_{daily}$ ) (Guo et al., 2016), or hourly mean temperatures ( $TV_{hourly}$ ) (Cheng et al., 2017). Also,  $TV_{daily}$  or  $TV_{hourly}$  has been applied separately in several multicity studies in China (Hu et al., 2019; Yang et al., 2018a; Zhang et al., 2017b) and Australia (Cheng et al., 2017), nationwide investigations in Braze (Zhao et al., 2018a) and England and Wales (Zhang et al., 2018b), as well as an international investigation (Guo et al., 2016).

Both TV<sub>daily</sub> and TV<sub>hourly</sub> are currently of great help to enhance the comprehensive understanding of health impact due to unstable temperatures, while some researchers recommend TV<sub>hourly</sub> rather than TV<sub>daily</sub> through auguring that TV<sub>hourly</sub> could theoretically better capture the temporal variation in temperature at a finer scale (Cheng et al., 2017; Zhang et al., 2018b). However, no research has provided population-based evidence regarding this debate, because prior epidemiologic studies generally linked TV<sub>daily</sub> or TV<sub>hourly</sub> separately with health. Here, this study aimed to compare the mortality effects associated with TV<sub>daily</sub> and TV<sub>hourly</sub> using large time-series datasets collected from China, United Kingdom and United States.

# 2. Materials and methods

# 2.1. Data collection

# 2.1.1. China data

Daily all-cause mortality data during 2006–2012 for 8 communities in southern China (Changsha, Wuhan (Jiang'an and Qiaokou), Hefei, Mananshan, Guilin, Nanning, Haikou) were collected from the Chinese Centre for Disease Prevention and Control. Meteorological data for the same period, including daily mean, minimum, and maximum temperature and mean relative humidity, were collected from the China Meteorological Data Network (http://data.cma.cn), which is administrated by the China Meteorological Administration.

Hourly temperature data for each community were acquired through the global hourly datasets of United States' National Centers for Environmental Information (NCEI, https://www.ncei.noaa.gov/). NCEI was established by the National Oceanic and Atmospheric Administration (NOAA) and aims to preserve, monitor, assess, and provide public access to the global environmental data and information including climate and historical weather (Chen et al., 2019; Jiao et al., 2019).

# 2.1.2. UK data

We acquired daily time-series data on weather and all-cause mortality in 10 Government Office Regions (i.e., Wales and 9 regions in England) from 1990 to 2012, from the example dataset for UK in a previous multi-country temperature-mortality study (Gasparrini et al., 2016). This dataset has been also made publicly available by Dr. Antonio Gasparrini on his personal web page (http://www.ag-myresearch. com/). A detailed description of these data can be found elsewhere (Armstrong et al., 2011; Gasparrini et al., 2012b, 2015).

Hourly temperature data for UK atmospheric monitoring stations between 1 January 1990 and 31 December 2012, were originally collected from the British Atmospheric Data Centre (BADC) (http:// archive.ceda.ac.uk/). The station-based hourly temperatures were then aggregated into regional-average measurements. More details about the temperature data integration can be found in our previous publication (Zhang et al., 2018b).

#### 2.1.3. US data

Daily all-cause mortality and meteorological data for 45 US metropolises during 1987–2000, were extracted from the publicly available National Morbidity, Mortality and Air Pollution Study (NMMAPS). The included 45 large urban communities were located across the seven regions in mainland America: North West (7), Upper Midwest (4), Industrial Midwest (10), North East (7), Southern California (3), South West (6), and South East (8). The details of this dataset could be found in previous publications (Peng et al., 2005; Samet et al., 2000). Hourly temperatures for the 45 US communities from January 1, 1987 to December 31, 2000 were acquired through Local Climatological Data (LCD) of NCEI (https://www.ncdc.noaa.gov/cdo-web/datatools/lcd/). LCD provides public access to the historical weather data for airport stations located within the United States and its territories, as well as many international cities.

## 2.2. Temperature variability index

Two composite indexes, namely TV<sub>daily</sub> and TV<sub>hourly</sub>, were used for exposure assessment of short-term temperature variability in our study. Consistent with previous investigations, TV<sub>daily</sub> was generated from the standard deviations (SD) of several days' daily minimum and maximum temperatures (Guo et al., 2016; Zhang et al., 2017b), whereas TV<sub>hourly</sub> was developed by calculating SDs of hourly temperatures during the exposure days (Cheng et al., 2017; Hu et al., 2018; Zhang et al., 2018b). These two measurements can account for both intra- and inter-day temperature variability, and overcome the strong collinearity when introducing intra- and inter-day TV into the model at the same time. To better understand TV-mortality associations, we assessed separately the mortality effects of TV exposure along various days (from lag 0-1 days to lag 0-10 days). For instance, TV at lag 0-1 days (TV<sub>0-1</sub>) was derived by calculating the SD of temperature exposure on the same day and 1 days before,  $TV_{0-2}$  was the SD for the preceding 3 days' exposure, and so on.

# 2.3. Data analysis

TV-mortality associations were investigated using a three-stage analytic approach separately for China, UK, and USA. First, we applied a time-series regression for each location to derive location-specific TVmortality curves. A second-stage meta-analysis was then performed to pool these estimated associations for each country. Finally, we calculated mortality fraction attributable to TV based on above-described location-specific and pooled estimates. Similar analytic strategy has also been adopted in several previous large-scale studies (Gasparrini and Armstrong, 2013; Gasparrini et al., 2012a).

All the analyses were performed using R software (version 3.3.2, http://www.R-project.org). We used "dlnm" package to create DLNM framework for temperature in the first-stage analysis, and the "metafor" package to perform the second-stage meta-analysis. All statistical tests were two-sided, and effects of p < 0.05 were considered statistically significant.

# 2.3.1. First-stage time-series regression

A standard time-series quasi-Poisson regression analysis (Peng et al., 2006) was performed to assess location-specific TV-mortality relationships. As previous studies reported, our preliminary analysis found an approximately linear dose-response curve between TV and mortality. We thereby included a linear term for TV in our final regression analysis. Several covariates were included in our regression model: (1) a naturel cubic spline (NCS) with 7 degrees of freedom (df) per year for calendar time to remove the long-term trends and seasonality (Ma et al., 2019; Yang et al., 2015); (2) indicator variable for day of the week (DOW); (3) 3 df NCS at equally spaced quantiles for the current day's mean relative humidity (Lin et al., 2018; Zhang et al., 2017a); (4) a flexible "cross-basis" term for mean temperature created by distributed lag nonlinear model (DLNM), modelling exposure-lag-response associations between temperature and mortality (Gasparrini, 2011; Gasparrini et al., 2010). Specifically, the effect of temperature exposure was speculated using a NCS with 3 internal knots (10th, 75th, and 90th) while the lagged-response association was modelled with a NCS with 2 internal knots at equally spaced log-values (Yang et al., 2015; Zhang et al., 2019). A maximum lag of 21 days was chosen to fully control for the confounding effects of both low and high temperatures, which was motivated by prior multi-country investigations (Gasparrini et al., 2015; Guo et al., 2014). Given that different definitions of the "crossbasis" term for temperature may introduce some uncertainties (Li et al., 2018; Zhang et al., 2019), we also tested modelling choices of maximum lag and internal knots in our sensitivity analyses.

## 2.3.2. Second-stage meta-analysis

For each country, we pooled location-specific estimates on TVmortality associations derived from the first-stage time series analysis, using random-effects meta-analysis through maximum likelihood estimation (MLE) (Viechtbauer, 2010). Location-specific and pooled estimates of TV effects on mortality were presented as excess mortality risk (%) and its 95% confidence interval (95% CI) associated with per 1 °C increase in TV index along different exposure days.

To illustrate the potential effect modification in the TV-mortality association, we additionally fitted a number of MLE-based meta-regression models by separately incorporating some geographical (e.g., latitude and longitude) and climatological (e.g., temperature and humidity) factors as predicators (Cheng et al., 2017; Yang et al., 2018a). The modified effects of these quantitative predictors were expressed as percentage changes in mortality (and 95% CIs) per an IQR (interquartile range) increase in the distribution of each predictor. We also compared TV-associated effects between countries by creating dummy variables and indicating China as the reference.

# 2.3.3. Third-stage assessment of attributable fraction

To estimate TV-attributable mortality burden, we first calculated attributable number of all-cause deaths (AD) caused by TV on each day of the whole series (Cheng et al., 2017; Hu et al., 2019). For a specific location, the formula for AD calculation is given as follows:

# $AD_i = D_i \times (RR_i - 1) / RR_i$

Where  $AD_i$  denotes the attributable death number on day *i*,  $D_i$  is the observed death number on day *i*,  $RR_i$  refers to the relative risk associated with TV exposure on day *i*.

By summing up  $AD_i$  during the whole series, total attributable deaths can be then obtained for each location. The sum of location-specific ADs generated the national-level AD estimate in each country. Attributable fractions (AF) of mortality (location-specific and country-level) were consequently provided by the ratios of total AD to the corresponding total number of observed deaths (Gasparrini et al., 2015).

### 2.3.4. Sensitivity analysis

To check the robustness of our main results, we performed several sensitivity analyses. Specifically, we tested the modelling choices of our first-stage time-series regression, by varying the dfs for calendar time, maximum lag days and internal knots for temperature.

# 3. Results

Table 1 gives the descriptive statistics of the included communities/ regions. The 63 locations (Fig. 1) from China (8 communities), UK (10 regions) and USA (45 metropolises), covered a broad span of latitudes (from 20.0°N to 55.0°N) and longitudes (from 122.7°W to 118.3°E). Our dataset totally consisted of 23, 089, 328 all-cause death cases, including 93, 750 from China, 7,573,716 from UK and 15, 421, 862 from USA, respectively. Mean temperatures varied substantially across locations, ranging from 8.8 °C in Minneapolis/St. Paul to 26.5 °C in Phoenix (Table S1). Large differences between TV<sub>daily</sub> and TV<sub>hourly</sub> were consistently observed in the three countries. In China, for instance, country-average temperature variability was 4.7 °C (3.8–5.2) for TV<sub>daily</sub> and 2.8 °C (2.4–3.1) for TV<sub>hourly</sub> respectively. Location-specific summary characteristics were presented in the supplementary material (Table S1).

Fig. 2 illustrates a clear comparison between  $TV_{hourly}$  and  $TV_{daily}$  at lag 0–1 days, in terms of their overall distributions for Wuhan,

#### Table 1

Summary characteristics of the included communities/regions in China, United Kingdom and United States.

Characteristics	Country				
	China	United Kingdom	United States		
Communities/regions (number)	8	10	45		
Latitude (°N) <sup>a</sup>	20.0-31.5	51.0-55.0	25.8-47.7		
Longitude (°E) <sup>a</sup>	108.1-118.3	9.5–11.6	71.1°W –122.7°W		
Study period (year)	2006-2012	1990-2012	1987-2000		
Total deaths (number)	93, 750	7, 573, 716	15, 421, 862		
Annual mean temperature (°C) <sup>b</sup>	18.8 (16.3–23.9)	10.4 (9.5–11.7)	14.9 (8.8-26.5)		
Annual mean humidity (%) <sup>b</sup>	73.7 (68.8-80.5)	74.7 (67.4–78.3)	65.5 (28.9–75.2)		
Annual mean TV <sub>daily</sub> (°C) <sup>b</sup>	4.7 (3.8–5.2)	4.4 (4.0–4.8)	6.5 (3.9–11.1)		
Annual mean TV <sub>hourly</sub> (°C) <sup>b</sup>	2.8 (2.4–3.1)	2.2 (1.8–2.5)	3.8 (2.2–5.4)		

<sup>a</sup> Ranges of location-specific latitudes or longitudes.

<sup>b</sup> Mean location-specific temperature, humidity or TV (range).

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Fig. 1. Locations of the 63 communities across China (a), UK (b), and USA (c).



Fig. 2. Distributions of temperature variability indexes at lag 0–1 days generated from daily and hourly temperatures in Wuhan, 2006–2012 (a), London, 1990–2012 (b), and Los Angeles, 1987–2000 (c).

2006–2012 (a), London, 1990–2012 (b), and Los Angeles, 1987–2000 (c), respectively. As expected, the  $TV_{daily}$  series is largely shifted towards wider ranges when comparing with  $TV_{hourly}$  series. Additionally, both distributions of  $TV_{daily}$  and  $TV_{hourly}$  changed very slightly when extending exposure days from 0–1 to 0–10 days (Fig. S1).

Fig. 3 shows the pooled exposure-response curves for TV-mortality associations in each country. In despite of a relatively wide uncertainty in China, approximately linear relationships were consistently identified for  $TV_{daily}$  and  $TV_{hourly}$ . Clear evidence was observed on increased risks associated with high TV exposures in all three countries, while China tended to exhibit larger mortality effects.

Fig. 4 demonstrates effect estimates of TV-mortality associations across various exposure days, presented as percent changes (%, 95% CIs) associated with per 1 °C increase in TV<sub>daily</sub> and TV<sub>hourly</sub>. Effect estimates of TV<sub>daily</sub> and TV<sub>hourly</sub> for various exposure days were comparable in China and USA, while UK exhibited smaller effects of TV<sub>daily</sub> than those of TV<sub>hourly</sub> at short lags such as 0–1 days. In the three countries, generally similar lag patterns of TV effects were consistently observed for TV<sub>daily</sub> and TV<sub>hourly</sub>. Specifically, TV effects increased to some extent with the number of exposure days, and tended to be relatively stable around exposures along 0–7 days, despite slight increases observed at longer exposure periods (e.g., 0–10 days) in UK. To ease the interpretation, we mainly chose TV<sub>0–7</sub> and TV<sub>0–10</sub> as the representative exposures to report our subsequent results.

Table 2 summarizes the mortality risks attributable to  $TV_{daily}$  and  $TV_{hourly}$  along lag 0–7 and lag 0–10 days. Generally, most effect estimates (i.e., both excess mortality risks and attributable fractions) increased to some extent from lag 0–7 to 0–10 days. A 1 °C rise in  $TV_{daily}$  and  $TV_{hourly}$  at lag 0–7 days was associated with mortality increases of 0.93% (95% CI: 0.12, 1.74) and 0.97% (0.18, 1.77) in China, 0.33% (0.15, 0.51) and 0.41% (0.21, 0.60) in UK, and 0.55% (0.41, 0.70) and 0.51% (0.35, 0.66) in USA, respectively. Larger attributable fractions were estimated using  $TV_{daily}$  than those using  $TV_{hourly}$ , with estimates at 0–10 days of 3.69% (0.51, 6.75) vs. 2.59% (0.10, 5.01) in China, 1.14% (0.54, 1.74) vs. 0.98% (0.55, 1.42) in UK, and 2.57% (1.97, 3.16) vs. 1.67% (1.15, 2.18) in USA, respectively.

Tables 3S2Table 3 and Table S2 explore the potential modifying effects of several location-level predictors on TV-mortality associations

by performing meta-regression analysis using different exposure days. Compared with UK and USA, China exhibited relatively larger excess mortality risks associated with temperature variability. Among the selected geographic and climatologic factors, we only observed significant modifying effects of latitude and average temperature. At lag 0–7 days, for example, increase in mortality associated with 1 °C rise in TV<sub>daily</sub>, showed a change of -0.17% (95% CI: -0.30, -0.05) and 0.22% (95% CI: 0.05, 0.39) for an IQR increase of latitude (9.5 °N) and average temperature (6.9 °C), respectively. Consistently, these results indicated higher vulnerability to TV-induced mortality risks in warmer locations.

The sensitivity analyses present the mortality estimates of TV-associated ERR and AF by changing the dfs for calendar time, maximum lag days and internal knots for temperature (Table S3), suggesting that our main findings from  $TV_{daily}$  and  $TV_{hourly}$  were generally robust to modelling choices.

# 4. Discussion

To the best of our knowledge, this is the first large-scale study to compare mortality risks associated with temperature variability using daily and hourly exposure metrics. Our multi-country analyses provided strong evidence of increased mortality triggered by large TV exposure in China, UK, and USA. Despite largely consistent TV-mortality associations identified for both TV indexes, we also observed some differences when separately attributing mortality fraction to  $TV_{daily}$  and  $TV_{hourly}$ . These findings would provide some important implications for better understanding of health burden caused by unstable temperatures, thus promoting future public health decision-making so as to fight against global climate change.

Previous epidemiologic investigations focused mostly on associating health outcomes with DTR, a common index for intra-day TV exposure assessment. Here, we could also take inter-day TV into consideration by generating the standard deviations of several days' daily or hourly temperatures (i.e.,  $TV_{daily}$  and  $TV_{hourly}$ ). Given no uniform TV definitions proposed before, the application of these two composite TV indexes has been increasingly considered capable to introduce a more comprehensive assessment for temperature variability (Guo et al.,



Fig. 3. Country-average exposure-response curves (smoothing using natural cubic splines with df = 3) between  $TV_{daily}$ ,  $TV_{hourly}$  and mortality in China, UK and USA. The continuous bold lines represent the estimated mortality risks and the grey areas are the 95% confidence intervals.

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Fig. 4. Mortality changes (%, 95% CIs) associated with per 1 °C increase in TV<sub>daily</sub> and TV<sub>hourly</sub> along various exposure days. The solid dots are the average effect estimates and the error bars represent the 95% confidence intervals.

2016; Hu et al., 2019). Calculation of  $TV_{daily}$  merely relies on very few temperature values (i.e., maximum and minimum temperatures), and fails to account for the temporal variation in temperature.  $TV_{daily}$  tends to show a large exaggeration of the tenuous hourly variations as illustrated in Fig. 2. By contrast,  $TV_{hourly}$  is generated from the standard deviation of finer-scale temperature monitoring records. The hourly

temperature records provide sufficient data to better capture the variable temperature within a short period of time, and could reduce exposure measurement error for temperature variability. From this perspective,  $TV_{hourly}$  can better reflect the actual patterns of whole-day temperature fluctuations (Cheng et al., 2017; Zhang et al., 2018b). Despite this, our results also supported the recent argument that  $TV_{daily}$ 

# Table 2

Estimated excess mortality risks and attributable fractions (%, 95% CIs) due to TV <sub>daily</sub> and TV <sub>hourly</sub> along selected exposure days in Chi	na, UK, and USA.
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Lag/country	ERR (%, 95% CI)		AF (%, 95% CI)	AF (%, 95% CI)	
	TV <sub>daily</sub>	TV <sub>hourly</sub>	TV <sub>daily</sub>	TV <sub>hourly</sub>	
Lag 0–7					
China	0.93 (0.12, 1.74)	0.97 (0.18, 1.77)	3.69 (0.51, 6.75)	2.59 (0.10, 5.01)	
UK	0.33 (0.15, 0.51)	0.41 (0.21, 0.60)	1.14 (0.54, 1.74)	0.98 (0.55, 1.42)	
USA	0.55 (0.41, 0.70)	0.51 (0.35, 0.66)	2.57 (1.97, 3.16)	1.67 (1.15, 2.18)	
Lag 0–10					
China	1.09 (0.22, 1.96)	1.26 (0.36, 2.17)	4.04 (0.62, 7.34)	3.03 (0.36, 5.62)	
UK	0.42 (0.18, 0.66)	0.46 (0.21, 0.71)	1.31 (0.61, 2.01)	1.07 (0.58, 1.57)	
USA	0.57 (0.44, 0.70)	0.51 (0.35, 0.68)	2.83 (2.13, 3.53)	1.84 (1.27, 2.40)	

Abbreviations: ERR, excessive relative risk; AF, attributable fraction; CI, confidence interval.

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#### Table 3

Estimated percent changes (%, 95% CIs) in the association between temperature variability at lag 0–7 days and mortality per an IQR increase in community-level predictors.

Predictor	IQR	$TV_{daily}$		TV <sub>hourly</sub>	
		Estimate (95% CI)	p value	Estimate (95% CI)	p value
Country					
China	-	Reference		Reference	
UK	-	-0.59(-1.41, 0.23)	0.158	-0.55(-1.14, 0.31)	0.209
USA	-	-0.37(-1.17, 0.44)	0.370	-0.45 (-1.29, 0.40)	0.296
Latitude	9.5 °N	-0.17 (-0.30, -0.05)	0.008	-0.14(-0.28, 0.01)	0.066
Longitude	93.5 °E	-0.15(-0.35, 0.06)	0.158	-0.07 (-0.30, 0.16)	0.555
Average temperature	6.9 °C	0.22 (0.05, 0.39)	0.011	0.20 (0.01, 0.40)	0.040
Temperature range	22.0 °C	-0.00(-0.20, 0.20)	0.989	-0.16(-0.37, 0.06)	0.152
Average DTR	3.0 °C	0.12 (-0.04, 0.28)	0.153	0.08(-0.11, 0.26)	0.407
Average humidity	8.5%	-0.04(-0.15, 0.08)	0.543	0.01(-0.12, 0.06)	0.874

Abbreviations: IQR, interquartile range; DTR, diurnal temperature range; CI, confidence interval.

could act well as the surrogate when estimating the acute death or hospitalization risks associated with TV (Guo et al., 2016; Zhang et al., 2017b; Zhao et al., 2018a). In this multi-city investigation, we identified generally similar exposure-response associations of  $TV_{daily}$  and  $TV_{hourly}$  with mortality risks. The potential overestimation of the attributable mortality burden, however, should be well noted when using  $TV_{daily}$  instead of  $TV_{hourly}$ . Here, we thereby recommend the choice of  $TV_{hourly}$  for future research, so as to achieve more comprehensive understanding of health burden in relation to unstable weather.

In this multi-country study, we observed increased mortality risks associated with exposures to large TV. A 1  $^\circ C$  rise in TV  $_{\rm hourly}$  at lag 0–7 days, for instance, was associated with an increase in mortality of 0.97% (0.18, 1.77) in China, 0.41% (0.21, 0.60) in UK, and 0.51% (0.35, 0.66) in USA, respectively. This finding coincides with large bodies of prior DTR-mortality investigations conducted in China (Zhou et al., 2014), UK (Zhang et al., 2018a), and USA (Lim et al., 2015). Also, recent years have seen growing evidence based on TV<sub>daily</sub> (Guo et al., 2016; Yang et al., 2018a; Zhao et al., 2018b) or  $TV_{hourly}$  (Cheng et al., 2017; Hu et al., 2019; Zhang et al., 2018b) locally and regionally. Consistent with these multi-city studies, we also identified approximately linear increases in mortality as TV exposure raised. This short-term association could be partly explained by the response inefficiency of human's thermoregulatory system to the sudden temperature changes within a very short period (Hu et al., 2019; Yang et al., 2018a; Zhang et al., 2017b). Two elderly cohort studies conducted in New England (Shi et al., 2015) and 135 US cities (Zanobetti et al., 2012), also provided longitudinal perspective for the shortened survival induced by long-term increases in summer temperature variability. These increasing epidemiologic evidence for risk triggered by large TV exposure, in the context of climate change, highlights the need for global efforts to reduce population vulnerability to both extreme and unstable temperatures.

TV-mortality associations may vary by locations due to substantial differences in climate characteristics (Guo et al., 2016; Lee et al., 2018; Yang et al., 2018a). Pooled estimates of TV effects derived in our study were generally larger in Chinese communities than those derived in UK and US cities, but comparable to a recent nationwide study in Japan. We estimated an increase of 0.93% (95% CI: 0.12, 1.74) in all-cause mortality associated with a 1 °C rise in TV<sub>daily</sub> at lag 0-7 days, for example, while this estimate was 0.90% (0.82,0.98) for 47 Japanese prefectures (Ma et al., 2019). As for  $TV_{hourly}$ , the pooled mortality effect (0.97%, 0.18 to 1.77) for Chinese southern communities in this study was relatively smaller than that for Zhejiang province, China (1.5%, 1.3 to 1.7) (Hu et al., 2019), but stronger than that for Australia (0.51%, 0.33 to 0.69) (Cheng et al., 2017). Regardless of the risk differences between above research, we consistently attributed a notable fraction of mortality burden (ranging from 0.98% to 5.33%) to short-term TV exposure, which could be comparable to or higher than burden from high temperatures or heatwaves (Cheng et al., 2019b).

As illustrated in prior evidence, city-level characteristics (e.g., demographic, sociological and climatologic) may have an influence on population vulnerability to temperature variability (Cheng et al., 2016; Ma et al., 2019; Yang et al., 2018a). Also, our study provided suggestive evidence of potential modifying effects of latitude and temperature on TV-mortality relationship, showing that persons in warmer locations exhibited higher vulnerability to mortality risk induced by large TV. This finding echoed to several recent large-scale time-series studies in China (Yang et al., 2018a), Australia (Cheng et al., 2017), and UK (Zhang et al., 2018a), as well as a previous combined analysis of four US cohorts of elderly people (Zanobetti et al., 2012). For example, for each 1 °C rise in mean temperature, TV<sub>hourly</sub>-related death risk increase was 0.09% (95% CI: 0.03 to 0.15) in five Australian capital cities (Cheng et al., 2017), and TV<sub>daily</sub>-associated increase was 0.08% (0.01-0.15) in 31 major Chinese cities (Yang et al., 2018a). Nevertheless, another multi-country study from 372 locations (Guo et al., 2016) showed inconsistent results when using short (0-1 days) and longer TV exposures (0-7 days). Using data spanning over 40 years in 47 Japanese prefectures, Ma and colleagues found no significant effect modification of latitude or temperature on TV<sub>daily</sub>-mortality associations (Ma et al., 2019). The underlying reasons for these less consistent findings across studies remained unclear to date, and further epidemiologic and mechanism researches are called for to help manage health risks of global, regional, and local climate change.

Several limitations of this study should be acknowledged. First, TVmortality associations estimated for China here were less representative, because we only included 8 southern communities in mainland China. Second, the datasets from China, UK, and USA covered quite different study periods, which may have weakened the comparability of TV-associated effects between countries. Third, in our main analyses, we did not consider the potential mediating, confounding or modifying effects of ambient air pollutants because of data unavailability. Additionally, we only investigated TV-associated all-cause mortality risk and burden, as age-cause specific mortality data was not included in our dataset.

# 5. Conclusions

In summary, our study added multi-country evidence for increased mortality risk associated with short-term exposure to large temperature variability. People in warmer locations may exhibit high vulnerability to TV-related mortality impacts. Daily and hourly TV exposure metrics produced generally comparable risk effects, but the attributable mortality burden tended to be higher using  $TV_{daily}$  instead of  $TV_{hourly}$ . Our findings may provide some important implications and directions for future research investigating TV-health relation, and contribute to efficient management of public health risks in the context of global climate change.

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# Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2019.108771.

#### Author contributions

Yunquan Zhang conceived and designed the experiments; Yunquan Zhang, Junzhe Bao, Zan Ding, and Qianqian Xiang collected the data; Yunquan Zhang and Qianqian Xiang performed the data analysis, and drafted the manuscript; Chuanhua Yu, Hung Chak Ho, Shengzhi Sun, Kejia Hu, and Ling Zhang helped revise the manuscript. All authors read and approved the final manuscript.

# **Conflicts of interest**

The authors declare they have no competing financial interests.

# References

- Armstrong, B.G., et al., 2011. Association of mortality with high temperatures in a temperate climate: England and Wales. J. Epidemiol. Community Health 65, 340–345.
- Chen, D., et al., 2019. Hourly associations between exposure to ambient particulate matter and emergency department visits in an urban population of Shenzhen, China. Atmos. Environ. 209, 78–85.
- Cheng, J., et al., 2017. The mortality burden of hourly temperature variability in five capital cities, Australia: time-series and meta-regression analysis. Environ. Int. 109, 10–19.
- Cheng, J., et al., 2019b. Impacts of heat, cold, and temperature variability on mortality in Australia, 2000-2009. Sci. Total Environ. 651, 2558–2565.
- Cheng, J., et al., 2016. The burden of extreme heat and heatwave on emergency ambulance dispatches: a time-series study in Huainan, China. Sci. Total Environ. 571, 27–33.
- Gasparrini, A., 2011. Distributed lag linear and non-linear models in R: the package dlnm. J. Stat. Softw. 43, 1–20.
- Gasparrini, A., Armstrong, B., 2013. Reducing and meta-analysing estimates from distributed lag non-linear models. BMC Med. Res. Methodol. 13, 1.
- Cheng, J., Xu, Z., Bambrick, H., Su, H., Tong, S., Hu, W., 2019. Impacts of exposure to ambient temperature on burden of disease: a systematic review of epidemiological evidence. Int. J. Biometeorol. 63, 1099–1115.
- Gasparrini, A., et al., 2010. Distributed lag non-linear models. Stat. Med. 29, 2224–2234.
  Gasparrini, A., et al., 2012a. Multivariate meta-analysis for non-linear and other multiparameter associations. Stat. Med. 31, 3821–3839.
- Gasparrini, A., et al., 2012b. The effect of high temperatures on cause-specific mortality in England and Wales. Occup. Environ. Med. 69, 56–61.
- Gasparrini, A., et al., 2016. Changes in susceptibility to heat during the summer: a multicountry analysis. Am. J. Epidemiol. 183, 1027–1036.
- Gasparrini, A., et al., 2015. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet 386, 369–375.
- Guo, Y., et al., 2014. Global variation in the effects of ambient temperature on mortality: a systematic evaluation. Epidemiology 25, 781–789.
- Guo, Y., et al., 2016. Temperature variability and mortality: a multi-country study. Environ. Health Perspect. 124, 1554–1559.
- Hajat, S., et al., 2010. Health effects of hot weather: from awareness of risk factors to effective health protection. Lancet 375, 856–863.
- Hu, K., et al., 2018. Temperature variability and mortality in rural and urban areas in Zhejiang province, China: an application of a spatiotemporal index. Sci. Total

Environ. 647, 1044-1051.

- Hu, K., et al., 2019. Temperature variability and mortality in rural and urban areas in Zhejiang province, China: an application of a spatiotemporal index. Sci. Total Environ. 647, 1044–1051.
- Huang, C., et al., 2013. Managing the health effects of temperature in response to climate change: challenges ahead. Environ. Health Perspect. 121, 415–419.
- Jiao, A., et al., 2019. Impact of summer heat on mortality and years of life lost: application of a novel indicator of daily excess hourly heat. Environ. Res. 172, 596–603.Lee, W., et al., 2018. Mortality burden of diurnal temperature range and its temporal
- changes: a multi-country study. Environ. Int. 110, 123–130. Li, G., et al., 2018. Projected temperature-related years of life lost from stroke due to global warming in a temperate climate city, asia: disease burden caused by future
- climate change. Stroke 49, 828–834.
   Lim, Y.H., et al., 2015. Diurnal temperature range and short-term mortality in large US communities. Int. J. Biometeorol. 59, 1311–1319.
- Lin, H., et al., 2018. Daily exceedance concentration hours: a novel indicator to measure acute cardiovascular effects of PM2.5 in six Chinese subtropical cities. Environ. Int. 111, 117–123.
- Lin, H., et al., 2013. Temperature changes between neighboring days and mortality in summer: a distributed lag non-linear time series analysis. PLoS One 8, e66403.
- Ma, C., et al., 2019. The association between temperature variability and cause-specific mortality: evidence from 47 Japanese prefectures during 1972-2015. Environ. Int. 127, 125–133.
- Peng, R.D., et al., 2006. Model choice in time series studies of air pollution and mortality. J. R. Stat. Soc. A 169, 179–203.
- Peng, R.D., Dominici, F., Pastor-Barriuso, R., Zeger, S.L., Samet, J.M., 2005. Seasonal analyses of air pollution and mortality in 100 US cities. Am. J. Epidemiol. 161 (6), 585–594.
- Samet, J.M., Zeger, S.L., Dominici, F., Curriero, F.C., Coursac, I., Dockery, D.W., Schwartz, J., Zanobetti, A., 2000. The national morbidity, mortality, and air pollution study. Res. Rep. Health Eff. Inst. 94. https://doi.org/10.3201/eid0604.000425.
- Shi, L., et al., 2015. Impacts of temperature and its variability on mortality in New England. Nat. Clim. Chang. 5, 988–991.
- Song, X., et al., 2017. Impact of ambient temperature on morbidity and mortality: an overview of reviews. Sci. Total Environ. 586, 241–254.
   Vicedo-Cabrera, A.M., et al., 2016. Associations of inter- and intraday temperature
- change with mortality. Am. J. Epidemiol. 183, 286-293. Viechtbauer, W., 2010. Conducting meta-analyses in R with the metafor package. J. Stat.
- Softw. 36, 1–48. Watts, N., et al., 2015. Health and climate change: policy responses to protect public
- health. Lancet 386, 1861–1914. Yang, J., et al., 2015. Cardiovascular mortality risk attributable to ambient temperature
- in China. Heart 101, 1966–1972. Yang, J., et al., 2018a. Vulnerability to the impact of temperature variability on mortality
- in 31 major Chinese cities. Environ. Pollut. 239, 631–637. Yang, J., et al., 2018b. Diurnal temperature range in relation to death from stroke in
- China. Environ. Res. 164, 669–675.
- Ye, X., et al., 2012. Ambient temperature and morbidity: a review of epidemiological evidence. Environ. Health Perspect. 120, 19–28.
- Zanobetti, A., et al., 2012. Summer temperature variability and long-term survival among elderly people with chronic disease. Proc. Natl. Acad. Sci. U. S. A. 109, 6608–6613.Zhan, Z., et al., 2017. Temperature change between neighboring days and mortality in
- United States: a nationwide study. Sci. Total Environ. 584–585, 1152–1161.
- Zhang, Y., et al., 2018a. Association of diurnal temperature range with daily mortality in England and Wales: a nationwide time-series study. Sci. Total Environ. 619–620, 291–300.
- Zhang, Y., et al., 2019. Socio-geographic disparity in cardiorespiratory mortality burden attributable to ambient temperature in the United States. Environ. Sci. Pollut. Res. 26, 694–705.
- Zhang, Y., et al., 2017a. Impact of temperature on mortality in Hubei, China: a multicounty time series analysis. Sci. Rep. 7, 45093.
- Zhang, Y., et al., 2017b. Impact of temperature variation on mortality: an observational study from 12 counties across Hubei Province in China. Sci. Total Environ. 587–588, 196–203.
- Zhang, Y., et al., 2018b. Temporal and seasonal variations of mortality burden associated with hourly temperature variability: a nationwide investigation in England and Wales. Environ. Int. 115, 325–333.
- Zhao, Q., et al., 2018a. Spatiotemporal and demographic variation in the association between temperature variability and hospitalizations in Brazil during 2000-2015: a nationwide time-series study. Environ. Int. 120, 345–353.
- Zhao, Q., et al., 2018b. Temperature variability and hospitalization for cardiac arrhythmia in Brazil: a nationwide case-crossover study during 2000-2015. Environ. Pollut. 246, 552–558.
- Zhou, X., et al., 2014. Acute effects of diurnal temperature range on mortality in 8 Chinese cities. Sci. Total Environ. 493, 92–97.