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Impact of diurnal temperature range on mortality in a high plateau area in southwest China: A time series analysis

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HIGHLIGHTS

- The effect of DTR on daily mortality was estimated in a high plateau city with a large DTR in China.
- A time-series analysis with 7 years of daily mortality data was used to assess the effect of DTR.
- The effect of DTR on mortality was non-linear, with J- or U-shaped curves.
- Relative risk assessments showed strong monotonic increases starting at DTR 16 °C.
- Males and people <75 years old were more susceptible to extreme high DTR than females and older people.

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ABSTRACT

Background: Diurnal temperature range (DTR) is an important meteorological indicator that reflects weather stability and is associated with global climate change and urbanization. Previous studies have explored the effect of DTR on human health in coastal cities with small daily temperature variations, but we have little evidence for high plateau regions where large DTRs usually occur. Using daily mortality data (2007–2013), we conducted a time-series analysis to assess the effect of DTR on daily mortality in Yuxi, a high plateau city in southwest China. Methods: Poisson regression with distributed lag non-linear model was used to estimate DTR effects on daily mortality, controlling for daily mean temperature, relative humidity, sunshine duration, wind speed, atmospheric pressure, day of the week, and seasonal and long-term trends.

Results: The cumulative effects of DTR were J-shaped curves for non-accidental, cardiorespiratory and cardiovascular mortality, with a U-shaped curve for respiratory mortality. Risk assessments showed strong monotonic increases in mortality starting at a DTR of approximately 16 °C. The relative risk of non-accidental morality with extreme high DTR at lag 0 and 0–21 days was 1.03 (95% confidence interval: 0.95–1.11) and 1.33 (0.94–1.89), respectively. The risk of mortality with extreme high DTR was greater for males and age <75 years than females and age \ge 75 years.

Conclusions: The effect of DTR on mortality was non-linear, with high DTR associated with increased mortality. A DTR of 16 °C may be a cut-off point for mortality prognosis and has implications for developing intervention strategies to address high DTR exposure.

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Abbreviations: CI, confidence interval; df, degrees of freedom; DLNM, distributed lag non-linear model; DTR,, diurnal temperature range; ICD-10, the Tenth Revision of the International Classification of Diseases; Q-AIC, quasi-Akaike information criteria; RR, relative size.

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1. Introduction

Climate change and temperature variation are associated with increased frequency, intensity and duration of adverse weather events (e.g., heat waves, cold spells, El Niños and storms) and have drawn the attention of researchers, especially concerning the adverse impacts on human health (Curriero et al., 2002; Iniguez et al., 2010; Yang et al., 2013). The association of daily ambient temperatures and

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mortality has been extensively demonstrated in various geographic regions, populations and climatic zones worldwide (Basu and Samet, 2002; Curriero et al., 2002; Iniguez et al., 2010; Medina-Ramon et al., 2006; Yu et al., 2011). Typically, the effects of daily ambient temperatures on mortality have been shown to be non-linear, following V-, U-, W-, J-, or inverse J-shaped curves that usually indicate increases in mortality at temperatures below the cold threshold or above the hot threshold (Curriero et al., 2002; Iniguez et al., 2010; Medina-Ramon and Schwartz, 2007; Wu et al., 2013; Yu et al., 2011).

Previous studies usually adopted daily mean, minimum, maximum or apparent temperature as ambient temperature indicators to explore the effects of temperature on mortality (Basu and Samet, 2002; Saez et al., 1995; Wu et al., 2013). In recent years, diurnal temperature range (DTR) has been suggested as a predictor of mortality and found an independent risk factor for human health by an increasing number of epidemiological studies (Kan et al., 2007; Song et al., 2008; Yang et al., 2013). Calculated as the daily maximum temperature minus the daily minimum temperature within 1 day, DTR is an important meteorological indicator associated with global climate change and urbanization that reflects the stability of weather (Cheng et al., 2014; Xu et al., 2014; Zhou et al., 2014).

Most previous studies have shown that mortality risk depends on exposure to the current day's DTR and on the exposure experienced during several previous days ("lag" or delayed effects) (Braga et al., 2001; Guo et al., 2011; Vutcovici et al., 2014). Among time-series studies, the generalized additive model has been commonly used to quantify the effect of DTR on mortality and calculate the lag effects, because daily mortality counts typically follow the Poisson distribution and the effect of DTR on health is potentially nonlinear (Song et al., 2008). Recently, a new methodological framework, the distributed lag non-linear model (DLNM), has been used for simultaneously representing the nonlinear and distributed lag effects between a predictor and an outcome in time series data (Gasparrini, 2014; Gasparrini et al., 2010). Developed on the basis of a "cross-basis" function, DLNM is a flexible model in understanding and investigating the relationship between DTR and mortality (Gasparrini et al., 2010; Goldberg et al., 2011).

The effect of DTR on mortality has been explored in China (Kan et al., 2007; Song et al., 2008; Zhou et al., 2014), Korea (Lim et al., 2013; Lim et al., 2012), Finland (Holopainen et al., 2013) and Canada (Vutcovici et al., 2014). However, most of the cities under study were high-income and located in low-altitude regions or coastal areas with low DTR. The impact of DTR on daily mortality in a high plateau area, with low atmospheric pressure, thin air and large DTR, has not been reported. In this study, we aimed to estimate the effect of DTR on mortality in Yuxi, a high-altitude city with a large DTR, in Yunnan Province, south-west of China.

2. Materials and methods

2.1. Study area and population

Yuxi city is on the western edge of the Yunnan–Guizhou Plateau, with complex geographic features including plateaus, mountains, valleys and basins. The area has a distinct subtropical plateau monsoon climate, with four spring-like seasons year round, giving the city a stable daily mean temperature but large temperature difference between day and night, morning or evening and daytime, indoor and outdoor, and sunny and shade locations. The area is 15,285 km² with a population of 2.30 million (1.18 million males) in 2010, as reported in the sixth national population census.

2.2. Mortality and meteorological data

Individual mortality data were collected from the Center for Disease Control and Prevention in the Hongta District and Tonghai County of Yuxi, which were included in the National Disease Surveillance Points. In 2010, these two districts contained 0.80 million residents, representing 34.55% of the population of Yuxi. Most of the people who live in these two districts are permanent residents, with low mobility.

A total of 28,201 registered deaths (15,581 males) occurred from January 1, 2007 to December 31, 2013, and included information on age, sex, date of birth, date of death, underlying cause of death, permanent address, educational attainment and occupation. The underlying causes of death in these two districts are usually assigned by medical personnel, and examination procedures are routinely performed to ensure accurate data. The daily mortality categories were classified according to the Tenth Revision of the International Classification of Diseases (ICD-10). Non-accidental mortality (ICD-10: A00-R99), cardiorespiratory mortality (ICD-10: I00-I99 and J00-J99), cardiovascular mortality (ICD-10: I00-I99) and respiratory mortality (ICD-10: J00-J99) were examined separately. Daily frequency of non-accidental deaths was summarized by gender and age (<75 and ≥75 years old).

Daily meteorological data including daily minimum temperature, maximum temperature, mean temperature, mean wind speed, sunshine duration, atmospheric pressure and mean relative humidity were obtained from the China Meteorological Data Sharing System for the same period. DTR was calculated as the difference between maximal and minimal temperatures within 1 day (Xu et al., 2014). During the study period, there were no missing values in the daily meteorological data except for daily sunshine duration (0.08% missing). All missing values were replaced by the median for the corresponding variables.

2.3. Statistical analysis

A quasi-Poisson generalized linear regression model combined with DLNM was used to estimate the effect of DTR on daily mortality, while controlling for daily mean temperature, relative humidity, sunshine duration, wind speed, atmospheric pressure, day of the week and the long-term trends of daily mortality, as suggested by previous studies (Gasparrini et al., 2010; Yang et al., 2012). The statistical model used in the analysis was as follows:

$$E(Y_t) = Exp\{ \alpha + \beta DTR_{t,l} + \lambda Temp_{t,l} + NS(Time_t, 7 \times 7) + NS(RH_t, 3) + NS(Sunshine_t, 3) + NS(WS_t, 3) + NS(AP_t, 3) + \gamma DOW_t \}$$

where t is the day of the observation (t = 1,2,3...2557), Y_t is the observed daily death counts and $E(Y_t)$ is the expected number of deaths on day t. Exp{ } is the natural exponential function; α is the intercept; DTR_{t l} is a matrix obtained by the DLNM to model non-linear and distributed lag effects of DTR over a lag of 0 (the current day) to l days, and β is the vector of coefficients for $DTR_{t,l}$; $Temp_{t,l}$ is a matrix obtained by applying the DLNM to mean temperature with the vector of coefficients of λ ; and NS() is the natural cubic spline. A nature cubic spline for time with 7 degrees of freedom (df) per year was used to describe the long-term trends and seasonality (Gasparrini et al., 2010). We also used natural cubic splines with 3 df at equally spaced quantiles for relative humidity (RH), sunshine duration (Sunshine), wind speed (WS) and atmospheric pressure (AP) as per previous studies (Gasparrini et al., 2010; Guo et al., 2011; Yang et al., 2013). The moving average of lag 0–2 days for relative humidity, sunshine duration, wind speed and atmospheric pressure was used. DOW_t is the day of the week effect (a categorical variable) on day t, and γ is the vector of coefficients.

We used a "natural cubic spline-natural cubic spline" DLNM, examining both the non-linear and lag effects of DTR on mortality with natural cubic splines. We placed spline knots at equally spaced values in the range of DTR, with the knots in the lag space placed equally on a logarithmic scale to mirror greater expected smoothness with increasing lag. The median value of DTR (10.2 °C) was used as the reference for calculating the relative risks (RRs) and 95% confidence intervals (CIs) across the study period (Guo et al., 2011; Yang et al., 2012). The RRs

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with lag up to 21 days were calculated for the overall effects because we found that the effects of DTR on daily mortality changed little for lags >3 weeks. Corresponding to the DTR, mean temperature was also controlled by a "natural cubic spline-natural cubic spline" DLNM for lag up to 21 days, with the median value of temperature (16.9 °C) as the reference. We also placed spline knots at equally spaced values in the range of temperature, with the knots in the lag space placed equally on a logarithmic scale. In choosing the df for lags and DTR and mean temperature, we used the quasi-Akaike information criterion (Q-AIC), a measure of fit, for quasi-Poisson models (Gasparrini, 2014; Gasparrini et al., 2010; Guo et al., 2011). Finally, DLNM models containing 4 df for DTR with 4 df for lag, and 5 df for mean temperature with 4 df for lag were selected by the lowest AIC value (Table S1).

To explore the single-day and cumulative effects of DTR on daily mortality over different lag days, we examined the mortality risks with DTR for lag 0, 5, 0–7 and 0–21 days. Furthermore, we stratified the full year into the warm season (April to September) and cold season (October to March of the next year) (Cao et al., 2009). In the seasonal analysis, a nature cubic spline for time with 4 df per season (6 months) was used to control for the seasonality. By comparing to the reference value of 10.2 °C, we quantified the effects of extreme high DTR (99th percentile of DTR distribution; 18.4 °C for the full year, 18.9 °C for the cold season and 17.3 °C for the warm season) on daily mortality categories.

The software R 3.0.1 (R Development Core Team, 2013) was used for all statistical analyses. The DLNM modeling framework was adequately implemented in the R package dlnm by using the extended version 2.0.9. All statistical tests were two-sided, and P < 0.05 was considered statistically significant.

3. Results

3.1. Data description

During the study period, from 2007 to 2013, the average daily mean temperature and relative humidity were 16.0 °C (range: -0.9 °C, 24.6 °C) and 68.5% (range: 25.0%, 100.0%), respectively (Table 1). The mean sunshine duration was 2208.7 h/year, and the minimum, mean and maximum DTR was 1.1 °C, 10.3 °C and 21.7 °C, respectively. The high plateau study area had a low atmospheric pressure with a mean of 810.15 hPa (Table 1). DTR was positively correlated with daily mean wind speed (r = 0.29, P < 0.01) and sunshine duration (r =

0.82, P < 0.01), and negatively correlated with relative humidity (r = -0.70, P < 0.01) and mean temperature (r = -0.21, P < 0.01).

The descriptive statistics for daily mortality categories by individual characteristics are in Table 2. Among 24,764 people with non-accidental deaths, 10,857 (43.84%) died of cardiovascular disease and 4527 (18.28%) died of respiratory disease. In a total of 2557 days, more males died, for a male-to-female sex ratio of 1.17:1, and people ≥ 75 years old accounted for 57.02% of all non-accidental deaths. The time series for all daily mortality categories and weather factors is in Fig. 1. We observed strong seasonal patterns with increases during the cooler months for all daily mortality categories and weather variables. The number of daily deaths and meteorological data had an analogous trend.

3.2. Effect of DTR on mortality

The overall effect of DTR on mortality categories is in Fig. 2, comparing the RRs for DTR by lag period (lag 0 to 21 days) with the reference DTR of 10.2 °C. The estimated effect of DTR was non-linear for all mortality categories, with high RRs at high DTR (Fig. 2). The cumulative effect of DTR on non-accidental, cardiorespiratory and cardiovascular mortality followed I-shaped curves, so the RRs changed slightly with low and moderate DTR (approximately 1), with rapid increases observed with high DTR (Fig. 3). We found a U-shaped relationship between DTR and respiratory mortality, with a low and flat cumulative RR in the intermediate DTR range and increases with both low and high DTRs (Fig. 3). In particular, the dose-response curves approximated a plateau at low DTR; at high DTR, we found a strong monotonic increase in number of deaths starting at approximately 16 °C (the 93rd percentile of DTR) (15.8 °C for non-accidental, 16.5 °C for cardiorespiratory, 16.7 °C for cardiovascular and 15.9 °C for respiratory mortality) (Fig. 3). The effect of low DTR on mortality was negligible, with prompt increase with high DTR (Figs. 2 and 3). Similar results were found in both cold and warm seasons (Figs. S1 and S2). Risk assessments in the cold (warm) season showed strong monotonic increases for nonaccidental, cardiorespiratory, cardiovascular and respiratory mortality starting at 16.6 °C (15.5 °C), 16.7 °C (15.7 °C), 16.9 °C (15.6 °C) and 15.0 °C (16.2 °C), respectively.

3.3. Effect of extreme high DTR on mortality

In terms of specific portions of curves, we focused on the estimated relative effect of extreme high DTR (99th percentile of DTR) on daily

Table 1Distribution of selected daily weather conditions by seasons, 2007–2013.

	$Mean \pm SD$	Minimum	25%	Median	75%	Maximum
Full year						
Mean temperature (°C)	16.0 ± 4.7	-0.9	12.2	16.9	20.0	24.6
DTR (°C)	10.3 ± 3.7	1.1	7.5	10.2	13.0	21.7
Mean wind speed (m/s)	2.7 ± 1.0	0.7	2.0	2.5	3.2	8.6
Mean relative humidity (%)	68.5 ± 14.6	25.0	60.0	72.0	79.0	100.0
Sunshine duration (h)	6.0 ± 3.9	0.0	2.2	6.8	9.6	12.9
Atmospheric pressure (hPa)	810.2 ± 3.2	802.7	807.8	810.0	812.3	822.2
Cold season						
Mean temperature (°C)	12.4 ± 3.6	-0.9	10.0	12.2	15.2	21.2
DTR (°C)	11.4 ± 3.9	1.1	8.8	11.8	14.3	21.7
Mean wind speed (m/s)	2.8 ± 1.0	0.7	2.1	2.7	3.4	8.6
Mean relative humidity (%)	65.3 ± 15.2	25.0	54.0	68.0	77.0	100.0
Sunshine duration (h)	6.8 ± 3.7	0.0	3.9	8.4	9.9	11.3
Atmospheric pressure (hPa)	811.6 ± 3.1	802.7	809.4	811.6	813.8	822.2
Warm season						
Mean temperature (°C)	19.6 ± 2.3	9.2	18.3	20.0	21.2	24.6
DTR (°C)	9.1 ± 3.2	1.2	6.9	8.9	11.2	19.9
Mean wind speed (m/s)	2.5 ± 0.9	0.7	1.9	2.3	2.9	7.5
Mean relative humidity (%)	71.7 ± 13.2	29.0	66.0	74.0	81.0	100.0
Sunshine duration (h)	5.3 ± 4.0	0.0	1.5	5.1	8.9	12.9
Atmospheric pressure (hPa)	808.7 ± 2.5	803.0	806.8	808.5	810.4	817.6

SD, standard deviation; 25%, 25th percentile; 75%, 75th percentile; DTR, diurnal temperature range.

Table 2 Distribution of daily mortality from non-accidental causes, by causes, gender and age, in Yuxi, China, $2007-2013\ (n=28,201)$.

	$Mean \pm SD$	Minimum	25%	Median	75%	Maximum
Non-accidental	9.7 ± 3.5	0	7	9	12	26
Cause-specific						
Cardiorespiratory	6.0 ± 2.7	0	4	6	8	19
Cardiovascular	4.3 ± 2.2	0	3	4	6	14
Respiratory	1.8 ± 1.4	0	1	2	3	8
Gender						
Male	5.2 ± 2.5	0	3	5	7	17
Female	4.5 ± 2.2	0	3	4	6	14
Age (years)						
<75	4.2 ± 2.1	0	3	4	6	15
≥75	5.5 ± 2.6	0	4	5	7	19
<75		-	_	-	_	

SD, standard deviation; 25%, 25th percentile; 75%, 75th percentile.

non-accidental mortality by causes and individual characteristics at different lag days. For a full year, the effect of extreme high DTR on non-accidental mortality was strongest at lag 0, declining over the following 2 days and then increasing again (Fig. S3). With a DTR of 10.2 °C as the reference, the RRs for non-accidental morality associated with extreme high DTR at lag 0 and 0–21 days in the full year, cold season and warm season were 1.03 (95% CI: 0.95–1.11) and 1.33 (0.94–1.89), 1.04 (0.95–1.15) and 2.05 (1.25–3.36), and 1.04 (0.91–1.19) and 0.84 (0.46–1.53),

respectively (Table 3). Compared with 10.2 °C, the cumulative effect of extreme high DTR over lag 0–21 days was significantly higher for non-accidental mortality, cardiorespiratory mortality, males and people <75 years old in the cold season but decreased significantly for respiratory mortality in the warm season (Table 3). Males were more susceptible to extreme high DTR than females in the full-year and cold season, with the opposite result observed in the warm season. Susceptibility to extreme high DTR was greater for people <75 than \geq 75 years old (Table 3).

3.4. Sensitivity analysis

When changing the degrees of freedom 6–8 per year for time and 2–4 for 4 meteorological factors (relative humidity, sunshine duration, wind speed and atmospheric pressure) (Fig. S4), the estimated effect of DTR on non-accidental mortality did not substantially change, which suggests that the results were relatively robust in these respects. Furthermore, the results were similar when excluding above 4 meteorological factors one by one or completely from the main model (Fig. S5). For completeness, all of the above 4 meteorological factors were retained in the main model. The delayed effect of extreme high DTR (18.4 °C relative to 10.2 °C) on non-accidental mortality changed little in different models (Table S2). The robust results were similar for cardiorespiratory, cardiovascular and respiratory mortality (results not shown).

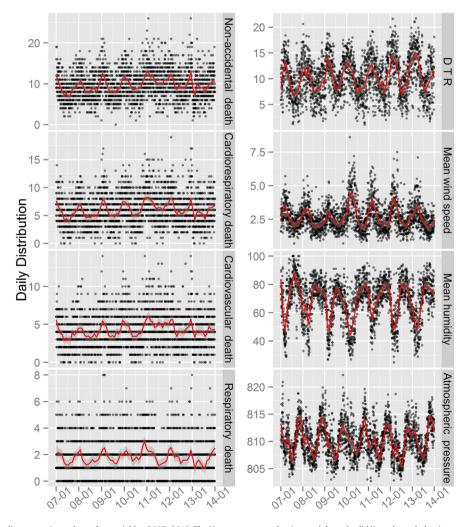


Fig. 1. Time series of daily mortality categories and weather variables, 2007–2013. The X-axes represent the time and the red solid lines through the time series are LOESS smoothing with a span of 5%. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

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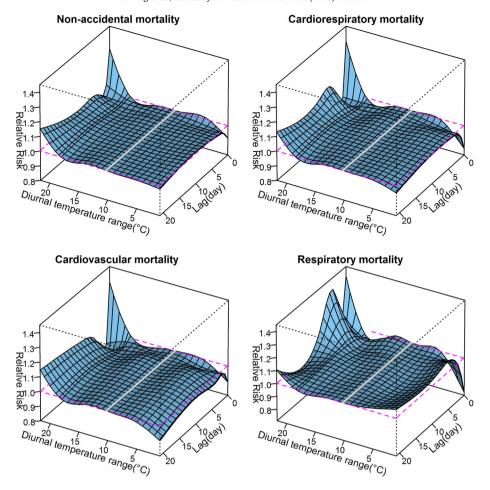


Fig. 2. Relative risk values for daily mortality categories (non-accidental, cardiorespiratory, cardiovascular and respiratory) and diurnal temperature range (DTR) by lag period. The Z-axes represent the relative increase in daily counts of mortality with DTR, and the other axes represent DTR and lag period (lag 0 to 21 days). Highlighted are the references at 10.2 °C (gray lines).

4. Discussion

The effect of DTR on mortality has been studied in low altitude regions with low DTR (Holopainen et al., 2013; Lim et al., 2012; Yang et al., 2013; Zhou et al., 2014), but the effect of high DTR on mortality has been little studied (Luo et al., 2013; Vutcovici et al., 2014). To our knowledge, this is the first attempt to explore the effect of DTR on non-accidental, cardiorespiratory, cardiovascular and respiratory mortality in a high-altitude city in southwest China with a large range in daily temperature. Using an advanced statistical method (i.e., DLNM), we identified a specific DTR threshold value above which daily mortality counts abruptly increased with increasing DTR. Focusing on the impact of extreme high DTR on daily mortality, we also identified subpopulations and mortality causes particularly susceptible to extreme high DTR. We found strong monotonic increases in mortality starting at a DTR of approximately 16 °C. The risk of mortality with extreme high DTR was greater for males and people <75 years old than females and people ≥ 75 years old. Our findings have implications for developing intervention strategies to prevent high DTR exposure.

In the present study, we found that the cumulative effect of DTR on daily mortality was non-linear, following J-shaped curves for non-accidental, cardiorespiratory and cardiovascular mortality but a U-shaped curve for respiratory mortality. However, more than half of related previous studies assumed and demonstrated a linear relationship between DTR and mortality with evidence of increasing mortality with increasing DTR in different regions, including cities in China (Cao et al., 2009; Yang et al., 2013; Zhou et al., 2014) and Korea (Lim et al., 2012). In agreement with our findings, an elderly population in Montreal, Canada,

showed a non-linear relationship between lag 0–30 days DTR and non-accidental mortality (Vutcovici et al., 2014). Moreover, Luo et al. (2013) found a U-shaped relationship between DTR and daily mortality in Guangzhou, China, claiming a stronger effect of higher and lower DTR than moderate DTR on mortality.

Notably, our findings revealed that the relative increase in daily death counts changed little at low DTR but showed a strong monotonic increase in cumulative DTR-related mortality starting at a threshold of approximately 16 °C. Plotting the cumulative effect of DTR accumulated over the concurrent day up to 30 days of lag, Vutcovici et al. (2014) observed that the daily death counts monotonically increased starting at about 10 °C. In Brisbane, Australia, Xu et al. (2014) reported that the effect of DTR on emergency department admissions for childhood diarrhea rapidly increased with DTR > 10 °C. DTR had a significant effect on daily mortality or morbidity (e.g., emergency room admissions or hospital admissions) in different regions: with increased DTR, the risk of DTR-associated health conditions increased accordingly (Liang et al., 2008; Vutcovici et al., 2014). People should be concerned about the impact of high DTR on human health and take effective protective measures. Our findings highlight the urgent need to strengthen awareness of the effects of high DTR exposure, especially diurnal variation in temperature > 16 °C.

The underlying physiological mechanisms of DTR on daily mortality are not clear, although there are some explanations for the observed adverse health effect of DTR. Sudden temperature changes might release inflammatory mediators associated with mast cells, increase cardiorespiratory workload and induce the onset of cardiorespiratory events (Imai et al., 1998; Keatinge et al., 1986). A large DTR might increase

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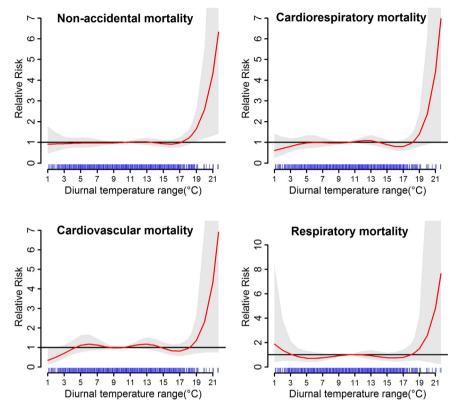


Fig. 3. The estimated cumulative effects of DTR over 21 days on mortality categories (non-accidental, cardiorespiratory, cardiovascular and respiratory). The red smooth lines are relative risks and the gray regions are the pointwise 95% confidence intervals. The reference value is 10.2 °C. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

the risk of cardiovascular disease onset by increasing blood pressure, oxygen uptake, heart rate, and cardiac workload (Liang et al., 2008; Vutcovici et al., 2014). Elevated heart rate and reduced time-domain

heart-rate variability with increments of DTR might explain in part the mechanisms of DTR on cardiovascular death (Lim et al., 2013). As well, sudden temperature changes could lead to pathophysiological

Table 3Single-day and cumulative effects of extreme high DTR^a on daily non-accidental mortality for lag periods by causes, gender and age in Yuxi, China, 2007–2013.

	Lag 0	Lag 5	Lag 0-7	Lag 0-21
Full year				
Non-accidental	1.03 (0.95-1.11)	1.00 (0.97-1.03)	1.06 (0.88-1.27)	1.33 (0.94-1.89)
Cardiorespiratory	1.02 (0.93-1.12)	1.00 (0.96-1.03)	0.95 (0.76-1.19)	1.10 (0.71-1.69)
Cardiovascular	1.04 (0.93-1.16)	0.98 (0.94-1.03)	0.91 (0.70-1.20)	1.07 (0.64-1.81)
Respiratory	0.97 (0.82-1.15)	1.03 (0.96-1.10)	1.05 (0.70-1.59)	1.16 (0.52-2.58)
Male	1.05 (0.94-1.16)	1.01 (0.97-1.05)	1.19 (0.93-1.53)	1.60 (0.98-2.60)
Female	1.00 (0.90-1.12)	0.99 (0.95-1.04)	0.92 (0.71-1.20)	1.08 (0.65-1.78)
<75 years old	1.07 (0.95-1.20)	1.00 (0.96-1.05)	1.10 (0.83-1.46)	1.69 (0.98-2.92)
≥75 years old	1.00 (0.90-1.10)	1.00 (0.96-1.04)	1.03 (0.82-1.30)	1.13 (0.72-1.77)
Cold season				
Non-accidental	1.04 (0.95-1.15)	1.02 (0.98-1.06)	1.17 (0.90-1.51)	2.05 (1.25-3.36)*
Cardiorespiratory	1.07 (0.95-1.20)	1.02 (0.97-1.08)	1.19 (0.87-1.63)	1.86 (1.02-3.41)*
Cardiovascular	1.06 (0.92-1.23)	1.01 (0.95-1.08)	1.11 (0.76-1.63)	1.82 (0.87-3.80)
Respiratory	1.08 (0.86-1.35)	1.06 (0.97-1.17)	1.40 (0.79-2.48)	1.87 (0.61-5.71)
Male	1.08 (0.94-1.24)	1.01 (0.95-1.08)	1.25 (0.87-1.79)	2.26 (1.14-4.50)*
Female	1.01 (0.87-1.17)	1.03 (0.97-1.10)	1.09 (0.74-1.60)	1.85 (0.88-3.88)
<75 years old	1.10 (0.94-1.29)	1.02 (0.95-1.09)	1.04 (0.69-1.59)	2.13 (0.95-4.77)
≥75 years old	1.01 (0.88-1.14)	1.02 (0.97-1.08)	1.26 (0.91-1.75)	2.02 (1.08-3.78)*
Warm season				
Non-accidental	1.04 (0.91-1.19)	0.97 (0.92-1.02)	0.95 (0.68-1.33)	0.84 (0.46-1.53)
Cardiorespiratory	0.98 (0.82-1.16)	0.94 (0.88-1.00)	0.66 (0.42-1.02)	0.58 (0.26-1.27)
Cardiovascular	1.07 (0.87-1.32)	0.97 (0.90-1.04)	0.81 (0.48-1.35)	0.84 (0.33-2.11)
Respiratory	0.78 (0.57-1.08)	0.85 (0.75-0.97)	0.36 (0.15-0.82)	0.19 (0.04-0.86)*
Male	1.03 (0.86-1.25)	0.96 (0.89-1.03)	0.79 (0.49-1.27)	0.52 (0.22-1.20)
Female	1.05 (0.87-1.27)	0.99 (0.92-1.06)	1.17 (0.73-1.88)	1.48 (0.63-3.50)
<75 years old	1.06 (0.87-1.29)	0.99 (0.92-1.07)	1.17 (0.72-1.93)	1.13 (0.46-2.73)
≥75 years old	1.03 (0.86-1.23)	0.96 (0.89-1.02)	0.80 (0.51-1.25)	0.65 (0.29-1.46)

Data represent relative risk (95% confidence interval).

^a The 99th percentile of DTR distribution (18.4 °C for the full year, 18.9 °C for the cold season and 17.3 °C for the warm season) relative to 10.2 °C.

^{*} Statistically significant association (P < 0.05).

responses of the respiratory epithelium, which might explain some of the mechanisms associated with the effect of DTR on respiratory mortality (Graudenz et al., 2006). In any case, understanding the underlying mechanisms of DTR on human health is needed.

Although the cumulative effect of extreme high DTR on all mortality categories was not high during the full year, the RR was increased in the cold season and decreased in the warm season. Moreover, cardiovascular and respiratory mortality were obviously influenced by the change in weather. Our results agree with data for 8 Chinese cities, finding an approximately two-fold higher effect of DTR on non-accidental, cardiovascular and respiratory mortality in the cold season than the full year (Zhou et al., 2014). Increases in mortality with cardiovascular and respiratory diseases and the mechanism during the cold weather have been widely reported (Huang et al., 2015; Ou et al., 2013). Joint effect (i.e., the interaction) of DTR with the mean temperature on mortality might exist in our study, because the effect of DTR on mortality differed depending to different mean temperatures (e.g., effect of a DTR of 15 °C on mortality is not the same when the mean temperature is 5 °C compared to when there is 25 °C).

Yuxi city has a distinct subtropical plateau monsoon climate, with a relatively stable daily mean temperature but large DTR. In the warm season, the mean temperature (19.6 \pm 2.3 °C) is suitable for human body, even though the minimum mean temperature is 9.2 °C. However, in the cold season, not only the DTR is larger than that in warm season, but also both mean temperature (12.4 \pm 3.6 °C) and minimum mean temperature (-0.9 °C) are lower. The cardiorespiratory system is sensitive for lower temperature, and the compensation function may decrease. The RRs of DTR on mortality were relatively increased accordingly in the cold season. Therefore, the effect of DTR should be shown by seasons.

We found increased risk of non-accidental mortality for males and age < 75 years with extreme high DTR in the full year and cold season. However, previous research in Guangzhou (Yang et al., 2013) found that females and older adults had more risks with DTR than males and younger people. A multicity study in Korea (Lim et al., 2012) reported greater adverse health affects of DTR in older adults (\geq 75 years) than younger people in Seoul, Daejeon and Incheon, with greater adverse health effects in younger people in Daegu, Busan and Gwangju. As well, males were more sensitive to DTR than females in Daegu (Lim et al., 2012). From our results, younger people and males may play or work outdoors (e.g., those engaged in outdoor occupations) more often than females and older adults, which may greatly increase their exposure to large DTR. Females and older adults may spend more time at home, and the real personal exposure to indoor DTR might not be equal to the outdoor DTR. The differences in the DTR effect by age and sex might depend on region, populations or social behaviors (e.g., daily activity). Why males and relatively young people were more sensitive to extreme high DTR is not clear.

The limitations in our study should be acknowledged. First, generalizing the results of our study in a high altitude city to other geographic regions is cautioned, particularly for places with small daily variations in temperature and low altitude. Second, exposure measurement bias could have been introduced when we assumed that each person had the same exposure level of DTR. People who spend more time outdoors and lack protective measures against high DTR might have more DTR-related risks. Third, we could not include the air pollution index in the main analysis, because these data were not available. However, previous studies reported that the effect of DTR on mortality did not substantially differ with and without the air pollution index (Lim et al., 2012). Furthermore, the air quality of Yuxi is very good (e.g., daily mean PM₁₀, NO₂ and SO₂ during 2014 of 51.8, 20.2 and 23.2 µg/m³, respectively) and may not have a negative impact on the health of local people.

Our study may have implications for both the public health policy arena and research domain. Local residents need to strengthen their awareness of high DTR exposure, especially DTR > 16 °C. When the temperature rapidly changes within a single day, ambient corrective actions

need to be implemented, such as the adaptation of houses (e.g., using the air conditioning systems), spending less time outdoors or wearing more clothing when the temperature drops. The implementation of alert systems or health education about impending large temperature changes may reduce the impact of DTR on health.

5. Conclusions

The effect of DTR was non-linear for mortality in Yuxi, a high-altitude area of China, with increases in mortality starting at DTR approximately 16 $^{\circ}$ C. Mortality was particularly affected by extreme high DTR among males and people <75 years old. Our findings may have implications for developing intervention strategies to prevent high DTR exposure.

Conflict of interest statement

As the authors of the manuscript, we declare that there are no conflicts of interest.

Competing financial interests

The authors declare no competing financial interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.scitotenv.2015.05.012.

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