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Developing a novel indicator to estimate years of life lost attributable to temperature variability between neighboring days

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Abstract

The evidence is limited for the mortality burden of temperature variability between neighboring days. This study developed a novel indicator to measure temperature variability between neighboring days and quantify its mortality burden. Daily mortality and meteorological data during 2006–2017 from 364 locations across China were collected. We first employed a distributed lag non-linear model and multivariable meta-analysis to investigate the association between the diurnal temperature range (DTR) with the years of life lost (YLL) rate and the association between the nocturnal temperature range (NTR) with the YLL rate. Then, we calculated the weight temperature variability between neighboring days (weight-TVN) based on the attributable YLL rate of the DTR and NTR. The relationship between the weight-TVN and YLL rate was analyzed, and the attributable fraction (AF) of the YLL and weight-TVN related life loss per death was calculated to quantify the mortality burden. Stratified analyses were conducted by region, season, gender, age group and cause of death. The DTR-YLL rate curve and NTR-YLL rate curve were both J-shaped and a higher YLL rate attributable to DTR was observed than NTR. There was a significant association between the weight-TVN and YLL rate. An estimated AF of the weight-TVN was 6.02% (95%CI: 3.71%–8.33%). The average life loss per death due to weight-TVN was 0.93 year (95%CI: 0.57–1.29). Stratification analyses showed that the AFs of weight-TVN were relatively larger in southern China, in the cold season, in the elderly, females and patients with respiratory illnesses. Although the AF of weight-TVN among the young group (AF = 4.74%, 95%CI: 1.79%–7.69%) was lower than for the elderly (AF = 6.06%, 95%CI: 3.72%–8.41%), weight-TVN related life loss per death among the young population (1.51, 95%CI: 0.57–2.45) was much higher than in the elderly (0.59, 95%CI: 0.36–0.82). A novel indicator to measure temperature variability between neighboring days was developed, and temperature fluctuation between adjacent days significantly increased the mortality burden. Our results indicate that more attention should be paid to short-term temperature fluctuation.

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1. Introduction

Numerous epidemiological studies have demonstrated a significant association between ambient temperature and mortality (Field et al 2014, Watts et al 2017). Most results indicated that temperature-mortality relationships were generally V- or U-shaped, which means both high and low temperatures are associated with increasing mortality risks (Gasparrini et al 2015, Chen et al 2018). In the context of climate change, weather fluctuations such as sharp temperature change were predicted to occur more frequently (Faergeman 2008). An increasing number of researchers also reported that short-term temperature variation such as diurnal temperature change (DTR) and temperature change between neighboring days (TCN) play an independent role in human health (Xu et al 2014, Ikram et al 2015, Liu et al 2015, Cheng et al 2016).

TCN was usually employed as an exposure indicator when assessing the association between inter-day temperature variation and mortality in previous studies (Guo et al 2011, Lin et al 2013, Cheng et al 2014, Zhan et al 2017). TCN is calculated by the difference of mean temperature between adjacent days, and mainly captures large-scale shifts. However, temperature change between adjacent days includes cooling at nighttime and warming at daytime, and inter-day temperature variability (TV) may be captured fully by simultaneously considering the intensity and direction of inter-day temperature fluctuation. For example, if the daily maximum temperature, daily mean temperature and daily minimum temperature on the present day were 36 °C, 30 °C and 24 °C, respectively, and the corresponding temperatures on the previous day were 32 °C, 30 °C and 28 °C, respectively, we will calculate 0 °C of TCN. Actually, the inter-day temperature fluctuation included a 4 °C increase from the minimum to maximum temperature on the previous day, an 8 °C decrease from the maximum temperature on the previous day to the minimum temperature on the present day, and a 12 °C increase from the minimum to maximum temperature on the present day. Therefore, the magnitude and direction of the temperature fluctuation between adjacent days should be included in the measure of inter-day temperature variation.

Recently, a study developed a novel indicator to measure TV by calculating the standard deviation (SD) of daily maximum and minimum temperatures during the exposure days (Guo et al 2016, Yang et al 2018, Ma et al 2019). TV is an indicator that includes both intra-day and inter-day temperature change. A significant association between TV and mortality indicated that the intensity of TV has an impact on health. But temperature fluctuation between neighboring days also includes two directions: cooling or warming. Several studies found that health effects varied with the direction of the temperature change (Ebi et al 2004, Schneider et al 2008, Kakitsuba 2019). For example, it was previously found that the diurnal change in human tympanic temperature and skin temperature was significantly larger in the condition of short-term increasing temperature compared with the condition of short-term decreasing temperature (Kakitsuba 2019). But few studies investigated the effect of inter-day temperature variations considering both the intensity and direction of temperature fluctuation. Thus, we developed a novel indicator (weight-TVN) to measure TV based on the process of temperature change between neighboring days.

In addition, most previous studies used death count as a health outcome, and this indicator cannot provide an ideal representation of the mortality burden attributable to TV because it gives equal weight to every death at different ages. Years of life lost (YLL) is an indicator of premature death. It is recognized as a more precise indicator of mortality burden because it considers both the number of deaths and age at death by assigning higher weights to deaths that occur at younger ages (Hay et al 2017). Moreover, since the size of the YLL largely depended on the population size of study locations, YLLs should be adjusted by population, such as using the YLL rate (i.e. YLL/10^6 population) in order to compare YLLs between different regions.

In this study, we developed a novel indicator (weight-TVN) to scale TV between neighboring days, and examine the association between TV between neighboring days and YLL based on the data from 364 counties or districts in China. We further quantified the mortality burden attributed to TVN by calculating attributable fractions (AFs) and life loss per death. Our findings are helpful to better understand the mechanism of health effects of short-term temperature fluctuation.

2. Material and methods

2.1. Study locations and data collection

The present study included 364 counties or districts covering seven geographical regions around mainland China (figure 1). In order to ensure enough daily death counts for each study point in model fitting, only locations with a population over 200,000 or mortality rates larger than 4% were included. Location-specific daily mortality records from Yunnan, Guangdong, Hunan, Zhejiang and Jilin provinces (from 1 January 2013–31 December 2017) were collected from the corresponding provincial mortality surveillance system and daily death data in other locations (from 1 January 2006–31 December 2011) were collected from China’s disease surveillance points system (DSPs). Provincial mortality surveillance systems are administrated by the corresponding provincial Center for Disease Control and Prevention (CDC) and DSPs are administrated by the Chinese CDC. They recorded all deaths and population counts at the sites.
and yielded a nationally representative annual sample of deaths. According to the 10th Revision of the International Classification of Diseases, (ICD-10), mortality data were classified into the following groups: non-accidental causes (codes: A00-R99), cardiovascular disease (CVD, codes I00-I99) and respiratory disease (RESP, codes J00-J98).

We calculated individual YLLs by matching the age and gender of every death to the life table for the corresponding province. The provincial life table was calculated using a method provided by the WHO (2013) using provincial mortality and demographical data, which were collected from the 2010 Population Census of China. Then, daily YLLs of each location were quantified by summing all individual YLLs on the same day. We stratified the daily YLLs by cause of death (non-accidental causes, CVD or RESP), gender (male or female), age (0–64 or 65+ years old) and region (northern China or southern China, divided by the north-south demarcation zone in China, which was developed based on the geographic information system (GIS) with some quantitative methods) (Zhang et al. 2012). We further computed the YLL rate (per 10^5 population) of each subgroup by dividing the daily YLLs by the population size of the group.

Daily meteorological data from 698 climate stations across China were derived from the China Meteorological Data Sharing Service System (http://data.cma.cn/), including mean temperature (Tm), maximum temperature (Tmax), minimum temperature (Tmin) and relative humidity (RH). The missing rates of daily weather variables were less than 0.01% (0.004% ~ 0.01%), and we imputed the missing values with the mean of values within two days before and after the missing data. We employed the Australian National University Splines (ANUSPLIN), an interpolation package based on the thin plate smoothing spline function, to interpolate the daily Tm grid at 0.01° × 0.01° resolution for all of China from 698 daily weather station observations. Longitude and latitude were taken into account as independent spline variables and elevation was regarded as a covariate. Ten-fold cross-validation was used to confirm the prediction accuracy of the interpolation method for daily Tm [R^2 = 0.96, root mean squared prediction error (RMSE) = 2.37 °C] (figure S1 (available online at stacks.iop.org/ERL/15/105010/mmedia)). We also interpolated the daily RH grid, daily Tmax grid and daily Tmin grid using ANUSPLIN. The result of ten-fold cross-validation shows that the R^2 of the RH, Tmax and Tmin were 0.81, 0.94 and 0.94, respectively (figure S1). Daily meteorological data from all 364 locations were extracted from the corresponding interpolated grid.

was the only ambient air pollutant obtained during the whole study period (2006–2017), so we used it as an agency of air quality. Daily average PM_{10} data during 2006–2017 were obtained from the National Urban Air Quality Real-time Publishing Platform (http://106.37.208.233:20035/), which is administrated by the China National Environmental

![Figure 1. Geographic distribution of 364 Chinese locations in the present study.](image-url)
Monitoring Centre. The missing rate of daily PM\(_{10}\) was 0.01%, and the way of imputing the missing values was the same as for meteorological data. Since an air quality monitoring system cannot cover all the selected locations, we established a random forest model to estimate the daily PM\(_{10}\) at each location using the following predictors: daily Tm, daily RH, daily PM\(_{10}\), latitude, longitude and altitude of each included air quality monitoring station, population density, length of road, types of land use and GDP per capita at each monitoring station using a radius of 1300 m (Liu et al 2019a, 2019b). One smooth temporal basis function was also included in the model to control the long-term and seasonal trend of PM\(_{10}\) concentrations. The result of ten-fold cross-validation for the model showed that the R\(^2\) was 0.78 and RMSE was 13.2 µg m\(^{-3}\) (figure S1). The population density data in 2015 were obtained from the GeoData Institute of the University of Southampton (www.worldpop.org.uk), and the GIS data (geographic map, road density, land use data and GDP per capita) were obtained from the Data Center for Resources and Environmental Sciences (www.resdc.cn).

### 2.2. Calculation of weight-TV between neighboring days

TV between neighboring days includes the warming process from nighttime to daytime and cooling process from daytime to nighttime. We calculated the indicators based on the diurnal temperature range (DTR, calculated as the subtraction of Tmin from Tmax) and nocturnal temperature range (NTR, calculated as the subtraction of the present day Tmin from the previous day Tmax). We first separately fitted the DTR-YLL rate association and NTR-YLL rate association using a two-stage analytic approach. The attributable YLL rates of DTR and NTR derived from the DTR-YLL rate or NTR-YLL rate associations were utilized as corresponding weights to calculate the weight-TV between neighboring days (weight-TVN).

#### 2.2.1. Two-stage analytic approach to model DTR-YLL or NTR-YLL associations.

DTR-YLL rate or NTR-YLL rate associations were estimated by a two-stage analytic approach. In the first stage, we applied a distributed lag non-linear model (DLNM) incorporated with a Gaussian distribution function to estimate the location-specific associations of DTR or NTR with the YLL rate. The DLNM models were described as follows (Gasparrini et al 2010).

\[
E(Y_t) = \alpha + cb(DTR_t, NTR_t, lag) + cb(Tm_t, lag) + ns(RH_t, df) + ns(time_t, df) + \beta_1 DOW_t + \beta_2 PM_{10}t.
\]

Cross-basis function (cb) was employed to estimate the non-linear and lagged effects of exposure, in which a quadratic B-spline with three knots (10th, 50th, 90th) of location-specific exposure distributions, and a natural cubic B-spline with an intercept and three internal knots were placed at equally spaced values in the log scale with the maximum lag up to 21 d (Gasparrini et al 2015, Chen et al 2018). Cross-basis functions of Tm and cross-basis function of DTR or NTR were both introduced into the DLNM model. RH and time trends were controlled for using natural cubic spline (ns) with three degrees of freedom (df) for RH and 8df per year for the time trend. The values of the df were chosen by the Akaike Information Criterion. A categorical variable was used to control the confounding effect of day of the week.

In the second stage, we employed a multivariate meta-analysis method with random effects models to pool the location-specific associations obtained from the first stage. We respectively referred the DTR and NTR corresponding to the minimum YLL rate as optimal values, and deemed them the reference for calculating an attributable YLL rate. The attributable YLL rate of DTR and NTR was used to calculate the weight-TVN.

#### 2.2.2. Calculation of weight-TVN.

TV between neighboring days (48 h) includes DTR and NTR at the previous day, and DTR and NTR at the present day. Attributable YLLs caused by DTR and NTR were used as weights to calculate the weight-TVN.

\[
TVN = \frac{YLL_{DTR} + YLL_{NTR} + DTR_{pre} \times YLL_{DTRpre} + NTR_{pre} \times YLL_{NTRpre}}{YLL_{DTR} + YLL_{NTR} + YLL_{DTRpre} + YLL_{NTRpre}},
\]

where \(YLL_{DTR}\) and \(YLL_{NTR}\), respectively, denote attributable YLL corresponding to DTR and NTR in the present day; \(DTR_{pre}\) and \(NTR_{pre}\), respectively, denote DTR and NTR in the previous day; \(YLL_{DTRpre}\) and \(YLL_{NTRpre}\), respectively, denote attributable YLL corresponding to DTR and NTR in the previous day.

We calculated the weight-TVN stratified by region (northern China and southern China), gender, age group (≥65 years old, 0–64 years old), causes of death (non-accidental causes, CVD or RESP) and season (May to October for the warm season, remainder of the year for the cold season). In the stratification analyses by season, we used a natural cubic spline with 5 df per year for time in the DLNM model.

### 2.3. Mortality burden of weight-TVN

The two-stage analytic approach abovementioned was employed to investigate the association of weight-TVN and YLL rate. In the first stage, the DLNM model was applied to estimate location-specific associations between weight-TVN and YLL rate. Cross-basis function of weight-TVN and cross-basis function of temperature were both included in the
Table 1. Summary of the daily YLL rate and meteorological factors across 364 locations in China.

|                              | Mean ± SD | Minimum | P25  | P50  | P75  | Maximum |
|------------------------------|-----------|---------|------|------|------|---------|
| YLL rate (/10^5 population)  | Nationwide| 23.6 ± 16.0 | 0.0  | 13.2 | 21.3 | 31.0    | 969.9   |
|                              | Northern China| 23.8 ± 21.1 | 0.0  | 11.2 | 20.5 | 31.9    | 774.7   |
|                              | Southern China| 23.5 ± 14.5 | 0.0  | 13.6 | 21.5 | 30.8    | 969.3   |
|                              | Warm season  | 22.2 ± 15.3 | 0.0  | 12.4 | 20.1 | 29.3    | 720.3   |
|                              | Cold season  | 24.9 ± 16.6 | 0.0  | 14.2 | 22.6 | 32.7    | 969.9   |
| Age 0–64                     | 14.2 ± 14.8 | 0.0    | 13.2 | 21.3 | 30.8 | 969.9   |
| Age 65+                      | 107.5 ± 74.7| 0.0   | 59.8 | 97.1 | 142.1| 3030.2  |
| Males                        | 27.7 ± 2.8  | 0.0   | 17.2 | 23.9 | 37.8 | 1907.5  |
| Females                      | 19.2 ± 19.2 | 0.0   | 6.9  | 15.4 | 26.7 | 1430.0  |
| CVD                          | 8.3 ± 8.2   | 0.0   | 2.8  | 6.5  | 8.3  | 379.2   |
| RESP                         | 2.4 ± 4.2   | 0.0   | 0.0  | 1.2  | 3.4  | 595.4   |
| Mean temperature (°C)        | 15.9 ± 9.9  | −32.3 | 9.5  | 17.5 | 23.4 | 35.6    |
| Relative humidity (%)        | 72.8 ± 14.1 | 6.0   | 65.0 | 75.0 | 83.0 | 100.0   |

DTR (°C)                      Nationwide| 8.8 ± 3.9 | 0.0   | 5.8  | 8.5  | 11.2 | 28.1    |
|                              | Northern China| 11.4 ± 4.1 | 0.0  | 8.4  | 11.2 | 14.3   | 28.1    |
|                              | Southern China| 8.2 ± 3.6  | 0.0  | 5.4  | 7.9  | 10.5   | 24.6    |
|                              | Warm season   | 8.5 ± 3.4  | 0.0  | 6.2  | 8.3  | 10.4   | 26.6    |
|                              | Cold season   | 9.0 ± 4.0  | 0.0  | 5.4  | 8.8  | 12.3   | 28.1    |
| NTR (°C)                     Nationwide| 8.8 ± 3.7 | −3.8   | 6.1  | 8.6  | 11.2 | 29.1    |
|                              | Northern China| 11.4 ± 3.7 | −3.8 | 8.8  | 11.4 | 14.0   | 29.1    |
|                              | Southern China| 8.2 ± 3.5  | −3.5 | 5.7  | 8.1  | 10.4   | 26.1    |
|                              | Warm season   | 8.5 ± 3.2  | −1.8 | 6.4  | 8.4  | 10.5   | 27.2    |
|                              | Cold season   | 9.0 ± 4.2  | −3.8 | 5.8  | 8.9  | 12.0   | 29.1    |

Note: YLL rate: years of life lost per 10^5 population; CVD: cardiovascular diseases; RESP: respiratory diseases; DTR: diurnal temperature range; NTR: nocturnal temperature range; SD: standard deviation.

DLNM model (lags to 21 d), with a natural cubic spline control for long-term trend (8 df per year), a natural cubic B-spline function of RH (3 df) and a categorical variable of day of the week. In the second stage, multivariate meta-analysis with random effects models was employed to pool the location-specific associations of weight-TVN and temperature with YLL rate. The MYTVN (weight-TVN corresponding to minimum YLL rate) and MYT (temperature corresponding to minimum YLL rate) was re-centered based on the location-specific MYTVN and MYT identified in the first stage and were defined as the optimal weight-TVN and temperature.

To quantify the mortality burden of non-optimal weight-TVN and its component, we further calculated AFs of weight-TVN and mean life loss per death attributable to weight-TVN. We first estimated the location-specific daily YLLs attributable to non-optimal weight-TVN by calculating the product of population size in each location and cumulative YLL rate of daily weight-TVN devised from curves of weight-TVN and YLL rate. The ratio of the total daily YLL attributable to non-optimal weight-TVN and total daily YLL provided AF of weight-TVN and the ratio of total daily YLL attributable to non-optimal weight-TVN and total daily death provided the mean life loss per death attributable to weight-TVN. A 95% confidence interval (95% CI) of AF and weight-TVN related YLLs per death were calculated using 95% CI of attributable YLLs for weight-TVN.

We also calculated AF of non-optimal temperature and its component based on the cumulative associations of temperature and YLL rate. We divided the non-optimal temperature into four components, including extremely cold, moderately cold, moderately hot, and extremely hot, defined as the ≤2.5th percentile, 2.5th percentile to the MYT, MYT to the 97.5th percentile and ≥97.5th percentile of temperature, respectively.

R software version 3.6.0 was used to perform data analysis, with the ‘dlnm’ package for fitting the DLNM model, and the ‘mvmeta’ package for multivariate meta-analysis.

2.4. Sensitivity analyses
Sensitivity analyses were performed on the parameters for the community-specific model of the weight-TVN and YLL rate to test the robustness of our results. We changed the maximum lag periods to 14 and 28 d, and modified the df of time from 6 to 8 per year to fit the models.

We also estimated the association of the TV with YLL rate using the same two-stage analytic approach abovementioned. The TV was calculated by the SD of the Tmax and Tmin during the preceding two days.
3. Results

3.1. Descriptive statistics
The general characteristics of the YLL rate and meteorological factors in the 364 locations are shown in Table 1. The average daily YLL rate was 23.6 years per 100,000. Geographically, the average daily YLL rate in northern China (23.8) was slightly higher than that in southern China (23.5). Compared with the warm season (22.2), a higher average daily YLL rate was observed in the cold season (24.4) and warm season (24.3) in northern China. Similarly, in southern China, the average daily YLL rate in the cold season (23.7) was higher than that in the warm season (22.5).
Table 2. Summary of daily weight-TVN by region, gender, age and cause of death.

| Region            | Mean ± SD | Minimum | P25  | P50  | P75  | Maximum |
|-------------------|-----------|---------|------|------|------|---------|
| Nationwide        | 9.2 ± 3.3 | −1.0    | 7.2  | 9.0  | 11.1 | 26.5    |
| Northern China    | 12.0 ± 3.9| −0.1    | 9.9  | 12.7 | 14.5 | 26.5    |
| Southern China    | 8.6 ± 3.0 | −1.1    | 6.8  | 8.5  | 10.3 | 23.4    |
| Warm season       | 8.8 ± 3.1 | −0.8    | 6.8  | 8.4  | 10.4 | 24.2    |
| Cold season       | 9.7 ± 3.8 | −1.4    | 7.2  | 9.7  | 12.3 | 26.5    |
| Age 0–64          | 9.1 ± 3.2 | −0.8    | 7.1  | 9.0  | 11.0 | 26.5    |
| Age 65+           | 9.2 ± 3.4 | −1.3    | 7.1  | 8.9  | 11.1 | 26.5    |
| Males             | 9.1 ± 3.2 | −1.4    | 7.1  | 8.9  | 11.0 | 26.5    |
| Females           | 9.2 ± 3.4 | −0.9    | 7.2  | 9.2  | 11.3 | 26.5    |
| CVD               | 9.2 ± 3.4 | −1.4    | 7.2  | 9.1  | 11.2 | 26.5    |
| RESP              | 9.3 ± 3.3 | −1.6    | 7.3  | 9.2  | 11.2 | 26.5    |

Note: CVD: cardiovascular diseases; RESP: respiratory diseases; SD: standard deviation.

found in the cold season (24.9). The daily means of the Tm and RH were respectively 15.9 °C and 72.8%. The average daily DTR and NTR nationwide during the study period were both 8.8 °C, and higher DTR and NTR were observed in northern China and in the cold season.

3.2. TV between neighboring days
The exposure-response associations between DTR or NTR were both ‘J’ shaped (figure 2). The attributable YLL rates of DTR were significantly higher than NTR for most groups except for the young population (0–64 years old). The attributable YLL rate of DTR and NTR in southern China was generally higher than that in northern China. Compared with the warm season, a higher effect of DTR and NTR was found in the cold season.

The mean daily weight-TVN was 9.2 °C nationwide. A higher weight-TVN was observed in northern China and in the cold season (12.0 °C and 9.7 °C), compared with southern China and in the warm season (8.6 °C and 8.8 °C). The weight-TVNs among other subgroups are presented in table 2. Average correlations between DTR, NTR, weight-TVN and other weather factors are shown in table S1. Average Pearson correlations between DTR and NTR with weight-TVN were 0.86 and 0.87, respectively.

3.3. Exposure-response association of weight-TVN and YLL rate
The cumulative exposure-response associations between weight-TVN and YLL rates were also J-shaped, with an MYTVN of 4.2 °C nationwide. We found a more significant effect of weight-TVN in southern China with MYTVN of 3.7 °C, compared with the effect of weight-TVN in northern China with MYTVN of 10.4 °C. Generally, the YLL rate attributable to weight-TVN was greater in the cold season than that in the warm season. A higher effect of weight-TVN was observed in the elderly (⩾65 years old) and CVD, compared with young populations (0–64 years old) and RESP, respectively (figure 3).

3.4. Mortality burden attributable to weight-TVN
Estimated AFs associated with non-optimal weight-TVN are shown in table 3. The total AF of YLLs caused by weight-TVN was 6.02% (95%CI: 3.71%–8.33%), most of which was from high weight-TVN (AF = 5.82%, 95%CI: 3.61%–8.61%). The AF of weight-TVN in southern China was 6.64% (95%CI: 3.92%–9.35%), while it was not statistically significant in northern China. The AF in the cold season was 10.31% (95%CI: 6.42%–14.19%), while AF was not significant in the warm season. A higher AF of weight-TVN for the elderly (⩾65 years old), female and RESP was observed, compared with the young, male and CVD, respectively.

An average of 0.93 (95%CI: 0.57–1.29) year life loss per death resulted from weight-TVN nationwide, in which 0.90 (95%CI: 0.56–1.24) year was from high weight-TVN. The mean life loss per death attributable to weight-TVN in southern China and in the cold season was 1.01 (95%CI: 0.60–1.42) years and 1.19 (95%CI: 0.70–1.68) years, respectively, but life loss per death attributable to weight-TVN in northern China and in the warm season was not significant. The weight-TVN related life loss per death was 1.51 (95%CI: 0.57–2.45) for the young population, much higher than that for the elderly (YLL = 0.59, 95%CI: 0.36–0.82). Higher weight-TVN related life loss per death was observed for males and RESP, compared with females and CVD respectively.

3.5. Sensitivity analyses
Sensitivity analyses showed that the cumulative associations of weight-TVN with YLL rates were relatively stable to the changes of maximum lag days and df for the long-term trends (figure S2).

TV-YLL rate associations were also J shaped and were relatively similar to weight-TVN and YLL rate associations, which indicated that weight-TVN is a reliable metric of TV (figure S3).
4. Discussion

The present study developed a novel indicator to measure TV between neighboring days. Through analyzing a large time-series data set including 364 locations in China, we found that weight-TVN was associated with an increase in mortality burden. To the best of our knowledge, this is the first study to simultaneously consider the intensity and direction of temperature fluctuation to estimate the life loss per death attributed to temperature fluctuation between adjacent days.

Previous studies, using TCN as the indicator of TV between neighboring days, found that positive TCN elevated mortality risk while negative TCN reduced mortality risk, especially in the cold season (Lin et al. 2013, Cheng et al. 2014, Zhan et al. 2017). The physiological mechanism is hard to explain why temperature decrease from the previous day was associated with reduced mortality because the human automatic thermoregulation system cannot fully adapt to sudden temperature change, irrespective of whether it is positive or negative (Garrett et al. 2009, Halonen et al. 2011a, 2011b; Martinez-Nicolas et al. 2015). Moreover, TCN is an indicator calculated by the difference of Tmb between adjacent days and does not consider the temperature change between daytime and nighttime. Substantial evidence

Figure 3. Overall cumulative associations of weight-TVN and YLL rate along lag 0–21 d with 95% CI.
YLL rate: years of life lost per 10^5 population; CVD: cardiovascular diseases; RESP: respiratory diseases.
has shown that DTR plays an independent role in mortality (Ding et al 2015, Lim et al 2015, Lee et al 2018). The present study also found that both DTR and NTR were associated with an increase in the YLL rate. Thus, the impact of TV between neighboring days on health was fully captured by taking into account the temperature fluctuation between daytime and nighttime (DTR and NTR).

Several studies used daily TV or hourly TV to characterize both intra- and inter-day TV, and found that TV was a risk factor of mortality (Guo et al 2016, Zhang et al 2017a, 2018, Hu et al 2019b). However, TV is calculated by the SD of daily Tmax and daily Tmin or hourly temperature records during exposure days, ignoring the direction of temperature change. Previous study analyzed the association between temperature changes (defined as at least 3 °C decrease in Tmax or 3 °C increase in Tmin) and cardiovascular and stroke morbidity in three Californian regions, and found the magnitude of increase in morbidity was different for temperature increase and temperature decrease (Ebi et al 2004). Another study analyzed the influence of weather on blood pressure, arrhythmia and ischemia, and found the change in heart function was associated with the direction of temperature (Schneider et al 2008). The present study also found that the magnitude of increase in the YLL rate caused by DTR (process of increasing temperature) was different compared with NTR (process of decreasing temperature), which suggested that the effect of temperature change not only depends on the intensity, but the direction of TV. Thus, this study explored a novel indicator to calculate TV between neighboring days based on the effects of both DTR and NTR.

We observed that weight-TVN was associated with a significant increase in the YLL rate, which is generally in line with those previous studies using TV as an indicator of TV between adjacent days. Previous studies show that mortality risks related to short-term (0–1 d) TV were higher in warm regions than that in cold regions (Guo et al 2016, Lee et al 2018), consistent with the finding in the present study that attributable YLL rates of weight-TVN were greater in southern China than in northern China. This spatial heterogeneity may be from adaptation capacities to local climate, as well as socio-economic and healthcare characteristics (Nielsen et al 1993, Odhiambo Sewe et al 2018, Hu et al 2019a).

We estimated that 6.02% YLLs are attributable to weight-TVN, most of which are from high weight-TVN (5.82%), which was higher compared with AF of TV (4.11%) estimated in the present study (table S1). The possible reason is that weight-TVN considered both the effect of intensity and direction of TV compared with TV. Our findings were comparable with AF (5.33%) of TV estimated in Zhejiang, China (Hu et al 2019b). We also estimated AF of non-optimal temperature to be 8.27% (table S1). Although AF of weight-TVN was lower than non-optimal temperatures, it was still several times greater than extreme cold (AF = 0.77%) and extreme heat (AF = 0.17%). Our results highlight an urgent need for the public health authorities to pay enough attention to TV. For example, developing an early warning system, and risk communication and community involvement were suggested to inform the governments and the public, especially vulnerable sectors of the population such as the elderly and people with chronic diseases, about the impending sharp temperature change, and to have necessary adaption policies to reduce the health impact of short-term TV in time.

Some studies also reported that there is seasonal variation of associations between TV and mortality, in spite of less consistent evidence observed in different studies. Stronger TV-mortality associations in the warm season were observed in Hubei, China, and a higher mortality burden of TV in the warm season was estimated in England (Zhang et al 2017b, 2018), whereas several other studies found that a greater health impact associated with TV was observed in the cold season (Cheng et al 2014, Zhou et al 2014). In the present study, we found a significantly higher mortality burden attributable to weight-TVN in the cold season. A previous multi-country analysis reported inconsistent season patterns of TV-mortality association in different countries (Guo et al 2016). One possible reason for the difference is that indicators used to measure TV were inconsistent in various investigations. Moreover, various geographic and socio-economic conditions in different regions may result in the different season pattern of health effect caused by TV.

We first estimated life loss per death due to weight-TVN stratified by region, season, gender, age and cause of death in order to describe the mortality burden of weight-TVN presented by each death. It is a more informative indicator for policy authorities to understand the health impact of weight-TVN and tailor preventive actions, targeting high-risk populations (Majdan et al 2017). An average of 0.93 (95%CI: 0.57–1.29) year life loss was associated with weight-TVN per death. The difference of weight-TVN related year life loss per death between males and females was small. We found higher weight-TVN related year life loss per death for RESP compared with CVD, respectively, which was generally coherent with previous studies, which observed a higher mortality effect of TV among RESP (Wang et al 2013, Zhou et al 2014, Hu et al 2019b). Most likely, sudden temperature changes may result in pathophysiological responses of the respiratory epithelium at a tissue level, causing bronchospasms and inflammatory changes (D’Amato et al 2018). Substantial evidence has demonstrated that the elderly were more vulnerable to TV. We also found a higher mortality burden of weight-TVN (AF = 6.58%) for the elderly individuals.
### Table 3. MYTVN, AFs attributable to weight-TVN and mean life loss attributable to weight-TVN per death at the national level and in different subgroups.

| Group              | MYTVN (°C, MYP (%)) | AF (%; 95%CI) of TVN | Life loss (years; 95%CI) caused by TVN |
|--------------------|----------------------|-----------------------|---------------------------------------|
|                    |                      | Total | Low weight-TVN | High weight-TVN | Total | Low weight-TVN | High weight-TVN |
| Nationwide         | 4.2 (7.1)            | 6.02 (3.71,8.33)     | 0.20 (0.10,0.31) | 5.82 (3.61,8.02) | 0.93 (0.57,1.29) | 0.03 (0.02,0.05) | 0.90 (0.56,1.24) |
| Northern China     | 10.4 (27.6)          | 1.09 (−3.15,5.34)    | 0.52 (−0.94,1.98) | 0.57 (−2.21,3.35) | 0.18 (−0.53,0.89) | 0.09 (−0.16,0.33) | 0.10 (−0.37,0.56) |
| Southern China     | 3.7 (5.0)            | 6.64 (3.92,9.35)     | 0.12 (0.05,0.19) | 6.52 (3.88,9.16) | 1.01 (0.60,1.42) | 0.02 (0.01,0.03) | 0.99 (0.59,1.40) |
| Warm season        | 4.7 (7.2)            | 2.44 (−1.05,5.94)    | 0.13 (0.00,0.27) | 2.31 (−1.05,5.67) | 0.39 (−0.17,0.94) | 0.02 (0.00,0.04) | 0.37 (−0.17,0.90) |
| Cold season        | 4.4 (10.4)           | 7.89 (4.64,11.13)    | 0.48 (0.25,0.71) | 7.41 (4.40,10.42) | 1.19 (0.70,1.68) | 0.07 (0.04,0.11) | 1.11 (0.66,1.57) |
| Age 0-64           | 4.1 (6.8)            | 4.74 (1.79,7.69)     | 0.13 (0.00,0.25) | 4.61 (1.78,7.43) | 1.51 (0.57,2.45) | 0.04 (0.00,0.08) | 1.47 (0.57,2.37) |
| Age 65+            | 4.3 (6.8)            | 6.06 (3.72,8.41)     | 0.24 (0.13,0.34) | 5.83 (3.59,8.07) | 0.59 (0.36,0.82) | 0.01 (0.01,0.03) | 0.57 (0.35,0.79) |
| Males              | 3.9 (5.1)            | 5.94 (3.16,8.73)     | 0.11 (0.03,0.19) | 5.83 (3.13,8.54) | 0.95 (0.50,1.39) | 0.02 (0.00,0.03) | 0.93 (0.50,1.36) |
| Females            | 4.3 (8.8)            | 6.26 (3.44,9.08)     | 0.32 (0.14,0.50) | 5.95 (3.31,8.59) | 0.92 (0.50,1.33) | 0.05 (0.02,0.07) | 0.87 (0.48,1.26) |
| CVD                | 4.2 (8.0)            | 5.98 (3.26,8.71)     | 0.28 (0.15,0.40) | 5.71 (3.11,8.31) | 0.77 (0.42,1.12) | 0.04 (0.02,0.05) | 0.74 (0.40,1.07) |
| RESP               | 4.4 (7.6)            | 8.40 (4.21,12.59)    | 0.31 (0.10,0.51) | 8.09 (4.11,12.07) | 0.90 (0.45,1.35) | 0.03 (0.01,0.06) | 0.87 (0.44,1.30) |

Note: MYTVN: minimum YLL rate TVN; MYP: minimum YLL rate percentile of the TVN; CVD: cardiovascular diseases; RESP: respiratory diseases
than the young group (AF = 6.31%), but the weight-TVN related year life loss per death was higher among the young. The possible mechanism of higher mortality burden (AF) of weight-TVN for the elderly was related to a higher vulnerability to sudden temperature change for the older population, while greater YLL per death for the young was explained by early premature death when young people died. Our result indicated that though death among the young was relatively rare, the mortality burden of weight-TVN for each young death was much higher than the elderly. Thus, necessary adaption strategies for the young population should also be taken to mitigate the health impact of short-term temperature change.

Several limitations of the novel indicators should be acknowledged. First, the novel indicator we developed is not a purely meteorological measure. It was calculated based on the DTR-YLL rate and NTR-YLL rate relationships as weighting factors. The complex calculation is difficult to understand for the public. Second, since weight-TVN considers shorter-term temperature fluctuations such as DTR and NTR, it requires a more accurate exposure. For example, temperature exposure at night for a nine-to-five worker was more indoor temperature rather than atmospheric temperature. However, we used district-wide TV to measure individual exposure, which may induce exposure measurement errors. A limitation of the study is that periods in all locations were inconsistent due to the unavailability of death data. However, a study conducted in Shanghai indicated that the effect of ambient temperature on mortality did not substantially change during 2001–2012 (Yang et al 2015).

5. Conclusion

The present study developed a novel indicator to measure the TV between neighboring days. Our results showed that weight-TVN is associated with an increased mortality burden, especially in southern China and in the cold season. Although the total mortality burden of weight-TVN among the young population is smaller than in the elderly, weight-TVN related life loss per death for the young population is much higher than the elderly. These findings may have important implications for developing adaptation measures to reduce the health consequence of unstable weather conditions.

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Conflict of interest

The authors declare no conflict of interest.

Data available statement

Meteorological data can be accessed from the China Meteorological Data Sharing Service System (http://data.cma.cn/). The mortality data of this study are available from the corresponding author (mawj@gdiph.org.cn), upon reasonable request. The data are not publicly available because the information could compromise personal privacy.

Ethics approval

The study was approved by the Ethics Committee of Guangdong Provincial Center for Disease Control and Prevention (2019 025).

Author contributions

WM set up the collaborative network, designed the study and revised the manuscript. SC, JH and WG performed the statistical analysis and took the lead in drafting the manuscript and interpreting the results. MZ, MY, CZ, YX (Yize Xiao), BH, YX (Yanjun Xu), TL, JH, XX, LL, RH, ZH, JL, DJ, MQ, QZ, PY, YX, JX, WZ, XL, LG, YZ and CH collected and cleaned the data, and contributed to the interpretation of the results and preparation of the submitted version of the manuscript.

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