Letter to the Editor

Mortality Risk Attributed to Ambient Temperature in Nanjing, China*

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We examined the attributed fractions of all-cause, cardiovascular, and respiratory mortality that were attributed to extreme and moderate cold and heat during 2010-2016 in Nanjing. Our results showed that 12.81%, 19.78%, and 25.33% of all-cause, cardiovascular, and respiratory mortalities, respectively, were attributed to temperature. The highest attributed fractions for three types of mortality were at 4 °C and the attributed fractions were high around 4 °C, which falls within the moderate cold temperatures. Although moderate cold has lower RR than extreme cold, it occurred on more days than did extreme cold. Therefore, health burden caused by moderate cold requires further attention in the future.

Key words: Temperature; Mortality; Attributed fractions; Moderate cold

Previous studies have revealed that the association between temperature and morbidity/mortality varied greatly by weather conditions, geographical regions, socioeconomic status, and demographic characteristics[1]. Most temperature-related morbidity/mortality studies, however, were conducted in developed countries[2,3]. China has complex climate conditions over a large variety of terrestrial landscapes. Research on temperature-related mortality in different areas is lacking. In Nanjing, which is the capital of Jiangsu Province, the details of the association between temperature and mortality remain underexplored.

Based on data collected in Nanjing, we aimed to quantify the all-cause, cardiovascular, and respiratory mortality burden attributed to non-optimal ambient temperature, and the relative contributions of hot and cold temperatures. In addition, we aimed to further refine the temperature effects on three types of mortality through temperature stratification, including extreme and moderate cold and heat, with per 1 °C increments.

Daily hospital death data were collected from the Chinese Centers for Disease Control and Prevention (CDC) from January 1, 2010 to December 31, 2016. The cases were extracted and coded according to the International Classification of Diseases, tenth revision (ICD-10) for all (ICD10: A00-R99), respiratory (ICD10: J00-J99), and cardiovascular (ICD10: I00-I99) diseases. Daily meteorological data for the same time period were collected from the China Meteorological Data sharing Service System (http://data.cma.cn/). Weather variables included daily average temperature (°C), daily relative humidity (%), and daily average wind speed (m/s).

In recent years, distributed lag non-linear models (DLNMs)[4] have become powerful and popular epidemiological models to investigate the health effects of ambient temperature or air pollution. DLNM is a modeling framework, which combines a conventional exposure-response function and a lag-response function into a cross-basis function. Thus, it is able to simultaneously describe both nonlinear dependencies and lagged effects[4]. Based on the advantage of DLNMs, a quasi-Poisson regression with DLNM was adopted to investigate non-linear and lag effects of temperature on morality in Nanjing, China. The Poisson regression model is the following:

$$Log[E(Y_t|x)] = \beta Temp_{t,l} + ns(Time, 6 \times 7) + ns(Wind_t, 3) + ns(RH_t, 3) + DOW_t + Holiday_t + \alpha \quad (1)$$

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Where t is the day of the observation; $E(Y_t|x)$ denotes the estimated daily death counts on day t; $\beta Temp_{t,l}$ refers to the cross-basis matrix produced by DLNMs to model non-linear and distributed lag effects of ambient temperature over the current day (lag 0) to lag l days, and β denotes a vector of coefficients for $Temp_{t,l}$. Based on previous studies[5], a maximum lag of 21 days was chosen for the delayed effect of temperature change on mortality. Akaike's Information Criterion for quasi-Poisson (Q-AIC) is used to choose *df* for temperature and lags. ns( ) is a natural cubic spline of time with 7 degrees of freedom (*df*) per year to control for the long-term trends and seasonality. Natural cubic splines with 3 *df* for the current day's mean wind speed and relative humidity; day of the week (DOW) and public holidays (Holiday) were treated as dummy variables; α is the intercept.

The minimum mortality temperature (MMT) is considered as the optimum temperature with the lowest risk of mortality. The attributed numbers (ANs) caused by non-optimal temperatures is the sum of deaths during the current day and the next 21 days. The attributed fractions (AFs) is calculated by the ratio of ANs to the total deaths. The components caused by cold and hot temperatures are computed by summing the subsets corresponding to days with temperatures lower or higher than the MMT, respectively. In this study, the AFs and ANs of all-cause, cardiovascular, and respiratory mortalities that are attributed to cold and hot temperatures (i.e., temperatures below and above the MMT) were calculated. In addition, temperature is classified into extremely and moderately cold and hot by using three cut-off knots, including the 2.5th temperature percentile, the MMT, and the 97.5th temperature percentile. The AFs of three types of mortality caused by different temperature intervals was calculated. To further refine temperature effects on mortality, temperature was stratified per 1 °C and the AFs of each category was calculated. All analyses were performed with the software R (V3.4.4). The 'dlnm' package was used to fit the distributed lag non-linear model.

A total of 383,674 death cases were recorded during the study period, of which 37,517 and 163,509 deaths were due to respiratory and cardiovascular diseases, thus accounting for 9.78% and 42.62%, respectively, of all deaths (Table 1). The number of daily deaths had a significant fluctuation ranging from 81.0 to 277.0 cases. The daily average temperature was 16.6 °C. In addition, considerable variations were found in daily relative humidity (17.0%-99.0%) and daily average wind speed (0.2-8.9 m/s), reflecting the sub-tropical continental monsoon climate of Nanjing.

Figure 1 shows the overall cumulative exposure-response curves for three types of mortality, interpreted as RR cumulated over the entire lag period of 0-21 days. The diagrams showed that all temperature-mortality relationships were characterized by a J-shaped curve, indicating an increase in RR for both cold and hot temperatures. The risk increases almost linearly at low temperatures but shows steep non-linear increase at high temperatures. Statistics revealed (Table 2) that 12.81%, 19.78%, and 25.33% of all-cause, cardiovascular, and respiratory mortality, corresponding to 49,148, 32,342, and 9,503 deaths, were due to temperature. Cold temperature accounted for most of the death burden, showing 11.08%, 16.42%, and 21.96% of all-cause, cardiovascular, and respiratory mortality, corresponding to 42,511, 26,848, and 8,239 deaths, respectively. However, the death burden due to hot temperature was comparatively smaller, showing

Table 1. Descriptive Statistics on Death Numbers and Meteorological Variables in Nanjing, China (2010-2016)

Characteristics	Mean ± SD	Min	2.5th	50th	97.5th	Max
Specific-diseases						
All-cause	151.9 ± 25.4	81.0	111.0	149.0	210.0	277.0
Respiratory	14.9 ± 6.2	3.0	5.0	14.0	29.0	46.0
Cardiovascular	64.7 ± 15.8	26.0	41.0	62.0	101.0	149.0
Meteorological variables						
Mean T (°C)	16.6 ± 9.3	-6.7	-0.1	17.8	31.8	34.6
Wind (m/s)	2.8 ± 1.1	0.2	1.1	2.6	5.4	8.9
RH (%)	70.4 ± 1.4	17.0	41.0	71.0	94.0	99.0

Note. SD: standard deviation; T: temperature; RH: relative humidity; 2.5th, 50th, and 97.5th are the 2.5th, 50th, and 97.5th temperature percentile of daily average temperature, respectively.

1.73%, 3.35%, and 3.37% of all-cause, cardiovascular, and respiratory mortality, corresponding to 6,637, 5,494, and 1,264 deaths, respectively. Histograms show that most daily mean temperatures were below MMT. Temperature distributions emphasize that the cold temperature, although characterized by comparatively low RR, persists for more days than high temperature.

The attributed components were separated in extreme and moderate heat and cold by cut-off points, including the 2.5^{th} temperature percentile, the MMT, and the 97.5^{th} temperature percentile. The AFs of all-cause, cardiovascular, and respiratory mortality due to moderate cold were 10.12%, 14.77%, and 20.14%, respectively (Table 2). Moderate cold is responsible for most of the temperature-related death burden.These results were mainly caused by the high MMT and most of the mean daily temperatures fall within the range of moderate cold.

In order to further refine the temperature effects on the three types of mortality, temperature was stratified by 1 °C and the AFs for each category were calculated. Figure 2 depicts that the highest Afs

Table 2. Attributed Fractions (AFs) by Cause-specific Diseases Computed as Total and as Separated Components for Extreme and Moderate Cold and Heat, with 95% Empirical Confidence Intervals (*CI*)

Items	Attributed Mortality Fractions AFs (%, 95% empirical *CI*)		
	All-cause	Cardiovascular	Respiratory
Overall	12.81 (6.76, 18.86)	19.78 (12.32, 27.24)	25.33 (10.09, 40.57)
Cold	11.08 (4.47, 17.69)	16.42 (9.01, 23.83)	21.96 (8.30, 35.62)
Heat	1.73 (1.19, 2.27)	3.35 (2.64, 4.06)	3.37 (2.20, 4.54)
Extreme cold	0.96 (0.53, 1.39)	1.65 (1.21,2.09)	1.83 (0.75, 2.90)
Moderate cold	10.12 (3.74, 16.50)	14.77 (7.53, 22.01)	20.14 (6.44, 33.84)
Moderate heat	1.02 (0.63, 1.42)	2.01 (1.52, 2.49)	2.13 (1.20, 3.06)
Extreme heat	0.71 (0.54, 0.89)	1.35 (1.18, 1.52)	1.24 (1.01, 1.47)

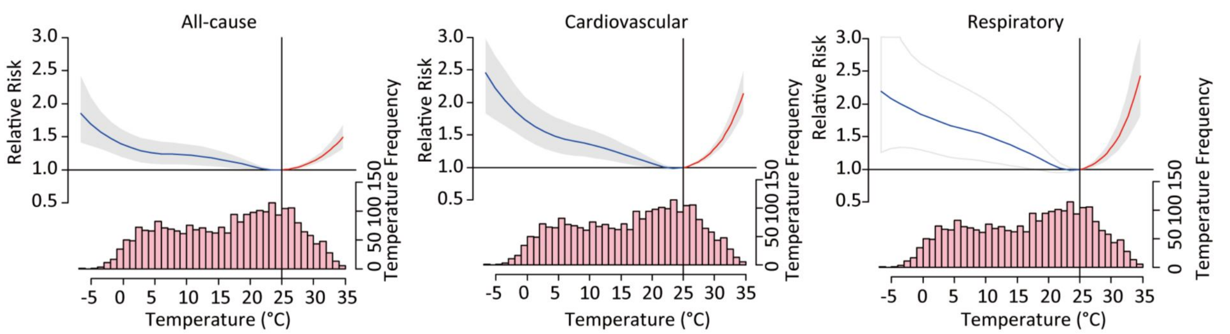

Figure 1. Overall cumulative exposure-response associations for three types of mortality in Nanjing, China, with histograms of the frequency of daily average temperature. Exposure-response relationships were evaluated as the best linear unbiased prediction [with 95% confidence interval (*CI*), shaded gray], with histograms of the frequency of daily temperature. Vertical solid lines represent city-specific minimum mortality temperatures.

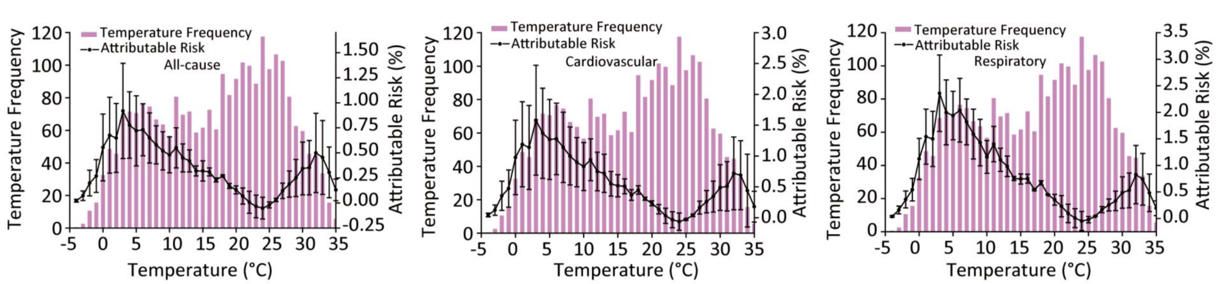

Figure 2. Attributed fractions (AFs) caused by per 1 °C of disease-specific mortality within 21 days in Nanjing, China, with a histogram of daily temperature.

were at 4 °C for three types of mortality and the AFs were high around 4 °C. According to our calculations, 57.3%, 55.3%, and 58.4% of temperature-related mortality of all-cause, cardiovascular, and respiratory causes, respectively, were observed when temperature was at the range of 0-10 °C.

To the best of our knowledge, systematic assessments of temperature-related mortality are rare. Our study used advanced statistical methods to quantify the extreme and moderate cold and heat effects on cause-specific mortality in Nanjing, China. The results revealed that cold was responsible for a high proportion of temperature-related death burden, whereas moderately cold temperature play a noticeable role in impact mortality. We further stratified temperature by 1 °C increments and revealed that there were high attributed mortality risks when temperature ranged from 0 °C to 10 °C in Nanjing.

In recent years, studies[6] have advanced our understanding on the biological mechanisms related to cold effects on human health, especially on cardiovascular and respiratory diseases. Exposure to cold is associated with cardiovascular stress reaction from certain affecting factors, including blood pressure, inflammatory cytokines, vasoconstriction, blood viscosity, and heart rate. Similarly, cold also leads to a series of immunological reactions such as persistent bronchoconstriction and suppression of mucociliary defense functions, thus resulting in increased risk of respiratory disease incidence and mortality.

Futhermore, We found the temperature interval between 0 °C and 10 °C accounted for 57.3%, 55.3%, and 58.4% of temperature-related mortality for all-cause, cardiovascular, and respiratory diseases, respectively. This temperature interval leads to high AFs of all three types of mortality and the main reasons are the following: the range from 0 °C to 10 °C is the normal temperature in Nanjing during the time of seasonal transition (e.g., autumn to winter or winter to spring). The atmosphere is usually frequent exchanges of cold and warm air masses during seasonal transitions, resulting in large amplitude of ambient temperature fluctuations. Studies[7] have indicated that large temperature fluctuations could cause the increase of the incidence of some weather-sensitive diseases, especially for the elderly or people with chronic diseases. In addition, due to global warming, the period of seasonal transition is curtailed, thus humans have less time to adapt to climate changes, which may be an other important factor for the onset of various diseases[8]. Hence, health burden caused by moderate cold requires more attention in the future.

Nevertheless, several limitations should be acknowledged. First, data regarding mortality were derived only from one city, which might limit extrapolation of our results to other cities or regions. Second, data on air pollutants were not controlled for in this study, because detailed air pollution data (e.g. $PM_{2.5}$, PM_{10}, and O_3) were not available. However, previous studies[9] have found that the effect of temperature on mortality did not change when controlling for air pollution.

In conclusion, cold weather was responsible for a high proportion of temperature-related death burden, whereas moderately cold temperature play a noticeable role in impact mortality. The AFs were high when temperature was between 0 °C and 10 °C. Although moderate cold has lower RR than extreme cold, it includes more days than extreme cold. Therefore, health burden caused by moderate cold requires further attention in the future. Our findings may have implications for the health impact associated with global climate change.

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