Letter to the Editor

Ambient Temperature and Outpatient Visits for Acute Exacerbation of Chronic Bronchitis in Shanghai: A Time Series Analysis*

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The association between ambient temperature and acute exacerbation of chronic bronchitis (AECB) was still unknown. Therefore, we performed an epidemiological study in a large hospital of Shanghai to explore the relationship about temperature and outpatient visit for AECB. We adopted a quasi-Poisson generalized additive models and distributed lag nonlinear models to estimate the accumulative effects of temperature on AECB across multiple days. We found significant non-linear effects of cold temperature on hospital visits for AECB, and the potential effect of cold temperature might last more than 2 weeks. The relative risks of extreme cold (first percentiles of temperature throughout the study period) and cold (10th percentile of temperature) temperature over lags 0-14 d were 2.98 [95% confidence intervals (CI): 1.77, 5.04] and 1.63 (95% CI: 1.21, 2.19), compared with the 25th percentile of temperature. However, we found no positive association between hospital visits and hot weather. This study showed that exposure to both extreme cold and cold temperatures were associated with increased outpatient visits for AECB in a large hospital of Shanghai.

Climate change has raised growing concerns in the associations between weather and health[1]. Epidemiological studies have shown that ambient temperature were nonlinearly associated with human health outcomes[2]. Acute exacerbation of chronic bronchitis (AECB) pose a substantial burden to patients, resulting in reduced lung function, increased morbidity and mortality, and long-term impairment in quality of life[3]. Approximately around 40%-50% of the exacerbations may be attributable to bacterial infections, and the remaining causes include viral infections or environmental irritants[4]. As one major environmental stimulus, temperature was rarely related to AECB in previous studies, especially in developing countries like Mainland China. Therefore, the objective of this study was to investigate the association between ambient temperature and outpatient visits of AECB in a large hospital of Shanghai, China.

The daily numbers of outpatient visits for AECB between January 1, 2010 and December 31, 2011 were obtained from Shanghai Yangpu District Central Hospital, which is also named by Yangpu Hospital, Tongji University. At the outpatient department, the diagnosis of AECB was completed by physicians based on patients' symptoms, inquiries, complaints, and findings on medical inspection. Then, the physicians must submit standard electronic documents through the internal computer network, which include basic information (name, gender, age, address, and telephones), as well as the primary diagnosis and treatment. We excluded floating population from our analyses whose permanent addresses were out of this district. Outpatient visits due to AECB were aggregated on a daily basis, and there were no missing daily values.

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The daily weather conditions (mean temperature and relative humidity) were collected from the Shanghai Meteorological Bureau. There were no missing values for weather data. In order to allow for the adjustment of the potential confounding effects of air pollution, we collected daily 24 h average concentrations on particulate matter less than 10 μm in aerodynamic diameter (PM_{10}), sulfur dioxide (SO_2), and nitrogen dioxide (NO_2) from a state-owned air quality monitoring station located in this district. The quality control for air quality data used in this study was under National Quality Control on Ambient Air Quality Monitoring Network.

We applied quasi-Poisson generalized additive models (GAM) to explore the association between temperature and outpatient visits of AECB because daily outpatient visits typically followed an overdispersed Poisson distribution. We then added a distributed lag nonlinear model (DLNM) in order to flexibly account for the potential lagged and nonlinear association[2,5]. The DLNM is developed on the basis of a 'cross-basis' function, which allows a simultaneous estimation of the non-linear association of temperature at each lag and obtain a cumulative estimate.

We incorporated several covariates in the model: 1) a natural cubic smooth function of calendar time with 7 degrees of freedom (df) per year, which excluded unmeasured long-term and seasonal trends in outpatient visits[6]; 2) air pollutants and relative humidity, which were constructed using the DLNM; and 3) an indicator variable for 'day of the week'. For the DLNM of temperature, we used a natural cubic spline with 5 df to account for the nonlinear effect of temperature. For the DLNMs of air pollutants and humidity, we selected a natural cubic spline of 3 df and a maximumlag of 3 d. For all the DLNMs, we used the natural cubic spline with 4 df for the lagged effects (lag space) of temperature, air pollutants, and humidity[7]. We estimated the association between temperature and AECB over the following lag periods: 0-3, 0-7, 0-14, and 0-21 d. A maximum lag of 21 d was used, because previous studies suggest that the effects of cold temperature could last for several weeks and the effects of high temperature were usually acute and immediate. Consistent with most previous meteorological epidemiological studies, we did not include atmospheric pressure and wind speed in the regression models.

Specifically, we calculated the relative risks (RRs) for AECB at extreme cold (first percentiles of temperature throughout the study period) and cold (10th percentiles of temperature) temperatures, compared with the 25th percentiles of temperature; and the RRs for outpatient visits at extreme hot (99th percentiles of temperature) and hot (90th percentiles of temperature) temperatures, compared with the 75th percentiles of temperature. The selection for cut-offs to define extreme cold, cold, hot, and extreme hot temperatures was somewhat arbitrary, but was consistent with choices of other published studies using the DLNM[5]. We then explore the age- and gender-specific associations between temperature and AECB. All statistical tests were two-sided, and values of $P<0.05$ were considered statistically significant. All of the analyses were performed using R software (version 2.15.1), with its 'dlnm' package to create the DLNM.

Table 1 shows the summary statistics in our study. During the study period, a total of 31,092 outpatient visits for AECB were included into our analysis. On average, there were approximately 43 cases per day. The average daily temperature and humidity were 17 °C and 68%, respectively. The 1th, 10th, 25th, 75th, 90th, and 99th percentiles of daily temperatureduring the study period were -0.2 °C, 3.7 °C, 9.4 °C, 25.0 °C, 29.3 °C, and 33.5 °C, respectively. The annual average concentrations were 79 μg/m^3 for PM_{10}, 30 μg/m^3 for SO_2, and 56 μg/m^3 for NO_2. Temperature was moderately correlated with air pollutants and relative humidity. PM_{10}, SO_2, and NO_2 were strongly correlated with each other (data not shown).

As indicated in Table 2, the association between temperature and AECB varied by lag periods. The RRs for cold and extreme cold temperatures increased with more lagged days. At lags 0-14 d, compared with the 25th percentile of temperature, the RR was 2.98 for extreme cold (1st percentile) and 1.63 for cold (10th percentile) temperatures, respectively. Our results were consistent with previous epidemiological studies, which found that ambient temperature was associated with the increased risk of respiratory mortality. For example, Wang et al.[8] found that the relative risk of respiratory morality associated with extreme cold temperature (1st percentile) over lags 0-21 d was 2.20 (95% CI: 1.01, 4.79), compared with the minimum-mortality temperature.

The relative risks also varied considerably by gender and age (see Table 3). The estimated associations of extreme cold and cold temperatures with AECB were significant for both genders, but the between-gender difference was statistically insignificant. We also found significant associations of extreme cold and cold temperatures in all age subgroups. For extreme cold temperature, the association among residents ≥65 years of age has a 2-fold bigger effect than those with 0-65 years of age. However, the difference was statistically insignificant across age subgroups for cold temperature.

Table 1. Summary Statistics of Daily Outpatient Visits for AECB, Weather Conditions and Air Pollutant Concentrations in the Study Area (2010-2011)

Variables	Mean±SD	Min	Percentile							Max
			P1	P10	P25	P50	P75	P90	P99	
NO. of daily outpatient visits for AECB	46±31	2	3	11	22	43	65	88	146	186
Meteorological measures (24 h average)										
Temperature (°C)	17.1±9.3	-2.2	-0.2	3.7	9.4	17.9	25.0	29.3	33.5	35.7
Humidity (%)	68.6±12.9	23.0	34.3	51.1	60.0	69.0	78.0	85.0	92.0	95.0
Air pollutants concentrations (24 h average, μg/m^3)										
PM_{10}	79.3±61.0	7.0	16.0	31.0	44.0	64.0	96.0	143.8	303.0	600.0
SO_2	30.0±17.3	6.0	7.3	12.0	16.0	26.0	40.0	54.0	78.0	134.0
NO_2	56.2±20.9	16.0	19.2	30.6	41.2	54.4	68.8	82.4	122.4	152.0

Note. Abbreviations: AECB, Acute exacerbation of chronic bronchitis; SD, standard deviation; PM_{10}, particulate matter less than 10 μm in aerodynamic diameter; SO_2, sulfur dioxide; NO_2, nitrogen dioxide.

Table 2. Cumulative Relative Risks and their 95% Confidence Intervals of Cold and Hot Temperatures on Outpatient Visits for Acute Exacerbation of Chronic Bronchitis over Multiple Lag Days

Lag Days	Extreme Cold[a]	Cold[b]	Hot[c]	Extreme Hot[d]
0-3	1.68 (1.22, 2.32)	1.23 (1.05, 1.44)	0.91 (0.75, 1.10)	0.81 (0.50, 1.32)
0-7	2.06 (1.39, 3.04)	1.33 (1.09, 1.62)	0.88 (0.68, 1.14)	0.82 (0.43, 1.56)
0-14	2.98 (1.77, 5.04)	1.63 (1.21, 2.19)	0.90 (0.65, 1.25)	0.94 (0.44, 2.00)
0-21	4.58 (2.51, 8.39)	1.91 (1.33, 2.75)	0.95 (0.64, 1.42)	1.06 (0.44, 2.56)

Note. [a]The 1st percentile of temperature relative to the 25th percentile of temperature throughout the study period; [b]The 10th percentile of temperature relative to the 25th percentile of temperature throughout the study period; [c]The 90th percentile of temperature relative to the 75th percentile of temperature throughout the study period; [d]The 99th percentile of temperature relative to the 75th percentile of temperature throughout the study period.

Table 3. Gender and Age-specific Relative Risks of Outpatient Visits of Acute Exacerbation of Chronic Bronchitis for Extreme Cold, Cold, Hot, and Extreme Hot Temperatures

Variables	Extreme Cold	Cold	Hot	Extreme Hot
Age (yrs.)				
0-65	1.83 (1.20, 2.78)	1.28 (1.04, 1.59)	0.94 (0.71, 1.24)	0.87 (0.44, 1.73)
≥66	3.80 (1.53, 9.45)	1.59 (1.00, 2.55)	0.64 (0.36, 1.16)	0.60 (0.14, 2.58)
Gender				
Male	2.31 (1.41, 3.78)	1.39 (1.08, 1.79)	0.86 (0.62, 1.19)	0.79 (0.35, 1.76)
Female	1.68 (0.96, 2.94)	1.24 (0.93, 1.65)	0.91 (0.63, 1.33)	0.88 (0.35, 2.22)

Note**.** The definition of extreme cold, cold, hot, and extreme hot temperatures are same with those in the footnotes of Table 2.

Our study found that older people were more sensitive to an exposure to extreme cold temperature. However, we did not observe significant difference between age subgroups for cold temperature. These findings was consistent with some previous studies which also have found that the elderly were at higher risk of mortality due to cold temperature[9]. It is plausible that old people has a high prevalence of chronic cardiopulmonary diseases, and thus are more susceptible to extreme cold temperature. Meanwhile, we did not observe significant modifying effect by gender, which were consistent with a previous study in California[10].

Our analysis had several strengths. Firstly, our study is the first to explore the association between ambient temperature and AECB in Mainland China. Secondly, this study investigated this association using an advanced statistical approach (i.e., DLNM), which can flexibly examine the lagged and nonlinear associations of temperature on health outcomes[11]. Three limitations should also be mentioned. First, this study was limited in one hospital in a city, so the representativeness of our results might not be sufficient. Second, this study was inherently an ecologic analysis, and thus potential confounding from individual-level risk factors could not be fully excluded. Third, we failed to control for the possibly confounding effects of fine particles and ozone because they were not routinely monitored in China during the study period. Therefore, further studies were needed to get a better understanding of the relationship between temperature and AECB.

In conclusion, our results demonstrated that exposure to extreme cold and cold temperature was associated with increased outpatient visits for AECB in a large hospital of Shanghai, China.

Conflict of Nterest Statement None of the authors has any conflict of interest to this paper.

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REFERENCES

1. Luber G, McGeehin M. Climate change and extreme heat events. Am J Prev Med, 2008; 35, 429-35.
2. Braga AL, Zanobetti A, Schwartz J. The effect of weather on respiratory and cardiovascular deaths in 12 U.S. Cities. Environ Health Perspect, 2002; 110, 859-63.
3. Mannino DM, Buist AS. Global burden of copd: Risk factors, prevalence, and future trends. Lancet, 2007; 370, 765-73.
4. Anthonisen NR, Manfreda J, Warren CP, et al. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. Ann Intern Med, 1987; 106, 196-204.
5. Chen RJ, Wang CC, Meng X, et al. Both low and high temperature may increase the risk of stroke mortality. Neurology, 2013; 81, 1064-70.
6. Peng RD, Dominici F, Louis TA. Model choice in time series studies of air pollution and mortality. J Roy Stat Soc a Sta, 2006; 169, 179-98.
7. Gasparrini A. Distributed lag linear and non-linear models in r: The package dlnm. J Stat Softw, 2011; 43, 1-20.
8. Wang C, Chen R, Kuang X, et al. Temperature and daily mortality in Suzhou, China: A time series analysis. Sci Total Environ, 2014; 466, 985-90.
9. Ma W, Yang C, Tan J, et al. Modifiers of the temperature-mortality association in Shanghai, China. Int J Biometeorol, 2012; 56, 205-7.
10. Basu R, Ostro BD. A multicounty analysis identifying the populations vulnerable to mortality associated with high ambient temperature in California. Am J Epidemiol, 2008; 168, 632-7.
11. Gasparrini A, Armstrong B, Kenward MG. Distributed lag non-linear models. Stat Med, 2010; 29, 2224-34.