Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China

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Complete List of Authors:	Liu, Yuan; Fudan University, School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education) Kan, Haidong; Fudan University, School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education); Fudan Tyndall Centre, Xu, Jianming; Shanghai Center for Urban Environmental Meteorology, ; Shanghai Key Laboratory of Meteorology and Health, Rogers, David; Health and Climate Foundation, Peng, Li; Shanghai Center for Urban Environmental Meteorology, ; Shanghai Key Laboratory of Meteorology and Health, Ye, Xiaofang; Shanghai Center for Urban Environmental Meteorology, ; Shanghai Key Laboratory of Meteorology and Health, Chen, Renjie; Fudan University, School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education) Zhang, Yue; Fudan University, School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education) Wang, Weibing; Fudan University, School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education); Fudan Tyndall Centre,
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Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China

Yuan Liu[1], Haidong Kan[1,2], Jianming Xu[3,4], David Rogers[5], Li Peng[3,4], Xiaofang Ye[3,4], Renjie Chen[1], Yue Zhang[1], and Weibing Wang [1,2]

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[1]School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education), Fudan University, Shanghai, China

[2]Fudan Tyndall Centre, Shanghai, China

[3]Shanghai Center for Urban Environmental Meteorology, Shanghai, China

[4]Shanghai Key Laboratory of Meteorology and Health, Shanghai, China

[5]Health and Climate Foundation, USA

Correspondence: Weibing Wang, Department of Epidemiology, School of Public Health, and Fudan Tyndall Centre, Fudan University, 138 Yi Xue Yuan Road, Shanghai 200032, China; Tel: +86 21 54237811; Fax: +86 21 54237710; E-mail: wwb@fudan.edu.cn

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Abstract

Objectives To explore the association between weather conditions and hospital admissions for pneumonia in Shanghai.

Design A time-series analysis was performed for a period of 4 years (Janarary 2008-December 2011). Generalized additive model yields to relative risks were also carried out.

Setting Shanghai, China.

Participants All daily hospital admissions for pneumonia obtained from the Shanghai health insurance system from January 1, 2008 to December 31, 2011 (n=99,403).

Results The relationship between mean temperature and pneumonia hospital admissions followed a V-shaped curve, with the optimum temperature (OT) at 13°C. When mean temperature was below the OT, temperature was associated with a 4.88% (95% confidence interval [CI]: 2.71%-7.09%) and 5.34% (95% [CI]: 2.04%-8.74%) increase in pneumonia hospital admissions in lag 4 using single-day lag structure and lag 0-7 using multi-day lag structure. When mean temperature ≥ OT, no significant associations between temperature and pneumonia hospital admissions were found. The magnitude of the effects of temperature varied across gender and age groups. Hospital admissions for pneumonia increased 15.99% (95%CI: 0.06%-34.46%) in cold period.

Conclusions Cold temperature may be one of the important risk factors for pneumonia hospitalizations. Prevention programs are needed to reduce the impact of cold temperature on pneumonia hospitalizations such as developing a weather

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warning system within a wide public health context.

Article summary

Article focus

- Pneumonia has been reported to be significantly influenced by meteorological factors
- The potential patterns of associations between weather conditions and pneumonia remain unclear in lots of countries especially in developing countries such as China.
- The study estimates the acute effects and lag influence of meteorological factors on hospital admissions for pneumonia.

Key messages

- The relationship between mean temperature and pneumonia hospital admissions followed a V-shaped curve, with the optimum temperature (OT) at 13°C.
- Cold temperature presented larger and more persistent effects and the magnitude of the effects of temperature varied with gender and age.

Strengths and limitations of this study

- Generalized additive models and two different lag structures were developed to explore the the possible interaction between meteorological factors and hospital admissions for pneumonia.
- we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure. This is expected to result in exposure misclassification.

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Background

Despite the availability of safe and effective antibiotics and vaccines for treatment and prevention, pneumonia is still a leading cause of death worldwide [1 2]. Pneumonia, in general lower respiratory tract infections, accounts for 6.6% of all deaths globally [3]. In adults, the incidences varied between 1.6 and 11 per 1,000 adults in different countries, with hospitalization proportions between 40% and 60% [4]. China is estimated to have 2.5 million pneumonia cases annually, of which 5% die from pneumonia-related diseases [5 6].

Climate change is potentially the largest global threat to human health [7]. In recent years, the association between meteorological factors and respiratory diseases has been observed extensively. Temperature has been reported to lead not only to direct deaths and illnesses but also to the aggravation of respiratory diseases [8 9]. Several studies have also found the association between temperature and daily respiratory deaths [10 11]. Generally, the curve between temperature and daily respiratory deaths followed V- or J-shaped [12 13]. In addition, time series studies on respiratory mortality have suggested that temperature has lag effects up to 3 weeks after exposure [14]. As one of the major disease of respiratory diseases, pneumonia has been reported to be significantly influenced by meteorological factors [11 15-17]. The relationships varied across areas with different weather patterns and latitudes. In Japan, for example, case number of *Mycoplasma pneumoniae* pneumonia increased significantly with increased average temperature and relative humidity [18]. However, neither hot nor cold temperatures had much effect on pneumonia death in hot cities in

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the USA [11].

Although pneumonia is recognized to result in substantial morbidity and mortality in some developed countries, the potential patterns of associations in other countries remain unclear, despite their populations being more sensitive to changes in weather conditions because of their poorer public health infrastructure and more vulnerable populations. We therefore performed a time-series analysis to estimate the acute effects and lag influence of meteorological factors on hospital admissions for pneumonia. Better understanding of the possible interaction will provide relevant information for developing public health plans and risk assessments in the ambient environment.

Materials and methods

Data collection

Shanghai is the most populous city in China, located at the eastern tip of the Yangtze River Delta, at latitude 31°14'N and longitude 121°29'E. The city comprises of 19 urban/suburban districts and counties, with a total area of 6341 square kilometers, and had a population of 23 million by the end of 2010, of which 14 million are registered population. The city features a moderate subtropical climate, with four distinct seasons and abundant rainfall.

For this analysis, the target population includes all registered population living in Shanghai with urban residents' basic medical insurance (hereafter population 1) or urban workers' basic medical insurance (hereafter population 2). Population 1 includes children, students and non-employed adults without new rural cooperative

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medical insurance. Population 2 includes employees, retirees and other insuranced participants. Daily hospital admissions for pneumonia incurred by residents of Shanghai from January 1, 2008 to December 31, 2011 were collected from the Shanghai Municipal Medical Insurance System. All forms of pneumonia coded J12-J18 according to the International Classification of Diseases, the tenth version (ICD-10) were included for analysis. Daily meteorological data (including mean temperature, relative humidity, precipitation and wind speed) was obtained from the Shanghai Center for Urban Environmental Meteorology. The weather data were measured at a fixed meteorlogical station located in Xuhui District of Shanghai.

Statistical methods

The hospital admissions for pneumonia and meteorological factors are linked by date and therefore can be analyzed with a time-series model [19]. As the number of daily hospital admissions is a type of low probability event and follows a Poisson distribution [20], a Poisson generalized additive model (GAM) approach was used to explore the association between meteorological factors and hospital admissions for pneumonia.

In order to examine the effect of meteorological factors on hospital admissions for pneumonia, we controlled the potential confounders such as long-term trend, the day of the week (DOW) and air pollutants. We first fitted nonparametric smoothing terms for trend on days and dummy variable for DOW. Thereafter, four meteorological factors were introduced into the model to explore the relationship between meteorological factors and hospital admissions for pneumonia. The independent

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model is described below:

$$\log E(Yt) = \alpha + s(\text{temperature}, df) + s(\text{relative humidity}, df) + s(\text{precipitation}, df) + s(\text{wind speed}, df) + s(\text{time}, df) + DOW + Z_t$$

where E (Yt) denotes the estimated daily hospital admissions for pneumonia counted on day t; α is the intercept; s() denotes a regression spline function for nonlinear variables [21]; time is the number of calendar days on day t; Z_t indicates the pollutant concentrations on day t; df is the degrees of freedom. The partial autocorrelation function (PACF) [22] was used to select the degrees of freedom of time trends until the absolute values of the sum of PACF for lags up to 30 reached a minimum. In the present study, the degree of freedom per year for time trends was 4. For meteorological factors, the selection of degrees of freedom was based on minimizing Akaike's Information Criterion (AIC) [23].

Additionally, we fitted linear terms for the mean temperature in the GAM model to explore the log-risk of daily hospital admissions for pneumonia associated with a unit increase of mean temperature. In examination of the lag effects of meteorological factors on hospital admissions for pneumonia, we developed two different lag structures: single-day lag and multi-day average starting from lag 0. For example, lag 0-1 stands for the 2-day moving average of current and previous day values.

Data preparation and analysis were carried out using EXCEL 2010, whereas regression models were fitted using the statistical software R version 3.0.1 by using the mgcv package.

Results

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Data description

Table 1 summarizes the basic statistics for our study. During the study period, totaling 1,461 days, 99,403 hospital admissions for pneumonia were recorded in Shanghai, a daily mean of 68.0 (range, 9.0–195.0). During the same time period, the mean daily temperature was 17.3°C (range, -3.4–35.7°C), reflecting the subtropical climate in Shanghai. The relative humidity, precipitation and wind speed averaged respectively at 69.4%, 30.9 mm and 2.9 m/s. Meanwhile, the mean daily concentrations of SO_2, NO_2 and PM_{10} were 35.6, 53.8 and 78.8 ug/m^3, respectively (Table 1).

Table 1 Summary statistics of daily hospital admissions for pneumonia and meteorological factors in Shanghai, 2008-2011

	Mean	SD	Min	P25	P75	Max
PHA[a]	68.0	27.3	9.0	50.0	85.0	195.0
Weather condition						
Mean temperature(°C)	17.3	9.2	-3.4	9.3	25.1	35.7
Relative humidity (%)	69.4	12.8	23.0	61.0	79.0	95.0
Precipitation(mm)	30.9	94.5	0.0	0.0	12.0	1284.0
Wind speed(m/s)	2.9	1.0	0.8	2.2	3.5	7.3
Air pollution						
SO_2(ug/m^3)	35.6	19.6	10.6	21.8	43.2	146.8
NO_2(ug/m^3)	53.8	20.5	12.4	39.4	64.5	141.7
PM_{10}(ug/m^3)	78.8	52.8	12.2	44.5	99.7	599.3

[a] PHA: pneumonia hospital admissions.

Daily hospital admissions and meteorological factors

Figure 1 shows the exposure-response (E-R) relationships between daily hospital admissions for pneumonia, and mean temperature, relative humidity, precipitation and wind speed, after adjusting for long-term trend, DOW and the air pollutants. The relationship between mean temperature and pneumonia hospital admissions followed a V-shaped, with a significant association (*P<0.001*) (Figure 1a). The optimum temperature (OT), corresponding to the lowest point in the E-R curve, was about 13°C; the risk of hospital admissions for pneumonia decreased at temperatures below the OT and then reversed the trend. In addition, GAM model did not find significance in associations between hospital admissions and relative humidity, precipitation, wind speed.

Lag effects of temperature on daily hospital admissions

As a V-shaped relationship between mean temperature and hospital admissions for pneumonia, we stratified the data by temperature above ("hot temperature") or below ("cold temperature") the OT. Then linear terms for the daily mean temperature were fitted in GAM models (Table 2). In single-day lag structures, significant associations (*P<0.01*) between cold temperature and hospital admissions for pneumonia were found at lag 2 to lag 5. Effect from cold temperature appears larger than that from hot temperature. The multi-day metrics of mean temperature exposure also showed a larger effect of cold temperature than hot temperature. The effects by cold temperature peaked at lag 0-6, with significance in lag 0-3 to lag 0-9. At the

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statistically significant maximum lag day (lag 0-6), a 1°C decrease in the 7-day moving average of mean temperature corresponded to a 5.34% (95%CI: 2.04%-8.74%) increase in hospital admissions for pneumonia. However, no significant associations between hot temperature and hospital admissions for pneumonia were found either in single-day or multi-day lag structures.

Table 2 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C change in mean temperature using alternative lags

Lag(d)[a]	OT(°C)	Cold temperature		Hot temperature	
		ER[b](%)	95%CI	ER(%)	95%CI
Single-day	13				
0		2.05	-0.61–4.78	0.80	-0.90–2.51
1		0.43	-2.07–3.01	0.41	-1.26–2.11
2		3.06*	0.72–5.47	0.04	-1.62–1.74
3		4.85**	2.65–7.09	0.37	-1.28–2.04
4		4.88**	2.71–7.09	1.28	-0.36–2.96
5		2.85*	0.65–5.10	1.16	-0.48–2.83
6		1.39	-0.81–3.64	1.21	-0.41–2.86
Multi-day	13				
0-1		0.03	-2.62–2.75	0.13	-1.66–1.96
0-2		1.57	-1.26–4.48	-0.08	-1.96–1.83
0-3		3.67*	0.84–6.59	-0.38	-2.39–1.67
0-4		4.88**	1.89–7.95	-0.42	-2.53–1.75

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0-5	5.21**	2.14–8.36	-0.62	-2.93–1.75
0-6	5.34**	2.04–8.74	-0.94	-3.42–1.60
0-7	5.10**	1.53–8.79	-0.48	-3.22–2.33
0-8	4.48*	0.72–8.37	-0.67	-3.47–2.21
0-9	4.01*	0.03–8.15	0.15	-2.81–3.20
0-10	1.43	-0.26–3.16	1.02	-0.52–2.59

[a] Lag 0 to lag 6: single-day lag from 0 to 6; lag 0-1 to lag 0-10: multi-day average of mean temperature (lag 0-1 means 2-day moving average of current and previous day values).

[b] ER means excess risk, ER= relative risk (RR) – 1.

* P <0.05. ** P <0.01.

Effects of cold temperature on different types of people

Since no significant associations between hot temperature and hospital admissions for pneumonia were found, we focused further analysis on the association between cold temperature and hospital admissions for pneumonia. Table 3 shows the different single-day lag effects of cold temperature on different population stratified by gender and age. We found significant effects of cold temperature in both males and females without a statistically significant difference by gender. The effects increased from lag 0, were greatest in lag 3 for male and in lag 4 for female, and then declined. In age-specific analysis, cold temperature was positively associated with pneumonia hospital admissions and was statistically significant in the categories over age 45. The OT for people who aged above 65 was 18°C, which was larger than that for those

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younger than 65.

Table 3 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in cold temperature stratified by gender and age.

	OT(°C)	ER[a] (%)						
		Lag0	Lag1	Lag2	Lag3	Lag4	Lag5	Lag6
Gender								
Male	13	-1.78	0.48	2.51	3.95**	3.77**	1.88**	0.57
Female	13	-2.25	0.38	3.62*	5.76**	6.01**	3.83	2.22
Age								
＜45	13	-1.36	-0.43	2.23	2.49	3.47	3.26	1.46
45-65	14	-2.81	-1.23	2.32	4.42**	4.88**	3.61*	2.52
65-75	18	-1.34	0.26	2.83	5.35**	5.51**	2.61	0.35
⩾75	18	-1.95	1.53	3.19*	4.47**	4.64**	2.41	1.10

[a] ER means excess risk, ER= relative risk (RR) – 1.

* P <0.05. ** P <0.01.

Figure 2 shows the single-day lag effects of cold temperature on different population. The effects reached maximum in the lag 3 on population 1 while in the lag 4 on population 2. A 1°C decrease of cold temperature corresponded to a 4.87% (95%CI: 2.67%-7.12%) increase in hospital admissions for pneumonia on population 2 in lag 4 while it was 4.13% (95%CI: 0.77%-7.60%) on population 1 in lag 3. The effects on population 2 appear larger and more persistent than that on population 1.

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Effect of cold period on pneumonia hospital admissions

Since cold temperature had large and persistent effects on pneumonia hospital admissions, we conducted a further analysis of cold temperature effects. We defined "cold period" as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) of temperature distribution during the study period; the "hot spot" for admissions refers to the day with daily pneumonia hospital admissions larger than the 75th percentile (85.0) of pneumonia hospital admissions.

Figure 3 shows pneumonia hospital admissions varied with daily mean temperature, while cold period is consistently corresponding to hot spots for pneumonia hospital admissions. We used cold period as a binary classification variable and fitted it in the GAM model. The result showed that hospital admissions for pneumonia increased 15.99% (95%CI: 0.06%-34.46%) in the cold period.

Discussion

This time-series analysis showed that ambient temperature was significantly associated with pneumonia hospital admissions, while relative humidity, precipitation and wind speed did not show the same. To our knowledge, this is the first effort to report the effects of meteorological factors on hospital admissions for pneumonia in China.

Generally, temperature appears V-, U-, or J-shaped variations with mortality or morbidity, with optimum temperature corresponding to the lowest point in temperature mortality curve [8 24]. The present study showed the relationship between mean

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temperature and pneumonia hospital admissions followed a V-shaped curve. Although the observation is consistent with the reported studies, our study showed the OT in Shanghai was 13°C, in comparison with 20°C in St. Paul [25], 16.5°C in Netherlands and 19°C in London [26]. Similar to the Beijing study [27], we found cold temperature presented larger effects. The fact that the peaks of respiratory syncytial virus and invasive pneumococcal disease were inversely correlated with temperature [28 29] and cold temperatures and therefore were favorable to the spread of influenza virus may partly explain the association [30].

We developed two different lag structures to examine the health effect of temperature. We observed statistically significant associations in both single-day and multi-day lag effects for cold temperature but none in both single-day and multi-day lag effects for hot temperature. Whereas, the multi-day lag structures showed that the effects from cold temperature lasted for 9 days. The findings were slightly different from other studies of morbidity. For example, Braga et al. study [11] found that the effect of cold temperatures persisted for days, whereas the effect of high temperatures was restricted to the day or the day before. Yu et al. research [31] demonstrated that cold temperature had 21 days lag effects, while hot temperature appears to exhibit short-term, acute effects.

Given the established importance of seasonal variation in mortality and morbidity excesses of respiratory diseases [32], several research studies have reported particularly on the relationship between extremely cold climatic episodes and mortality and morbidity, noting the tendency for a winter mortality increase after the occurrence

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of cold spells [33]. However, there is neither a uniform and agreed definition of a cold spell [34] nor a precise definition of the period for which such events should be studied. Our criteria for identifying cold period are to combine time and temperature thresholds, which is similar to other studies [35 36]. Our study found that there was a 15.99% increase of pneumonia hospital admissions in cold period. The cold period had significant effects on pneumonia hospital admissions. Further studies are needed to explore the cold temperature effects on pneumonia are from cold temperature itself, the cold period or their interaction.

Cold temperature effects on different types of people were observed. The effect of cold temperature on population 2 was larger and more persistent than that on population 1. Hospital admissions for pneumonia in population 2 increased by 0.67% and 1.06% more than that in population 1 associated with a 1°C decrease of cold temperature in lag 3 and lag 4. Probable reasons were that population 2 included employees and retirees but most people in population 1 were non-employed adults and students. The employees have more work pressure and have fewer opportunities to exercise, which might weaken their immunity. The elderly people are usually more susceptible to heat- or cold-related health risks [37 38]. The magnitude of the effects of temperature varied with gender and age. The OT for $\geqslant$65 age groups was higher than that for $<$65 age groups, which meant that elderly people were more vulnerable to cold weather for pneumonia hospital admissions. Cold temperature only had effect on people older than 45. In this age group, the ability to regulate body temperatures is reduced, and sweating thresholds are generally elevated compared with younger

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people [39].

Our study has several limitations. First, we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure. This is expected to result in exposure misclassification. Secondly, our study only contains data hospitalizations for pneumonia, and excludes less severe cases. Therefore, meteorological factors' effects on hospital admissions of pneumonia we observed may not be applied to the effects on the incidence of pneumonia.

CONCLUSION

We observed significant associations between meteorological factors and daily pneumonia hospital admissions in Shanghai. Cold temperature presented larger and more persistent effects and the magnitude of the effects of temperature varied with gender and age. Cold period had significant effects on pneumonia hospital admissions. Prevention programs may be needed to reduce the impact of cold temperature such as developing a weather warning system within a wide public health context.

Competing interests The authors declare that they have no competing interests.

Authors' contributions JX, LP and XY provided and organized data; YL, YZ and RC conducted the study, performed data analysis, and LY drafted the manuscript; WW, HK and DR reviewed and edited the manuscript, and WW conceived the study and

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contributed to the study design. All authors read and approved the final manuscript.

Authors' information [1]School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education), Fudan University, Shanghai, China.[2]Fudan Tyndall Centre, Shanghai, China. [3]Shanghai Center for Urban Environmental Meteorology, Shanghai, China. [4]Shanghai Key Laboratory of Meteorology and Health, Shanghai, China. [5]Health and Climate Foundation, USA.

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References

1. World Health Organization (2008) The top 10 causes of death. Available: http://www.who.int/mediacentre/factsheets/fs310/en/ Accessed 19 Jan 2010
2. Rudan I, O'Brien KL, Nair H, et al. Epidemiology and etiology of childhood pneumonia in 2010: estimates of incidence, severe morbidity, mortality, underlying risk factors and causative pathogens for 192 countries. Journal of global health 2013;**3**(1):10401 doi: 10.7189/jogh.03.010401 [published Online First: Epub Date].
3. Mathers C BC, and Moesgaard Iburg K. WHO. Global Burden of Disease in 2002: data sources, methods and results. Ref Type: Generic.
4. Polverino E Fau - Torres Marti A, Torres Marti A. Community-acquired pneumonia. (1827-1596 (Electronic))
5. Guan X, Silk BJ, Li W, et al. Pneumonia incidence and mortality in Mainland China: systematic review of Chinese and English literature, 1985-2008. PloS one 2010;**5**(7):e11721 doi: 10.1371/journal.pone.0011721 [published Online First: Epub Date].
6. Li-xian HE, Xue-hua C. Contentions on the pathogenic spectrum of community-acquired pneumonia and the first experimental application of antibiotic agents. Chinese Journal of Practical Internal Medicine 2007;**27**(2):110-13 doi: 10.3969/j.issn.1005-2194.2007.02.012 [published

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Online First: Epub Date].

7. Shea KM, Truckner RT, Weber RW, Peden DB. Climate change and allergic disease. The Journal of allergy and clinical immunology 2008;**122**(3):443-53; quiz 54-5 doi: 10.1016/j.jaci.2008.06.032 [published Online First: Epub Date].

8. Curriero FC, Heiner KS, Samet JM, Zeger SL, Strug L, Patz JA. Temperature and mortality in 11 cities of the eastern United States. American journal of epidemiology 2002;**155**(1):80-7

9. Haines A, McMichael AJ, Epstein PR. Environment and health: 2. Global climate change and health. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 2000;**163**(6):729-34

10. Braga AL, Zanobetti A, Schwartz J. The time course of weather-related deaths. Epidemiology 2001;**12**(6):662-7

11. Braga AL, Zanobetti A, Schwartz J. The effect of weather on respiratory and cardiovascular deaths in 12 U.S. cities. Environmental health perspectives 2002;**110**(9):859-63

12. Farajzadeh M, Darand M. Analyzing the influence of air temperature on the cardiovascular, respiratory and stroke mortality in tehran. Iranian Journal of Environmental Health Science & Engineering 2009;**6**(4):261-70

13. Liu L, Breitner S, Pan X, et al. Associations between air temperature and cardio-respiratory mortality in the urban area of Beijing, China: a time-series analysis. Environmental Health 2011;**10**(1):51

14. Huynen MM, Martens P, Schram D, Weijenberg MP, Kunst AE. The impact of heat

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waves and cold spells on mortality rates in the Dutch population. Environmental health perspectives 2001;**109**(5):463-70

15. Ye Y, Zulu E, Mutisya M, Orindi B, Emina J, Kyobutungi C. Seasonal pattern of pneumonia mortality among under-five children in Nairobi's informal settlements. The American journal of tropical medicine and hygiene 2009;**81**(5):770-5 doi: 10.4269/ajtmh.2009.09-0070 [published Online First: Epub Date].
16. Egondi T, Kyobutungi C, Kovats S, Muindi K, Ettarh R, Rocklov J. Time-series analysis of weather and mortality patterns in Nairobi's informal settlements. Global health action 2012;**5**:23-32 doi: 10.3402/gha.v5i0.19065 [published Online First: Epub Date].
17. Lim YH, Hong YC, Kim H. Effects of diurnal temperature range on cardiovascular and respiratory hospital admissions in Korea. The Science of the total environment 2012;**417-418**:55-60 doi: 10.1016/j.scitotenv.2011.12.048 [published Online First: Epub Date].
18. Onozuka D, Hashizume M, Hagihara A. Impact of weather factors on Mycoplasma pneumoniae pneumonia. Thorax 2009;**64**(6):507-11 doi: 10.1136/thx.2008.111237 [published Online First: Epub Date].
19. Zeger SL, Irizarry R, Peng RD. On time series analysis of public health and biomedical data. Annual review of public health 2006;**27**:57-79 doi: 10.1146/annurev.publhealth.26.021304.144517 [published Online First: Epub Date].

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20. Cao J, Li W, Tan J, et al. Association of ambient air pollution with hospital outpatient and emergency room visits in Shanghai, China. The Science of the total environment 2009;**407**(21):5531-6 doi: 10.1016/j.scitotenv.2009.07.021 [published Online First: Epub Date].

21. Guo Y, Barnett AG, Yu W, et al. A large change in temperature between neighbouring days increases the risk of mortality. PloS one 2011;**6**(2):e16511 doi: 10.1371/journal.pone.0016511 [published Online First: Epub Date].

22. Kan H, London SJ, Chen H, et al. Diurnal temperature range and daily mortality in Shanghai, China. Environmental research 2007;**103**(3):424-31 doi: 10.1016/j.envres.2006.11.009 [published Online First: Epub Date].

23. Hastie T, Tibshirani R. Generalized additive models for medical research. Statistical methods in medical research 1995;**4**(3):187-96

24. Kan HD, Jia J, Chen BH. Temperature and daily mortality in Shanghai: a time-series study. Biomedical and environmental sciences : BES 2003;**16**(2):133-9

25. Gouveia N, Hajat S, Armstrong B. Socioeconomic differentials in the temperature-mortality relationship in Sao Paulo, Brazil. International journal of epidemiology 2003;**32**(3):390-7

26. Patz JA, Campbell-Lendrum D, Holloway T, Foley JA. Impact of regional climate change on human health. Nature 2005;**438**(7066):310-7 doi: 10.1038/nature04188 [published Online First: Epub Date].

27. Mo Yun-zheng, Zheng Ya-an, Hui T, et al. Relationship between daily mean

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temperature and emergency department visits for respiratory diseases: a time-series analysis. (1671-167X (Print))

28. Yusuf S, Piedimonte G, Auais A, et al. The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus. Epidemiology and infection 2007;**135**(7):1077-90 doi: 10.1017/S095026880600776X [published Online First: Epub Date].

29. Murdoch DR, Jennings LC. Association of respiratory virus activity and environmental factors with the incidence of invasive pneumococcal disease. The Journal of infection 2009;**58**(1):37-46 doi: 10.1016/j.jinf.2008.10.011 [published Online First: Epub Date].

30. Lowen Ac Fau - Mubareka S, Mubareka S Fau - Steel J, Steel J Fau - Palese P, Palese P. Influenza virus transmission is dependent on relative humidity and temperature. (1553-7374 (Electronic)) doi: D - NLM: PMC2034399 EDAT- 2007/10/24 09:00 MHDA- 2007/11/14 09:00 CRDT- 2007/10/24 09:00 PHST- 2007/07/11 [received] PHST- 2007/09/05 [accepted] AID - 07-PLPA-RA-0426 [pii] AID - 10.1371/journal.ppat.0030151 [doi] PST - ppublish [published Online First: Epub Date].

31. Yu W, Mengersen K, Hu W, Guo Y, Pan X, Tong S. Assessing the relationship between global warming and mortality: Lag effects of temperature fluctuations by age and mortality categories. Environmental pollution 2011;**159**(7):1789-93 doi: http://dx.doi.org/10.1016/j.envpol.2011.03.039 [published Online First: Epub Date].

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For peer review only

32. Donaldson GC, Goldring JJ, Wedzicha JA. Influence of season on exacerbation characteristics in patients with COPD. Chest 2012;**141**(1):94-100 doi: 10.1378/chest.11-0281 [published Online First: Epub Date].

33. Revich B, Shaposhnikov D. Excess mortality during heat waves and cold spells in Moscow, Russia. Occupational and environmental medicine 2008;**65**(10):691-6 doi: 10.1136/oem.2007.033944 [published Online First: Epub Date].

34. Kysely J, Pokorna L, Kyncl J, Kriz B. Excess cardiovascular mortality associated with cold spells in the Czech Republic. BMC public health 2009;**9**:19 doi: 10.1186/1471-2458-9-19 [published Online First: Epub Date].

35. Ma W Fau - Yang C, Yang C Fau - Chu C, Chu C Fau - Li T, Li T Fau - Tan J, Tan J Fau - Kan H, Kan H. The impact of the 2008 cold spell on mortality in Shanghai, China. (1432-1254 (Electronic))

36. Monteiro A Fau - Carvalho V, Carvalho V Fau - Gois J, Gois J Fau - Sousa C, Sousa C. Use of "Cold Spell" indices to quantify excess chronic obstructive pulmonary disease (COPD) morbidity during winter (November to March 2000-2007): case study in Porto. (1432-1254 (Electronic))

37. Ye X, Wolff R, Yu W, Vaneckova P, Pan X, Tong S. Ambient temperature and morbidity: a review of epidemiological evidence. Environmental health perspectives 2012;**120**(1):19-28 doi: 10.1289/ehp.1003198 [published Online First: Epub Date].

38. Yu W, Mengersen K, Wang X, et al. Daily average temperature and mortality

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among the elderly: a meta-analysis and systematic review of epidemiological evidence. International journal of biometeorology 2012;**56**(4):569-81 doi: 10.1007/s00484-011-0497-3 [published Online First: Epub Date].

39. Kenney WL, Hodgson JL. Heat Tolerance, Thermoregulation and Aging. Sports Medicine 1987;**4**(6):446-56

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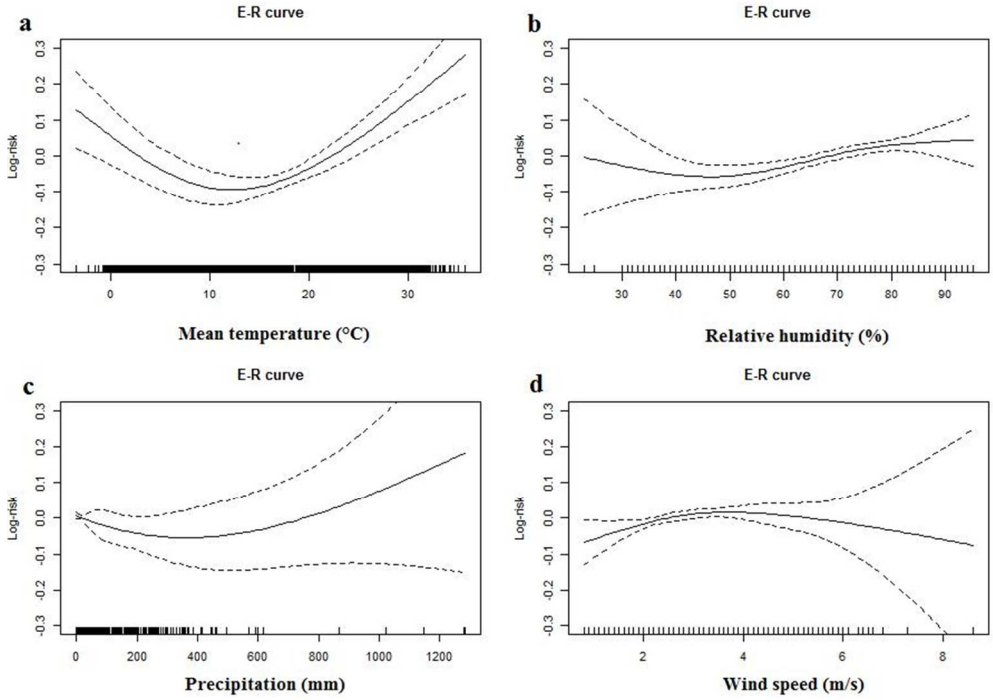

Figure 1 Smoothing plots of meteorological factors against hospital admissions for pneumonia. (a) mean temperature at lag 4; (b) relative humidity at lag 0; (c) precipitation at lag 0; (d) wind speed at lag 0. The solid lines indicate the estimated mean percentage of change in ED visits, and the dotted lines represent twice the standard error.
237x168mm (96 x 96 DPI)

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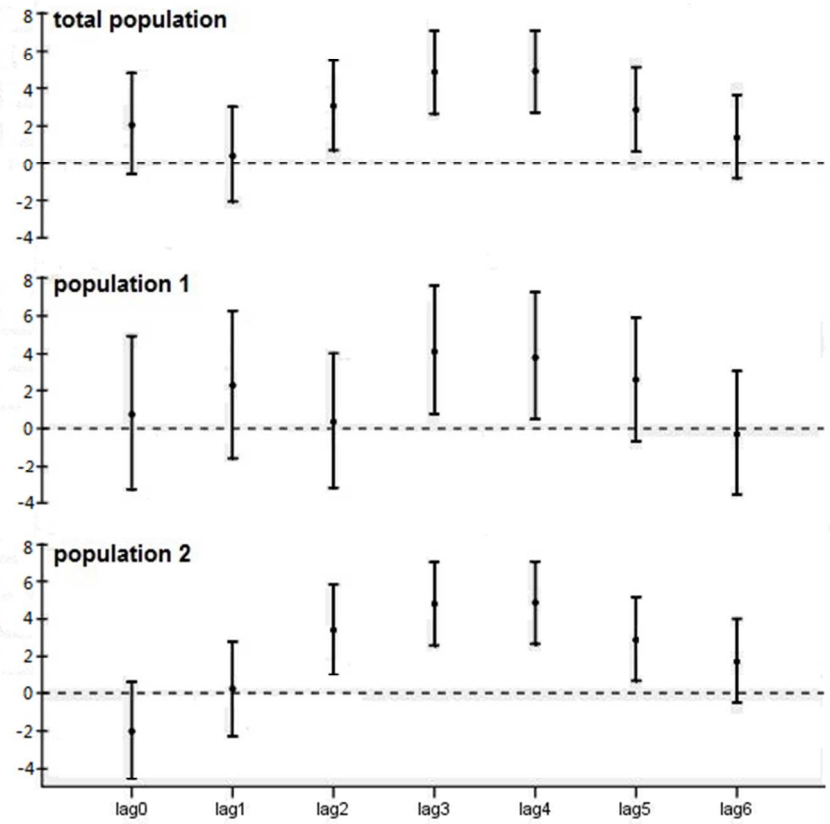

Figure 2 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in cold temperature using single-day lag structure by different population.
167x154mm (96 x 96 DPI)

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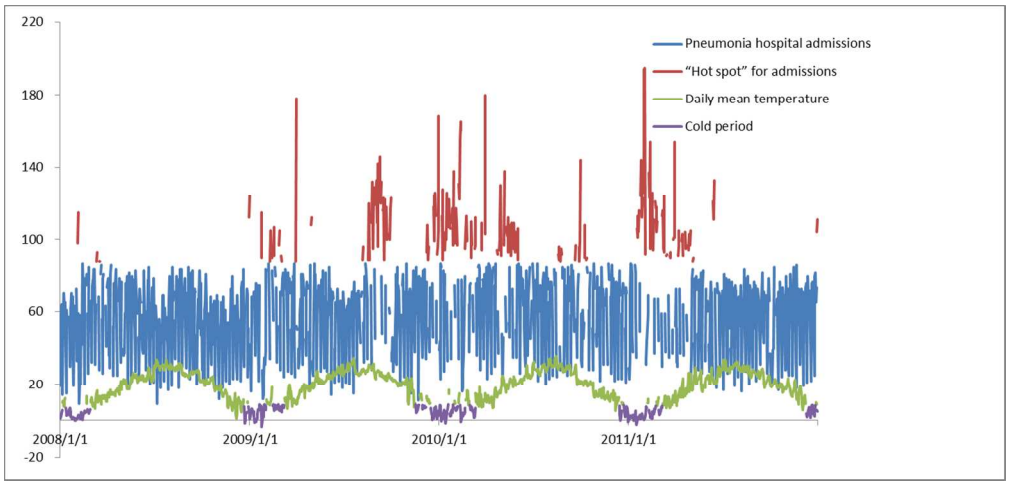

Figure 3 Daily mean temperature and daily pneumonia hospital admissions. Cold period means a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) of temperature distribution during the study period; "hot spot" for admissions means the day with daily pneumonia hospital admissions larger than the 75th percentile (85.0) of pneumonia hospital admissions.
380x180mm (96 x 96 DPI)

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China	1
		(b) **Objectives** To explore the association between weather conditions and hospital admissions for pneumonia in Shanghai. **Design** A time-series analysis was performed for a period of 4 years (Janarary 2008-December 2011). Generalized additive model yields to relative risks were also carried out. **Conclusions** Cold temperature may be one of the important risk factors for pneumonia hospitalizations.	2
Introduction			
Background/rationale	2	Although pneumonia is recognized to result in substantial morbidity and mortality in some developed countries, the potential patterns of associations in other countries remain unclear	4-5
Objectives	3	pneumonia has been reported to be significantly influenced by meteorological factors.	4-5
Methods			
Study design	4	A time-series analysis	6
Setting	5	Shanghai, China	5
Participants	6	All daily hospital admissions for pneumonia obtained from the Shanghai health insurance system from January 1, 2008 to December 31, 2011 (n=99,403).	5
Variables	7	The target population includes all registered population living in Shanghai with urban residents' basic medical insurance (hereafter population 1) or urban workers' basic medical insurance (hereafter population 2). we stratified the data by temperature above ("hot temperature") or below ("cold temperature") the optimum temperature (OT). We defined "cold period" as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) of temperature distribution during the study period; the "hot spot" for admissions refers to the day with daily pneumonia hospital admissions larger than the 75th percentile (85.0) of pneumonia hospital admissions.	5, 9, 13
Data sources/ measurement	8*	Daily hospital admissions for pneumonia incurred by residents of Shanghai from January 1, 2008 to December 31, 2011 were collected from the Shanghai Municipal Medical Insurance System. Daily meteorological data (including mean temperature, relative humidity, precipitation and wind speed) was obtained from the Shanghai Center for Urban Environmental Meteorology.	6

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		The weather data were measured at a fixed meteorlogical station located in Xuhui District of Shanghai.	
Bias	9	We controlled the potential confounders such as long-term trend, the day of the week (DOW) and air pollutants.	*6*
Study size	10	The target population includes all registered population living in Shanghai with urban residents' basic medical insurance or urban workers' basic medical insurance.	5
Quantitative variables	11	The hospital admissions for pneumonia and meteorological factors are linked by date and therefore can be analyzed with a time-series model.	6
Statistical methods	12	(a) a Poisson generalized additive model (GAM) approach was used to explore the association between meteorological factors and hospital admissions for pneumonia.	6
		(b) The partial autocorrelation function (PACF) was used to select the degrees of freedom of time trends	7
Results			
Participants	13*	All daily hospital admissions for pneumonia obtained from the Shanghai health insurance system from January 1, 2008 to December 31, 2011 (n=99,403).	8
Descriptive data	14*	During the study period, totaling 1,461 days, 99,403 hospital admissions for pneumonia were recorded in Shanghai, a daily mean of 68.0 (range, 9.0–195.0). During the same time period, the mean daily temperature was 17.3°C (range, -3.4–35.7°C), reflecting the subtropical climate in Shanghai. The relative humidity, precipitation and wind speed averaged respectively at 69.4%, 30.9 mm and 2.9 m/s. Meanwhile, the mean daily concentrations of SO2, NO2 and PM10 were 35.6, 53.8 and 78.8 ug/m3, respectively	8
Outcome data	15*	Optimum temperature (OT), excess risk (ER)	9-12
Main results	16	(a) The relationship between mean temperature and pneumonia hospital admissions followed a V-shaped curve, with the optimum temperature (OT) at 13°C. When mean temperature was below the OT, temperature was associated with a 4.88% (95% confidence interval [CI]: 2.71%-7.09%) and 5.34% (95% [CI]: 2.04%-8.74%) increase in pneumonia hospital admissions in lag 4 using single-day lag structure and lag 0-7 using multi-day lag structure. Hospital admissions for pneumonia increased 15.99% (95%CI: 0.06%-34.46%) in cold period.	9, 10, 13
		(b) We defined "cold period" as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) of temperature distribution during the study period; the "hot spot" for admissions refers to the day with daily pneumonia hospital admissions larger than the 75th percentile (85.0) of pneumonia hospital admissions.	13
Other analyses	17	Cold temperature effects on different types of people were observed. The magnitude of the effects of temperature varied with gender and age.	11, 12
Discussion			
Key results	18	The relationship between mean temperature and pneumonia hospital admissions followed a V-shaped curve, with the	13, 14, 15

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		optimum temperature (OT) at 13°C. Cold temperature presented larger and more persistent effects and the magnitude of the effects of temperature varied with gender and age.	
Limitations	19	we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure. This is expected to result in exposure misclassification.	16
Interpretation	20	Cold temperature may be one of the important risk factors for pneumonia hospitalizations.	16
Generalisability	21	The setting of this study was Shanghai, China. Although the results are consistent with the lots of other reported studies, it should be careful of generalizability to other populations.	
Other information			
Funding	22	This study was funded by the Global Environment Change Research in Fudan University (Grant No. EZH1829007/003), and the program of Key Discipline Development of Public Health of Shanghai (Grant No. 12GWZX0101).	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China: a time-series analysis

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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Infectious diseases
Keywords:	pneumonia, temperature, time-series, generalized additive model

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Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China: a time-series analysis

Yuan Liu[1], Haidong Kan[1,2], Jianming Xu[3,4], David Rogers[5], Li Peng[3,4], Xiaofang Ye[3,4], Renjie Chen[1], Yue Zhang[1], and Weibing Wang [1,2]

Running Title: Weather conditions and pneumonia hospitalization

[1]School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education), Fudan University, Shanghai, China

[2]Fudan Tyndall Centre, Shanghai, China

[3]Shanghai Center for Urban Environmental Meteorology, Shanghai, China

[4]Shanghai Key Laboratory of Meteorology and Health, Shanghai, China

[5]Health and Climate Foundation, USA

Correspondence: Weibing Wang, Department of Epidemiology, School of Public Health, and Fudan Tyndall Centre, Fudan University, 138 Yi Xue Yuan Road, Shanghai 200032, China; Tel: +86 21 54237811; Fax: +86 21 54237710; E-mail: wwb@fudan.edu.cn

Keywords: pneumonia, temperature, time-series, generalized additive model

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Abstract

Objectives To explore the association between weather conditions and hospital admissions for pneumonia in Shanghai.

Design A time-series analysis was performed for a period of 4 years (January 2008-December 2011). Generalized additive model were used to calculate the relative risks.

Setting Shanghai, China.

Participants All daily hospital admissions for pneumonia were obtained from the Shanghai health insurance system between January 1, 2008 and December 31, 2011 (n=99,403).

Results The relationship between mean temperature and pneumonia hospital admissions followed a V-shape curve, with an optimum temperature (OT) at 13°C. When mean temperature was below the OT, a 1°C decrease corresponded to a 4.88% (95% confidence interval [CI]: 2.71%-7.09%) and 5.34% (95% CI: 2.04%-8.74%) increase in pneumonia hospital admissions in lag 4 using single-day lag structure and lag 0-7 using multi-day lag structure. When mean temperature ≥ OT, no significant associations between temperature and pneumonia hospital admissions were found. The magnitude of the effects of temperature varied across gender and age groups. Hospitalizations for pneumonia increased 15.99% (95% CI: 0.06%-34.46%) in the cold period.

Conclusions Cold temperature may be one of the important risk factors for pneumonia hospitalizations. Prevention programs are needed to reduce the impact of

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cold temperature on pneumonia hospitalizations such as developing a weather warning system within a wide public health context.

Article summary

Article focus

- Pneumonia has been reported to be significantly influenced by meteorological factors
- The potential patterns of associations between weather conditions and pneumonia remain unclear in lots of countries especially in developing countries such as China.
- The study estimates the acute effects and time pattern of meteorological factors on hospital admissions for pneumonia.

Key messages

- The relationship between mean temperature and pneumonia hospital admissions followed a V-shape curve, with an optimum temperature (OT) at 13°C.
- Cold temperature caused larger and more persistent adverse effects and the magnitude of these effects of temperature varied with gender and age.

Strengths and limitations of this study

- Generalized additive models and two different lag structures were developed to explore the possible interaction between meteorological factors and hospital admissions for pneumonia.
- we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure.

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This is expected to result in exposure misclassification.

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Background

Despite the availability of safe and effective antibiotics and vaccines for treatment and prevention, pneumonia is still a leading cause of death worldwide [1 2]. Pneumonia, in general lower respiratory tract infections, accounts for 6.6% of all deaths globally [3]. In adults, the incidences varied between 1.6 and 11 per 1,000 adults in different countries, with hospitalization proportions ranging from 40% to 60% [4]. China is estimated to have 2.5 million pneumonia cases annually, of which 5% die from pneumonia-related diseases [5 6].

Climate change is potentially the largest global threat to human health [7]. In recent years, the association between meteorological factors and respiratory diseases has been observed extensively. Temperature has been reported to lead not only to direct deaths and illnesses but also to the aggravation of respiratory diseases [8 9]. Several studies have emphasized the relationships between temperature and daily respiratory deaths [10 11]. Generally, the curves between temperature and daily respiratory deaths were V- or J-shape [12 13]. In addition, time series studies on respiratory mortality have suggested that temperature has lag effects up to 3 weeks after exposure [14]. As one of the major disease of respiratory diseases, pneumonia has been reported to be significantly influenced by meteorological factors [11 15-17]. However, the relationships varied across areas with different weather patterns and latitudes. In Japan, for example, case number of *Mycoplasma pneumoniae* pneumonia increased significantly with increased average temperature and relative humidity [18]. Contrarily, neither hot nor cold temperatures had much effect on

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pneumonia death in hot cities in the USA [11].

Although pneumonia is recognized to result in substantial morbidity and mortality in some developed countries, the potential patterns of associations in other countries remain unclear. Whereas the populations of source limited countries may be more sensitive to changes in weather conditions because of their poorer public health infrastructure and vulnerability of the populations. We therefore performed a time-series analysis to estimate the acute effects and time pattern of meteorological factors on hospital admissions for pneumonia. Better understanding of the possible interaction will provide relevant information for developing public health plans and risk assessments in ambient environment.

Materials and methods

Data collection

Shanghai is the most populous city in China, located at the eastern tip of the Yangtze River Delta, at latitude 31°14'N and longitude 121°29'E. The city comprises of 19 urban/suburban districts and counties, with a total area of 6341 square kilometers, and had a population of over 23 million people by the end of 2010, of which 14 million are registered residents. The city features a moderate subtropical climate, with four distinct seasons and abundant rainfall.

For this analysis, the target population included all registered population living in Shanghai with urban residents' basic medical insurance (hereafter population 1) and urban workers' basic medical insurance (hereafter population 2). Population 1 included children, students and non-employed adults excluding those with new rural

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cooperative medical insurance. Population 2 included employees, retirees and other insuranced participants. Daily hospital admissions for pneumonia incurred by the two populations of Shanghai from January 1, 2008 to December 31, 2011 were collected from the Shanghai Municipal Medical Insurance System. All forms of pneumonia coded J12-J18 according to the International Classification of Diseases, the tenth version (ICD-10) were included for the analysis. Daily meteorological data (including mean temperature, relative humidity, precipitation and wind speed) were obtained from the Shanghai Center for Urban Environmental Meteorology. The weather data were measured at a fixed meteorological station located in the Xuhui District of Shanghai. Due to the probable confounding effects that air pollution and suspended particles may have on temperature and pneumonia, air pollution data (sulfur dioxide (SO2), nitrogen dioxide (NO2) and PM10) were also obtained from the Shanghai Center for Urban Environmental Meteorology.

Statistical methods

The hospital admissions for pneumonia and meteorological factors were linked by the date and therefore can be analyzed with a time-series model [19]. As the number of daily hospital admissions is a type of low probability event and follows a Poisson distribution [20], a Poisson generalized additive model (GAM) approach was used to explore the association between meteorological factors and hospital admissions for pneumonia.

In order to examine the effect of meteorological factors on hospital admissions for pneumonia, we controlled the potential confounders such as long-term trend, the day

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of the week (DOW) and air pollutants. We first fitted nonparametric smoothing terms for trend on days and dummy variable for DOW. Thereafter, four meteorological factors were introduced into the model to explore the relationship between meteorological factors and hospital admissions for pneumonia. The independent model is described below:

$$\log E(Yt) = \alpha + s(\text{temperature}, df) + s(\text{relative humidity}, df) + s(\text{precipitation}, df) + s(\text{wind speed}, df) + s(\text{time}, df) + DOW + Z_t$$

where E (Yt) denotes the estimated daily hospital admissions for pneumonia counted on day t; α is the intercept; s() denotes a regression spline function for nonlinear variables [21]; time is the number of calendar days on day t; Z_t indicates the pollutant concentrations on day t; df is the degrees of freedom. The partial autocorrelation function (PACF) [22] was used to select the degrees of freedom of time trends until the absolute values of the sum of PACF for lags up to 30 reached a minimum. Sensitivity analyses were performed to check whether the results were robust to the specification of parameters in the model. We found that the effects were stable when using 4 or 5 degrees of freedom per year for time. In addition, we modified degrees of freedom of smooth (4-5 df) for meteorological factors, and the estimates were not changed substantially. These sensitivity analyses resulted in the selection of 4 df per year to control for time trend and 4 df for meteorological factors. For meteorological factors, the selection of degrees of freedom was based on minimizing Akaike's Information Criterion (AIC) [23].

Additionally, we fitted linear terms for the mean temperature in the GAM to

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explore the log-risk of daily hospital admissions for pneumonia associated with a unit increase of mean temperature. In examination of the lag effects of meteorological factors on hospital admissions for pneumonia, we developed two different lag structures: single-day lag and multi-day average starting from lag 0. For example, lag 0-1 stands for the 2-day moving average of current and previous day values. Relative risk (RR) refers to the ratio of the probability of an event occurring, while excess risk (ER) is the change in risk of a given activity. We used ER to evaluate the association between daily hospital admissions for pneumonia and a unit change of mean temperature.

We defined “cold period” as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) and “hot spot” for admissions as the days with daily pneumonia hospital admissions larger than the 75th percentile (85).

Data preparation and analysis were carried out using EXCEL 2010, whereas regression models were fitted using the statistical software R version 3.0.1 by using the mgcv package.

Results

Data description

Table 1 summarizes the basic statistics for our study. During the study period, totaling 1,461 days, 99,403 hospital admissions for pneumonia were recorded in Shanghai with a mean of 68 (range, 9–195) per day. During the same time period, the mean daily temperature was 17.3°C (range, -3.4–35.7°C), reflecting the subtropical climate in Shanghai. A correlation matrix table for the meteorological and air pollution

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variables was provided in the Supplementary Table S2.

Table 1 Summary statistics of daily hospital admissions for pneumonia and meteorological factors in Shanghai, 2008-2011

	Mean	SD	Min	P25	P75	Max
PHA[a]	68	27	9	50	85	195
Weather condition						
Mean temperature(°C)	17.3	9.2	-3.4	9.3	25.1	35.7
Relative humidity (%)	69	13	23	61	79	95
Precipitation(mm)	30.9	94.5	0.0	0.0	12.0	1284.0
Wind speed(m/s)	2.9	1.0	0.8	2.2	3.5	7.3
Air pollution						
SO_2(ug/m^3)	36	20	11	22	43	147
NO_2(ug/m^3)	54	21	12	39	65	142
PM_{10}(ug/m^3)	79	53	12	45	100	599

[a] PHA: pneumonia hospital admissions.

Daily hospital admissions and meteorological factors

Figure 1 shows the exposure-response (E-R) relationships between daily hospital admissions for pneumonia, and mean temperature, relative humidity, precipitation and wind speed, after adjusting for long-term trend, DOW and the air pollutants in the GAM. The relationship between mean temperature and pneumonia hospital admissions followed a V-shape with a significant association (*P<0.001*) (Figure 1a). The optimum temperature (OT), corresponding to the lowest point in the E-R curve,

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was about 13°C. Below the OT, as temperatures increased, the risk of hospital admissions for pneumonia decreased and then reversed the trend above the OT. In addition, GAM did not find effects of relative humidity, precipitation, wind speed in pneumonia hospital admissions.

Lag effects of temperature on daily hospital admissions

As there was a V-shaped relationship between mean temperature and hospital admissions for pneumonia, we stratified the data by temperature above ("hot temperature") or below ("cold temperature") the OT. Then linear terms for the daily mean temperature were fitted in GAMs (Table 2). In single-day lag structures, significant associations (*P<0.01*) between cold temperature and hospital admissions for pneumonia were found at lag 2 to lag 5. Effect from cold temperature appears larger than that from hot temperature. The multi-day metrics of mean temperature exposure also showed a larger effect of cold temperature than that of hot temperature. The effects by cold temperature peaked at lag 0-6, with statistical significance in lag 0-3 to lag 0-9. At lag 0-6, a 1°C decrease in the 7-day moving average of mean temperature corresponded to a 5.34% (95%CI: 2.04%-8.74%) increase in hospital admissions for pneumonia. However, no adverse effects of hot temperature were found either in single-day or multi-day lag structures.

Table 2 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C change in mean temperature using alternative lags

Lag(d)[a]	OT(°C)	Cold temperature		Hot temperature	
		ER[b](%)	95%CI	ER(%)	95%CI

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Single-day	13				
0		-2.05	-4.78–0.61	0.80	-0.90–2.51
1		0.43	-2.07–3.01	0.41	-1.26–2.11
2		3.06*	0.72–5.47	0.04	-1.62–1.74
3		4.85**	2.65–7.09	0.37	-1.28–2.04
4		4.88**	2.71–7.09	1.28	-0.36–2.96
5		2.85*	0.65–5.10	1.16	-0.48–2.83
6		1.39	-0.81–3.64	1.21	-0.41–2.86
Multi-day	13				
0-1		0.03	-2.62–2.75	0.13	-1.66–1.96
0-2		1.57	-1.26–4.48	-0.08	-1.96–1.83
0-3		3.67*	0.84–6.59	-0.38	-2.39–1.67
0-4		4.88**	1.89–7.95	-0.42	-2.53–1.75
0-5		5.21**	2.14–8.36	-0.62	-2.93–1.75
0-6		5.34**	2.04–8.74	-0.94	-3.42–1.60
0-7		5.10**	1.53–8.79	-0.48	-3.22–2.33
0-8		4.48*	0.72–8.37	-0.67	-3.47–2.21
0-9		4.01*	0.03–8.15	0.15	-2.81–3.20
0-10		1.43	-0.26–3.16	1.02	-0.52–2.59

[a] Lag 0 to lag 6: single-day lag from 0 to 6; lag 0-1 to lag 0-10: multi-day average of mean temperature (lag 0-1 means 2-day moving average of current and previous day values).

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[b] ER means excess risk, ER= relative risk (RR) – 1.

* P <0.05. ** P <0.01.

Effects of cold temperature on different types of people

Since no significant effects of hot temperature in hospital admissions for pneumonia were found, we focused further analysis on the association between cold temperature and hospital admissions for pneumonia. The association between hot temperature and hospital admissions for pneumonia was showed in Supplementary Table S3. Table 3 shows the different single-day lag effects of cold temperature on different sub-populations. We found the adverse effects of cold temperature in both males and females without a statistically significant difference by gender. The effects increased from lag 0, with peaks in lag 3 for male and in lag 4 for female, and then declined. In age-specific analysis, cold temperature was positively associated with pneumonia hospital admissions and was statistically significant in the categories over age 45. The OT for people who aged above 65 was 18°C, which was larger than that for those younger than 65.

Table 3 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in cold temperature stratified by gender and age.

	No.	OT(°C)	ER[a] (%)						
			Lag0	Lag1	Lag2	Lag3	Lag4	Lag5	Lag6
Gender									
Male	50696	13	-1.78	0.48	2.51*	3.95**	3.77**	1.88**	0.57

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			(-4.49-1.00)	(-2.14-3.18)	(0.07,5.02)	(1.64,6.31)	(1.50-6.09)	(-0.42-4.24)	(-1.70-2.89)
Female	48706	13	-2.25	0.38	3.62*	5.76**	6.01**	3.83**	2.22
			(-5.05-0.64)	(-2.38-3.23)	(0.99-6.31)	(3.34-8.24)	(3.62-8.46)	(1.41-6.32)	(-0.23-4.73)
Age									
＜45	9567	13	-1.36	-0.43	2.23	2.49	3.47	3.26	1.46
			(-5.71-3.19)	(-4.68-4.01)	(-1.83-6.12)	(-1.45-6.50)	(-0.28-7.35)	(-0.52-6.99)	(-2.26-5.32)
45-65	25446	14	-2.81	-1.23	2.32	4.42**	4.88**	3.61*	2.52
			(-6.09-0.59)	(-4.44-2.09)	(-0.75-5.49)	(1.54-7.37)	(2.06-7.79)	(0.75-6.54)	(-0.39-5.51)
65-75	16198	18	-1.34	0.26	2.83	5.35**	5.51**	2.61	0.35
			(-4.98-2.43)	(-3.26-3.90)	(-0.54-6.31)	(2.20-8.60)	(2.42-8.68)	(-0.44-5.74)	(-2.62-3.41)
⩾75	48191	18	-1.95	1.53	3.19*	4.47**	4.64**	2.41	1.10
			(-4.77-0.95)	(-1.26-4.41)	(0.62-5.83)	(2.09-6.91)	(2.26-7.08)	(-0.01-4.88)	(-1.28-3.53)

[a] ER means excess risk, ER= relative risk (RR) – 1.

* P <0.05. ** P <0.01.

Figure 2 shows the single-day lag effects of cold temperature on different sub-population. The effects reached maximum in the lag 3 on population 1 while in the lag 4 on population 2. A 1°C decrease of cold temperature corresponded to a 4.87% (95%CI: 2.67%-7.12%) increase in hospital admissions for pneumonia on population 2 in lag 4 while it was 4.13% (95%CI: 0.77%-7.60%) on population 1 in lag 3. The effects on population 2 appear larger and more persistent than that on population 1.

Effect of cold period on pneumonia hospital admissions

Since cold temperature had large and persistent effects on pneumonia hospital

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admissions, we conducted a further analysis of cold temperature effects.

Figure 3 shows pneumonia hospital admissions varied with daily mean temperature, while cold period is related to hot spots for pneumonia hospital admissions. A 2 by 2 table to show the association between cold period and hot spots was provided in the Supplementary Table S1. We used cold period as a binary classification variable and fitted it in the GAM. The result showed that hospital admissions for pneumonia increased 15.99% (95%CI: 0.06%-34.46%) in the cold period.

Discussion

This time-series analysis showed that ambient temperature was significantly associated with hospital admissions for pneumonia, while relative humidity, precipitation and wind speed did not show the same. To our knowledge, this is the first to report the effects of meteorological factors on hospital admissions for pneumonia in China.

Generally, temperature appears V-, U-, or J-shape variations with mortality or morbidity, with OT corresponding to the lowest point in temperature mortality curve [8 24]. The present study showed a V-shape curve in the relationship between mean temperature and hospital admissions for pneumonia. Although the observation is consistent with the reported studies, we observed a different OT (13°C) in Shanghai, in comparison with 20°C in St. Paul [25], 16.5°C in Netherlands and 19°C in London [26]. Similar to the Beijing study [27], we found cold temperature presented larger

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effects. Other studies report that the peaks of respiratory syncytial virus and invasive pneumococcal disease were inversely correlated with temperature [28 29] and cold temperature was favorable to the spread of influenza virus [30], which might partly explain the association between cold temperature and hospital admissions for pneumonia.

We developed two different lag structures to examine the health effect of temperature. Statistically significant associations in both single-day and multi-day lag effects models for cold temperature were observed, whileneither single-day nor multi-day lag effects was found from hot temperature. These findings were slightly different from other studies on morbidity. For example, Braga et al. [11] described that the effect of cold temperatures persisted for days, whereas the effect of high temperatures was restricted to the day or the day before. Yu et al. [31] demonstrated that cold temperature had a lag time of 21 days, while hot temperature appears to exhibit short-term, acute effects.

Given the established importance of seasonal variation in mortality and morbidity excesses of respiratory diseases [32], several research studies have reported particularly on the relationship between extremely cold climatic episodes and mortality and morbidity, noting the tendency for a winter mortality increased after the occurrence of cold spells [33]. However, there is neither a uniform and agreed definition of a cold spell [34] nor a precise definition of the period for which such events should be studied. Our criteria for identifying cold period was to combine time and temperature thresholds, which is similar to other studies [35 36]. We found that

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there was a 15.99% increase of pneumonia hospital admissions in the cold period. Further studies are needed to explore if the cold temperature effects on pneumonia itself, or other factors.

The effects of cold temperature on different populations were observed. The effect of cold temperature on population 2 was larger and more persistent than that on population 1. Adverse effects of pneumonia hospitalizations of population 2 were larger (ER increased by 0.67% and 1.06% in lag 3 and lag 4 respectively) than that of population 1. The population 2 included employees and retirees while population 1 were mostly non-employed adults and students. The employees have more work pressure and have fewer opportunities to exercise, which might weaken their immunity; the elderly people are usually more susceptible to heat- or cold-related health risks [37 38]. The magnitude of the effects of temperature varied with gender and age. The OT for $\geqslant$65 age groups was higher than that for $<$65 age groups, indicating that elderly people had increased vulnerability to cold weather for pneumonia. Cold temperature only showed its effect on people older than 45. For residents in this age group, the ability to regulate body temperatures is reduced, and sweating thresholds are generally elevated in comparison with younger people [39].

Influenza epidemics, which generally occurs in the cold weather, have been accounted for as confounders in some studies[40]. Due to lack of reliable data, we didn't include the influenza epidemics as a control factor. However, the smooth function of time should have eliminated most such residual secular effects and there is no reason to expect an significant association of influenza with temperature (after

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controlling for time trend). In addition, many other studies have not included influenza as a confounder[12 41].

Our study has several limitations. First, we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure. This was expected to result in exposure misclassification. Secondly, our study only contained hospitalizations for pneumonia, but excluded less severe cases. Therefore, meteorological factors' effects on hospital admissions of pneumonia we observed may not be applied to the effects on the overall situation of pneumonia. Thirdly, the findings of this study should be cautious to generalize to other locations, particularly for places with different climates. In addition, the influence of ozone was not controlled for, because the data of ozone was not available.

CONCLUSION

We observed significant associations between meteorological factors and daily pneumonia hospital admissions in Shanghai. Cold temperature presented larger and more persistent effects and the magnitude of these effects of temperature varied with gender and age. Cold period had adverse effects on pneumonia hospital admissions. Prevention programs may be needed to reduce the impact of cold temperature such as developing a weather warning system within a wide public health context.

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Authors' contributions JX, LP and XY provided and organized data; YL, YZ and RC conducted the study, performed data analysis, and LY drafted the manuscript; WW, HK and DR reviewed and edited the manuscript, and WW conceived the study and contributed to the study design. All authors read and approved the final manuscript.

Competing interests The authors declare that they have no competing interests.

Data Sharing Statement: No additional data available

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Figure 1 Smoothing plots of meteorological factors against hospital admissions for pneumonia.

(a) mean temperature at lag 4; (b) relative humidity at lag 0; (c) precipitation at lag 0; (d) wind speed at lag 0. The solid lines indicate the estimated mean percentage of change in pneumonia hospital admissions, the dotted lines represent 95% confidence interval, and Log-risk represent Log(RR).

Figure 2 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in cold temperature using single-day lag structure by different sub-population.

Figure 3 Daily mean temperature and daily pneumonia hospital admissions. Cold period means a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C); "hot spot" for admissions means the day with daily pneumonia hospital admissions larger than the 75th percentile (85).

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References

1. World Health Organization (2008) The top 10 causes of death. Available: http://www.who.int/mediacentre/factsheets/fs310/en/ Accessed 19 Jan 2010
2. Rudan I, O'Brien KL, Nair H, et al. Epidemiology and etiology of childhood pneumonia in 2010: estimates of incidence, severe morbidity, mortality, underlying risk factors and causative pathogens for 192 countries. Journal of global health 2013;**3**(1):10401 doi: 10.7189/jogh.03.010401[published Online First: Epub Date]|.
3. Mathers C BC, and Moesgaard Iburg K. WHO. Global Burden of Disease in 2002: data sources, methods and results. Ref Type: Generic.
4. Polverino E Fau - Torres Marti A, Torres Marti A. Community-acquired pneumonia. (1827-1596 (Electronic))
5. Guan X, Silk BJ, Li W, et al. Pneumonia incidence and mortality in Mainland China: systematic review of Chinese and English literature, 1985-2008. PloS one 2010;**5**(7):e11721 doi: 10.1371/journal.pone.0011721[published Online First: Epub Date]|.
6. Li-xian HE, Xue-hua C. Contentions on the pathogenic spectrum of community-acquired pneumonia and the first experimental application of antibiotic agents. Chinese Journal of Practical Internal Medicine 2007;**27**(2):110-13 doi: 10.3969/j.issn.1005-2194.2007.02.012[published Online First: Epub Date]|.
7. Shea KM, Truckner RT, Weber RW, et al. Climate change and allergic disease. The Journal of allergy and clinical immunology 2008;**122**(3):443-53; quiz 54-5 doi: 10.1016/j.jaci.2008.06.032[published Online First: Epub Date]|.
8. Curriero FC, Heiner KS, Samet JM, et al. Temperature and mortality in 11 cities of the eastern United States. American journal of epidemiology 2002;**155**(1):80-7
9. Haines A, McMichael AJ, Epstein PR. Environment and health: 2. Global climate change and health. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 2000;**163**(6):729-34
10. Braga AL, Zanobetti A, Schwartz J. The time course of weather-related deaths. Epidemiology 2001;**12**(6):662-7
11. Braga AL, Zanobetti A, Schwartz J. The effect of weather on respiratory and cardiovascular deaths in 12 U.S. cities. Environmental health perspectives 2002;**110**(9):859-63
12. Farajzadeh M, Darand M. Analyzing the Influence of Air Temperature on the Cardiovascular, Respiratory and Stroke Mortality in Tehran. Iran J Environ Healt 2009;**6**(4):261-70
13. Liu L, Breitner S, Pan X, et al. Associations between air temperature and cardio-respiratory mortality in the urban area of Beijing, China: a time-series analysis. Environmental Health 2011;**10**(1):51
14. Huynen MM, Martens P, Schram D, et al. The impact of heat waves and cold

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spells on mortality rates in the Dutch population. Environmental health perspectives 2001;**109**(5):463-70
15. Ye Y, Zulu E, Mutisya M, et al. Seasonal pattern of pneumonia mortality among under-five children in Nairobi's informal settlements. The American journal of tropical medicine and hygiene 2009;**81**(5):770-5 doi: 10.4269/ajtmh.2009.09-0070[published Online First: Epub Date]|.
16. Egondi T, Kyobutungi C, Kovats S, et al. Time-series analysis of weather and mortality patterns in Nairobi's informal settlements. Global health action 2012;**5**:23-32 doi: 10.3402/gha.v5i0.19065[published Online First: Epub Date]|.
17. Lim YH, Hong YC, Kim H. Effects of diurnal temperature range on cardiovascular and respiratory hospital admissions in Korea. The Science of the total environment 2012;**417-418**:55-60 doi: 10.1016/j.scitotenv.2011.12.048[published Online First: Epub Date]|.
18. Onozuka D, Hashizume M, Hagihara A. Impact of weather factors on Mycoplasma pneumoniae pneumonia. Thorax 2009;**64**(6):507-11 doi: 10.1136/thx.2008.111237[published Online First: Epub Date]|.
19. Zeger SL, Irizarry R, Peng RD. On time series analysis of public health and biomedical data. Annual review of public health 2006;**27**:57-79 doi: 10.1146/annurev.publhealth.26.021304.144517[published Online First: Epub Date]|.
20. Cao J, Li W, Tan J, et al. Association of ambient air pollution with hospital outpatient and emergency room visits in Shanghai, China. The Science of the total environment 2009;**407**(21):5531-6 doi: 10.1016/j.scitotenv.2009.07.021[published Online First: Epub Date]|.
21. Guo Y, Barnett AG, Yu W, et al. A large change in temperature between neighbouring days increases the risk of mortality. PloS one 2011;**6**(2):e16511 doi: 10.1371/journal.pone.0016511[published Online First: Epub Date]|.
22. Kan H, London SJ, Chen H, et al. Diurnal temperature range and daily mortality in Shanghai, China. Environmental research 2007;**103**(3):424-31 doi: 10.1016/j.envres.2006.11.009[published Online First: Epub Date]|.
23. Hastie T, Tibshirani R. Generalized additive models for medical research. Statistical methods in medical research 1995;**4**(3):187-96
24. Kan HD, Jia J, Chen BH. Temperature and daily mortality in Shanghai: a time-series study. Biomedical and environmental sciences : BES 2003;**16**(2):133-9
25. Gouveia N, Hajat S, Armstrong B. Socioeconomic differentials in the temperature-mortality relationship in Sao Paulo, Brazil. International journal of epidemiology 2003;**32**(3):390-7
26. Patz JA, Campbell-Lendrum D, Holloway T, et al. Impact of regional climate change on human health. Nature 2005;**438**(7066):310-7 doi: 10.1038/nature04188[published Online First: Epub Date]|.
27. Mo Yun-zheng, Zheng Ya-an, Hui T, et al. Relationship between daily mean temperature and emergency department visits for respiratory diseases: a

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time-series analysis. (1671-167X (Print))
28. Yusuf S, Piedimonte G, Auais A, et al. The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus. Epidemiology and infection 2007;**135**(7):1077-90 doi: 10.1017/S095026880600776X[published Online First: Epub Date]|.
29. Murdoch DR, Jennings LC. Association of respiratory virus activity and environmental factors with the incidence of invasive pneumococcal disease. The Journal of infection 2009;**58**(1):37-46 doi: 10.1016/j.jinf.2008.10.011[published Online First: Epub Date]|.
30. Lowen Ac Fau - Mubareka S, Mubareka S Fau - Steel J, Steel J Fau - Palese P, et al. Influenza virus transmission is dependent on relative humidity and temperature. (1553-7374 (Electronic)) doi: D - NLM: PMC2034399 EDAT- 2007/10/24 09:00 MHDA- 2007/11/14 09:00 CRDT- 2007/10/24 09:00 PHST- 2007/07/11 [received] PHST- 2007/09/05 [accepted] AID - 07-PLPA-RA-0426 [pii] AID - 10.1371/journal.ppat.0030151 [doi] PST - ppublish[published Online First: Epub Date]|.
31. Yu W, Mengersen K, Hu W, et al. Assessing the relationship between global warming and mortality: Lag effects of temperature fluctuations by age and mortality categories. Environmental pollution 2011;**159**(7):1789-93 doi: http://dx.doi.org/10.1016/j.envpol.2011.03.039[published Online First: Epub Date]|.
32. Donaldson GC, Goldring JJ, Wedzicha JA. Influence of season on exacerbation characteristics in patients with COPD. Chest 2012;**141**(1):94-100 doi: 10.1378/chest.11-0281[published Online First: Epub Date]|.
33. Revich B, Shaposhnikov D. Excess mortality during heat waves and cold spells in Moscow, Russia. Occupational and environmental medicine 2008;**65**(10):691-6 doi: 10.1136/oem.2007.033944[published Online First: Epub Date]|.
34. Kysely J, Pokorna L, Kyncl J, et al. Excess cardiovascular mortality associated with cold spells in the Czech Republic. BMC public health 2009;**9**:19 doi: 10.1186/1471-2458-9-19[published Online First: Epub Date]|.
35. Ma W Fau - Yang C, Yang C Fau - Chu C, Chu C Fau - Li T, et al. The impact of the 2008 cold spell on mortality in Shanghai, China. (1432-1254 (Electronic))
36. Monteiro A Fau - Carvalho V, Carvalho V Fau - Gois J, Gois J Fau - Sousa C, et al. Use of "Cold Spell" indices to quantify excess chronic obstructive pulmonary disease (COPD) morbidity during winter (November to March 2000-2007): case study in Porto. (1432-1254 (Electronic))
37. Ye X, Wolff R, Yu W, et al. Ambient temperature and morbidity: a review of epidemiological evidence. Environmental health perspectives 2012;**120**(1):19-28 doi: 10.1289/ehp.1003198[published Online First: Epub Date]|.
38. Yu W, Mengersen K, Wang X, et al. Daily average temperature and mortality among the elderly: a meta-analysis and systematic review of epidemiological evidence. International journal of biometeorology 2012;**56**(4):569-81 doi:

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10.1007/s00484-011-0497-3[published Online First: Epub Date]|.

39. Kenney WL, Hodgson JL. Heat Tolerance, Thermoregulation and Aging. Sports Medicine 1987;**4**(6):446-56
40. Armstrong B. Models for the relationship between ambient temperature and daily mortality. Epidemiology 2006;**17**(6):624-31 doi: DOI 10.1097/01.ede.0000239732.50999.8f[published Online First: Epub Date]|.
41. Curriero FC, Heiner KS, Samet JM, et al. Temperature and mortality in 11 cities of the eastern United States. American journal of epidemiology 2002;**155**(1):80-87 doi: Doi 10.1093/Aje/155.1.80[published Online First: Epub Date]|.

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Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China: a time-series analysis

Yuan Liu[1], Haidong Kan[1,2], Jianming Xu[3,4], David Rogers[5], Li Peng[3,4], Xiaofang Ye[3,4], Renjie Chen[1], Yue Zhang[1], and Weibing Wang [1,2]

Running Title: Weather conditions and pneumonia hospitalization

[1]School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education), Fudan University, Shanghai, China

[2]Fudan Tyndall Centre, Shanghai, China

[3]Shanghai Center for Urban Environmental Meteorology, Shanghai, China

[4]Shanghai Key Laboratory of Meteorology and Health, Shanghai, China

[5]Health and Climate Foundation, USA

Correspondence: Weibing Wang, Department of Epidemiology, School of Public Health, and Fudan Tyndall Centre, Fudan University, 138 Yi Xue Yuan Road, Shanghai 200032, China; Tel: +86 21 54237811; Fax: +86 21 54237710; E-mail: wwb@fudan.edu.cn

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Abstract

Objectives To explore the association between weather conditions and hospital admissions for pneumonia in Shanghai.

Design A time-series analysis was performed for a period of 4 years (Januarary 2008-December 2011). Generalized additive model were used to calculate the relative risksyields to relative risks were also carried out.

Setting Shanghai, China.

Participants All daily hospital admissions for pneumonia were obtained from the Shanghai health insurance system betweenfrom January 1, 2008 to and December 31, 2011 (n=99,403).

Results The relationship between mean temperature and pneumonia hospital admissions followed a V-shaped curve, with the an optimum temperature (OT) at 13°C. When mean temperature was below the OT, a 1°C decrease corresponded to temperature was associated with a 4.88% (95% confidence interval [CI]: 2.71%-7.09%) and 5.34% (95% [CI]: 2.04%-8.74%) increase in pneumonia hospital admissions in lag 4 using single-day lag structure and lag 0-7 using multi-day lag structure. When mean temperature ≥ OT, no significant associations between temperature and pneumonia hospital admissions were found. The magnitude of the effects of temperature varied across gender and age groups. Hospitalizationsospital admissions for pneumonia increased 15.99% (95% CI: 0.06%-34.46%) in the cold period.

Conclusions Cold temperature may be one of the important risk factors for

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pneumonia hospitalizations. Prevention programs are needed to reduce the impact of cold temperature on pneumonia hospitalizations such as developing a weather warning system within a wide public health context.

Article summary

Article focus

- Pneumonia has been reported to be significantly influenced by meteorological factors
- The potential patterns of associations between weather conditions and pneumonia remain unclear in lots of countries especially in developing countries such as China.
- The study estimates the acute effects and time pattern~~lag influence~~ of meteorological factors on hospital admissions for pneumonia.

Key messages

- The relationship between mean temperature and pneumonia hospital admissions followed a V-shape~~d~~ curve, with ~~the~~ an optimum temperature (OT) at 13°C.
- Cold temperature ~~presented~~ caused larger and more persistent adverse effects and the magnitude of these effects of temperature varied with gender and age.

Strengths and limitations of this study

- Generalized additive models and two different lag structures were developed to explore the ~~the~~ possible interaction between meteorological factors and hospital admissions for pneumonia.
- we used available outdoor monitoring data of ambient meteorological factors

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derived from a monitoring station rather than measures of personal exposure. This is expected to result in exposure misclassification.

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Background

Despite the availability of safe and effective antibiotics and vaccines for treatment and prevention, pneumonia is still a leading cause of death worldwide [1 2]. Pneumonia, in general lower respiratory tract infections, accounts for 6.6% of all deaths globally [3]. In adults, the incidences varied between 1.6 and 11 per 1,000 adults in different countries, with hospitalization proportions ranging ~~between~~from 40% ~~and~~to 60% [4]. China is estimated to have 2.5 million pneumonia cases annually, of which 5% die from pneumonia-related diseases [5 6].

Climate change is potentially the largest global threat to human health [7]. In recent years, the association between meteorological factors and respiratory diseases has been observed extensively. Temperature has been reported to lead not only to direct deaths and illnesses but also to the aggravation of respiratory diseases [8 9]. Several studies have emphasized the relationships~~also found the association~~ between temperature and daily respiratory deaths [10 11]. Generally, the curves between temperature and daily respiratory deaths w~~as~~ere~~followed~~ V- or J-shape~~d~~ [12 13]. In addition, time series studies on respiratory mortality have suggested that temperature has lag effects up to 3 weeks after exposure [14]. As one of the major disease of respiratory diseases, pneumonia has been reported to be significantly influenced by meteorological factors [11 15-17]. However, ~~T~~the relationships varied across areas with different weather patterns and latitudes. In Japan, for example, case number of *Mycoplasma pneumoniae* pneumonia increased significantly with increased average temperature and relative humidity [18]. Contrarily~~However~~, neither

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hot nor cold temperatures had much effect on pneumonia death in hot cities in the USA [11].

Although pneumonia is recognized to result in substantial morbidity and mortality in some developed countries, the potential patterns of associations in other countries remain unclear~~,~~. ~~despite~~ Whereas the~~ir~~ populations of source limited countries ~~being~~may be more sensitive to changes in weather conditions because of their poorer public health infrastructure and ~~more~~ vulnerab~~le populations~~ility of the populations. We therefore performed a time-series analysis to estimate the acute effects and time pattern~~lag influence~~ of meteorological factors on hospital admissions for pneumonia. Better understanding of the possible interaction will provide relevant information for developing public health plans and risk assessments in ~~the~~ ambient environment.

Materials and methods

Data collection

Shanghai is the most populous city in China, located at the eastern tip of the Yangtze River Delta, at latitude 31°14'N and longitude 121°29'E. The city comprises of 19 urban/suburban districts and counties, with a total area of 6341 square kilometers, and had a population of over 23 million people by the end of 2010, of which 14 million are registered ~~population~~residents. The city features a moderate subtropical climate, with four distinct seasons and abundant rainfall.

For this analysis, the target population include~~s~~ all registered population living in Shanghai with urban residents' basic medical insurance (hereafter population 1) and ~~or~~ urban workers' basic medical insurance (hereafter population 2). Population 1

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~~includes~~ included children, students and non-employed adults ~~without~~ excluding those with new rural cooperative medical insurance. Population 2 ~~includes~~ included employees, retirees and other insuranced participants. Daily hospital admissions for pneumonia incurred by ~~residents~~ the two populations of Shanghai from January 1, 2008 to December 31, 2011 were collected from the Shanghai Municipal Medical Insurance System. All forms of pneumonia coded J12-J18 according to the International Classification of Diseases, the tenth version (ICD-10) were included for the analysis. Daily meteorological data (including mean temperature, relative humidity, precipitation and wind speed) were~~was~~ obtained from the Shanghai Center for Urban Environmental Meteorology. The weather data were measured at a fixed ~~meteorological~~meteorological station located in the Xuhui District of Shanghai. Due to the probable confounding effects that air pollution and suspended particles may have on temperature and pneumonia, air pollution data (sulfur dioxide (SO2), nitrogen dioxide (NO2) and PM10) were also obtained from the Shanghai Center for Urban Environmental Meteorology.

Statistical methods

The hospital admissions for pneumonia and meteorological factors were~~are~~ linked by the date and therefore can be analyzed with a time-series model [19]. As the number of daily hospital admissions is a type of low probability event and follows a Poisson distribution [20], a Poisson generalized additive model (GAM) approach was used to explore the association between meteorological factors and hospital admissions for pneumonia.

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In order to examine the effect of meteorological factors on hospital admissions for pneumonia, we controlled the potential confounders such as long-term trend, the day of the week (DOW) and air pollutants. We first fitted nonparametric smoothing terms for trend on days and dummy variable for DOW. Thereafter, four meteorological factors were introduced into the model to explore the relationship between meteorological factors and hospital admissions for pneumonia. The independent model is described below:

$\log E(Yt) = \alpha + s(\text{temperature}, df) + s(\text{relative humidity}, df) + s(\text{precipitation}, df) + s(\text{wind speed}, df) + s(\text{time}, df) + DOW + Z_t$

where E (Yt) denotes the estimated daily hospital admissions for pneumonia counted on day t; α is the intercept; s() denotes a regression spline function for nonlinear variables [21]; time is the number of calendar days on day t; Z_t indicates the pollutant concentrations on day t; df is the degrees of freedom. The partial autocorrelation function (PACF) [22] was used to select the degrees of freedom of time trends until the absolute values of the sum of PACF for lags up to 30 reached a minimum. Sensitivity analyses were performed to check whether the results were robust to the specification of parameters in the model. We found that the effects were stable when using 4 or 5 degrees of freedom per year for time. In addition, we modified degrees of freedom of smooth (4-5 df) for meteorological factors, and the estimates were not changed substantially. These sensitivity analyses resulted in the selection of 4 df per year to control for time trend and 4 df for meteorological factors. ~~In the present study, the degree of freedom per year for time trends was 4.~~ For meteorological factors, the

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selection of degrees of freedom was based on minimizing Akaike's Information Criterion (AIC) [23].

Additionally, we fitted linear terms for the mean temperature in the GAM ~~model~~ to explore the log-risk of daily hospital admissions for pneumonia associated with a unit increase of mean temperature. In examination of the lag effects of meteorological factors on hospital admissions for pneumonia, we developed two different lag structures: single-day lag and multi-day average starting from lag 0. For example, lag 0-1 stands for the 2-day moving average of current and previous day values. Relative risk (RR) ~~is~~refers to the ratio of the probability of an event occurring, while excess risk (ER) is the change in risk of a given activity. We used ER to evaluate the association between daily hospital admissions for pneumonia and a unit change of mean temperature.

We defined "cold period" as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) and "hot spot" for admissions as the days with daily pneumonia hospital admissions larger than the 75th percentile (85).

Data preparation and analysis were carried out using EXCEL 2010, whereas regression models were fitted using the statistical software R version 3.0.1 by using the mgcv package.

Results

Data description

Table 1 summarizes the basic statistics for our study. During the study period, totaling 1,461 days, 99,403 hospital admissions for pneumonia were recorded in

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Shanghai with , a daily mean of 68.0 (range, 9.0–195.0) per day. During the same time period, the mean daily temperature was 17.3°C (range, -3.4–35.7°C), reflecting the subtropical climate in Shanghai. A correlation matrix table for the meteorological and air pollution variables was provided in the Supplementary Table S2. The relative humidity, precipitation and wind speed averaged respectively at 69.4%, 30.9 mm and 2.9 m/s. Meanwhile, the mean daily concentrations of SO_2, NO_2 and PM_{10} were 35.6, 53.8 and 78.8 ug/m^3, respectively (Table 1).

Table 1 Summary statistics of daily hospital admissions for pneumonia and meteorological factors in Shanghai, 2008-2011

	Mean	SD	Min	P25	P75	Max
PHA[a]	68.0	27.3	9.0	50.0	85.0	195.0
Weather condition						
Mean temperature(°C)	17.3	9.2	-3.4	9.3	25.1	35.7
Relative humidity (%)	69.4	132.8	23.0	61.0	79.0	95.0
Precipitation(mm)	30.9	94.5	0.0	0.0	12.0	1284.0
Wind speed(m/s)	2.9	1.0	0.8	2.2	3.5	7.3
Air pollution						
SO_2(ug/m^3)	35.6	2019.6	110.6	221.8	43.2	1476.8
NO_2(ug/m^3)	543.8	210.5	12.4	39.4	64.5	1421.7
PM_{10}(ug/m^3)	798.8	532.8	12.2	454.5	10099.7	599.3

[a] PHA: pneumonia hospital admissions.

Daily hospital admissions and meteorological factors

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Figure 1 shows the exposure-response (E-R) relationships between daily hospital admissions for pneumonia, and mean temperature, relative humidity, precipitation and wind speed, after adjusting for long-term trend, DOW and the air pollutants in the GAM. The relationship between mean temperature and pneumonia hospital admissions followed a V-shaped, with a significant association (*P<0.001*) (Figure 1a). The optimum temperature (OT), corresponding to the lowest point in the E-R curve, was about 13°C.; Below the OT, as temperatures increased, the risk of hospital admissions for pneumonia decreased at temperatures below the OT and then reversed the trend above the OT. In addition, GAM model did not find find effectssignificance of relative humidity, precipitation, wind speed in associations between pneumonia hospital admissions and relative humidity, precipitation, wind speed.

Lag effects of temperature on daily hospital admissions

As there was a V-shaped relationship between mean temperature and hospital admissions for pneumonia, we stratified the data by temperature above ("hot temperature") or below ("cold temperature") the OT. Then linear terms for the daily mean temperature were fitted in GAM models (Table 2). In single-day lag structures, significant associations (*P<0.01*) between cold temperature and hospital admissions for pneumonia were found at lag 2 to lag 5. Effect from cold temperature appears larger than that from hot temperature. The multi-day metrics of mean temperature exposure also showed a larger effect of cold temperature than that of hot temperature. The effects by cold temperature peaked at lag 0-6, with statistically significance in lag

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0-3 to lag 0-9. At ~~the statistically significant maximum lag day (~~lag 0-6~~)~~, a 1°C decrease in the 7-day moving average of mean temperature corresponded to a 5.34% (95%CI: 2.04%-8.74%) increase in hospital admissions for pneumonia. However, no adverse ~~significant associations between~~effects of hot temperature ~~and hospital admissions for pneumonia~~ were found either in single-day or multi-day lag structures.

Table 2 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C change in mean temperature using alternative lags

Lag(d)[a]	OT(°C)	Cold temperature		Hot temperature	
		ER[b](%)	95%CI	ER(%)	95%CI
Single-day	13				
0		-2.05	-4.78~~0.61~~–0.61~~4.78~~	0.80	-0.90–2.51
1		0.43	-2.07–3.01	0.41	-1.26–2.11
2		3.06*	0.72–5.47	0.04	-1.62–1.74
3		4.85**	2.65–7.09	0.37	-1.28–2.04
4		4.88**	2.71–7.09	1.28	-0.36–2.96
5		2.85*	0.65–5.10	1.16	-0.48–2.83
6		1.39	-0.81–3.64	1.21	-0.41–2.86
Multi-day	13				
0-1		0.03	-2.62–2.75	0.13	-1.66–1.96
0-2		1.57	-1.26–4.48	-0.08	-1.96–1.83
0-3		3.67*	0.84–6.59	-0.38	-2.39–1.67
0-4		4.88**	1.89–7.95	-0.42	-2.53–1.75

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0-5	5.21**	2.14–8.36	-0.62	-2.93–1.75
0-6	5.34**	2.04–8.74	-0.94	-3.42–1.60
0-7	5.10**	1.53–8.79	-0.48	-3.22–2.33
0-8	4.48*	0.72–8.37	-0.67	-3.47–2.21
0-9	4.01*	0.03–8.15	0.15	-2.81–3.20
0-10	1.43	-0.26–3.16	1.02	-0.52–2.59

[a] Lag 0 to lag 6: single-day lag from 0 to 6; lag 0-1 to lag 0-10: multi-day average of mean temperature (lag 0-1 means 2-day moving average of current and previous day values).

[b] ER means excess risk, ER= relative risk (RR) – 1.

* P <0.05. ** P <0.01.

Effects of cold temperature on different types of people

Since no significant effects of hot temperature~~significant associations between hot temperature and~~ in hospital admissions for pneumonia were found, we focused further analysis on the association between cold temperature and hospital admissions for pneumonia. The association between hot temperature and hospital admissions for pneumonia was showed in Supplementary Table S3. Table 3 shows the different single-day lag effects of cold temperature on different sub-populations ~~stratified by gender and age~~. We found the adverse~~significant~~ effects of cold temperature in both males and females without a statistically significant difference by gender. The effects increased from lag 0, ~~were greatest~~with peaks in lag 3 for male and in lag 4 for female, and then declined. In age-specific analysis, cold temperature was positively

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associated with pneumonia hospital admissions and was statistically significant in the categories over age 45. The OT for people who aged above 65 was 18°C, which was larger than that for those younger than 65.

Table 3 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in cold temperature stratified by gender and age.

	No.	OT(°C)	ER[a] (%)					
			Lag0	Lag1	Lag2	Lag3	Lag4	Lag5
Gender								
Male	50696	13	-1.78 (-4.49-1.00)	0.48 (-2.14-3.18)	2.51* (0.07,5.02)	3.95** (1.64,6.31)	3.77** (1.50-6.09)	1.88** (-0.42-4.24)
Female	48706	13	-2.25 (-5.05-0.64)	0.38 (-2.38-3.23)	3.62* (0.99-6.31)	5.76** (3.34-8.24)	6.01** (3.62-8.46)	3.83** (1.41-6.32)
Age								
＜45	9567	13	-1.36 (-5.71-3.19)	-0.43 (-4.68-4.01)	2.23 (-1.83-6.12)	2.49 (-1.45-6.50)	3.47 (-0.28-7.35)	3.26 (-0.52-6.99)
45-65	25446	14	-2.81 (-6.09-0.59)	-1.23 (-4.44-2.09)	2.32 (-0.75-5.49)	4.42** (1.54-7.37)	4.88** (2.06-7.79)	3.61* (0.75-6.54)
65-75	16198	18	-1.34 (-4.98-2.43)	0.26 (-3.26-3.90)	2.83 (-0.54-6.31)	5.35** (2.20-8.60)	5.51** (2.42-8.68)	2.61 (-0.44-5.74)
⩾75	48191	18	-1.95 (-4.77-0.95)	1.53 (-1.26-4.41)	3.19* (0.62-5.83)	4.47** (2.09-6.91)	4.64** (2.26-7.08)	2.41 (-0.01-4.88)

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[a] ER means excess risk, ER= relative risk (RR) – 1.

* P <0.05. ** P <0.01.

Figure 2 shows the single-day lag effects of cold temperature on different sub-population. The effects reached maximum in the lag 3 on population 1 while in the lag 4 on population 2. A 1°C decrease of cold temperature corresponded to a 4.87% (95%CI: 2.67%-7.12%) increase in hospital admissions for pneumonia on population 2 in lag 4 while it was 4.13% (95%CI: 0.77%-7.60%) on population 1 in lag 3. The effects on population 2 appear larger and more persistent than that on population 1.

Effect of cold period on pneumonia hospital admissions

Since cold temperature had large and persistent effects on pneumonia hospital admissions, we conducted a further analysis of cold temperature effects. ~~We defined "cold period" as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) of temperature distribution during the study period; the "hot spot" for admissions refers to the day with daily pneumonia hospital admissions larger than the 75th percentile (85.0) of pneumonia hospital admissions.~~

Figure 3 shows pneumonia hospital admissions varied with daily mean temperature, while cold period is related~~consistently corresponding~~ to hot spots for pneumonia hospital admissions. A 2 by 2 table to show the association between cold period and hot spots was provided in the Supplementary Table S1. We used cold period as a binary classification variable and fitted it in the GAM ~~model~~. The result showed that hospital admissions for pneumonia increased 15.99% (95%CI: 0.06%-34.46%) in the cold period.

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Discussion

This time-series analysis showed that ambient temperature was significantly associated with hospital admissions for pneumonia ~~hospital admissions~~, while relative humidity, precipitation and wind speed did not show the same. To our knowledge, this is the first ~~effort~~ to report the effects of meteorological factors on hospital admissions for pneumonia in China.

Generally, temperature appears V-, U-, or J-shape~~d~~ variations with mortality or morbidity, with ~~optimum temperature~~OT corresponding to the lowest point in temperature mortality curve [8 24]. The present study showed ~~the relationship between mean temperature and pneumonia hospital admissions followed~~ a V-shape~~d~~ curve in the relationship between mean temperature and hospital admissions for pneumonia. Although the observation is consistent with the reported studies, ~~our study showed the~~we observed a different OT ~~in Shanghai was~~ (13°C) in Shanghai, in comparison with 20°C in St. Paul [25], 16.5°C in Netherlands and 19°C in London [26]. Similar to the Beijing study [27], we found cold temperature presented larger effects. Other studies report~~The fact~~ that the peaks of respiratory syncytial virus and invasive pneumococcal disease were inversely correlated with temperature [28 29] and cold temperature~~s and therefore~~ was~~ere~~ favorable to the spread of influenza virus [30], ~~those~~which might~~ay~~ partly explain the association ~~[30]~~ between cold temperature and hospital admissions for pneumonia.

We developed two different lag structures to examine the health effect of

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temperature. ~~We observed s~~Statistically significant associations in both single-day and multi-day lag effects models for cold temperature were observed, ~~but~~ while~~none in~~neither ~~both~~ single-day ~~and~~nor multi-day lag effects was found~~for~~ from hot temperature. ~~Whereas, the multi-day lag structures showed that the effects from of cold temperature lasted for 9 days.~~ Thi~~s~~ese~~e~~ findings were slightly different from other studies ~~of~~ on morbidity. For example, Braga et al. ~~study~~ [11] described~~found~~ that the effect of cold temperatures persisted for days, whereas the effect of high temperatures was restricted to the day or the day before. Yu et al.~~ research~~ [31] demonstrated that cold temperature had ~~21 days~~ a lag time of 21 days~~effects~~, while hot temperature appears to exhibit short-term, acute effects.

Given the established importance of seasonal variation in mortality and morbidity excesses of respiratory diseases [32], several research studies have reported particularly on the relationship between extremely cold climatic episodes and mortality and morbidity, noting the tendency for a winter mortality increased after the occurrence of cold spells [33]. However, there is neither a uniform and agreed definition of a cold spell [34] nor a precise definition of the period for which such events should be studied. Our criteria for identifying cold period was~~are~~ to combine time and temperature thresholds, which is similar to other studies [35 36]. We~~Our study~~ found that there was a 15.99% increase of pneumonia hospital admissions in the cold period~~. The cold period had adversesignificant effects on pneumonia hospital admissions~~. Further studies are needed to explore if the cold temperature effects on pneumonia ~~are from cold temperature~~ itself, ~~the cold period or their interaction~~or other

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factors.

~~Cold temperature~~ The effects of cold temperature on different ~~types of people~~populations were observed. The effect of cold temperature on population 2 was larger and more persistent than that on population 1. Adverse effects of ~~Hospital admissions for~~ pneumonia hospitalizations ~~in~~of population 2 ~~increased~~were larger ~~by~~(-ER increased by 0.67% and 1.06% ~~more~~in lag 3 and lag 4 respectively) than that ~~in~~ of population 1 ~~associated with a 1°C decrease of cold temperature in lag 3 and lag 4~~. ~~Probable reasons were that~~ The population 2 included employees and retirees ~~but~~ while ~~most people in~~ population 1 were mostly non-employed adults and students. The employees have more work pressure and have fewer opportunities to exercise, which might weaken their immunity~~. T~~; the elderly people are usually more susceptible to heat- or cold-related health risks [37 38]. The magnitude of the effects of temperature varied with gender and age. The OT for ⩾65 age groups was higher than that for ＜65 age groups, ~~which meant~~indicating that elderly people ~~were~~ had ~~more~~ increased vulnerab~~l~~ility~~e~~ to cold weather for pneumonia ~~hospital admissions~~. Cold temperature only ~~had~~ showed its effect on people older than 45. For residents ~~In~~in this age group, the ability to regulate body temperatures is reduced, and sweating thresholds are generally elevated in compar~~ed~~ison with younger people [39].

Influenza epidemics, which generally occurs in the cold weather, have been accounted for as confounders in some studies[40]. Due to lack of reliable data, we didn't include the influenza epidemics as a control factor. However, the smooth function of time should have eliminated most such residual secular effects and there

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is no reason to expect an significant association of influenza with temperature (after controlling for time trend). In addition, many other studies have not included influenza as a confounder[12 41].

Our study has several limitations. First, we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure. This wais expected to result in exposure misclassification. Secondly, our study only containeds ~~data~~ hospitalizations for pneumonia, but~~and~~ excludeds less severe cases. Therefore, meteorological factors' effects on hospital admissions of pneumonia we observed may not be applied to the effects on the overall situation ~~incidence~~ of pneumonia. Thirdly, the findings of this study should be cautious to generalize to other locations, particularly for places with different climates. In addition, the influence of ozone was not controlled for, because the data of ozone was not available.

CONCLUSION

We observed significant associations between meteorological factors and daily pneumonia hospital admissions in Shanghai. Cold temperature presented larger and more persistent effects and the magnitude of these effects of temperature varied with gender and age. Cold period had ~~significant effects~~adverse effects on pneumonia hospital admissions. Prevention programs may be needed to reduce the impact of cold temperature such as developing a weather warning system within a wide public health context.

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Competing interests The authors declare that they have no competing interests.

Authors' contributions JX, LP and XY provided and organized data; YL, YZ and RC conducted the study, performed data analysis, and LY drafted the manuscript; WW, HK and DR reviewed and edited the manuscript, and WW conceived the study and contributed to the study design. All authors read and approved the final manuscript.

Authors' information [1]School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education), Fudan University, Shanghai, China.[2]Fudan Tyndall Centre, Shanghai, China. [3]Shanghai Center for Urban Environmental Meteorology, Shanghai, China. [4]Shanghai Key Laboratory of Meteorology and Health, Shanghai, China. [5]Health and Climate Foundation, USA.

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References

1. World Health Organization (2008) The top 10 causes of death. Available: http://www.who.int/mediacentre/factsheets/fs310/en/ Accessed 19 Jan 2010
2. Rudan I, O'Brien KL, Nair H, et al. Epidemiology and etiology of childhood pneumonia in 2010: estimates of incidence, severe morbidity, mortality, underlying risk factors and causative pathogens for 192 countries. Journal of global health 2013;**3**(1):10401 doi: 10.7189/jogh.03.010401[published Online First: Epub Date]|.
3. Mathers C BC, and Moesgaard Iburg K. WHO. Global Burden of Disease in 2002: data sources, methods and results. Ref Type: Generic.
4. Polverino E Fau - Torres Marti A, Torres Marti A. Community-acquired pneumonia. (1827-1596 (Electronic))
5. Guan X, Silk BJ, Li W, et al. Pneumonia incidence and mortality in Mainland China: systematic review of Chinese and English literature, 1985-2008. PloS one 2010;**5**(7):e11721 doi: 10.1371/journal.pone.0011721[published Online First: Epub Date]|.
6. Li-xian HE, Xue-hua C. Contentions on the pathogenic spectrum of community-acquired pneumonia and the first experimental application of antibiotic agents. Chinese Journal of Practical Internal Medicine 2007;**27**(2):110-13 doi: 10.3969/j.issn.1005-2194.2007.02.012[published Online First: Epub Date]|.
7. Shea KM, Truckner RT, Weber RW, Peden DB. Climate change and allergic disease. The Journal of allergy and clinical immunology 2008;**122**(3):443-53; quiz 54-5 doi: 10.1016/j.jaci.2008.06.032[published Online First: Epub Date]|.
8. Curriero FC, Heiner KS, Samet JM, Zeger SL, Strug L, Patz JA. Temperature and mortality in 11 cities of the eastern United States. American journal of epidemiology 2002;**155**(1):80-7
9. Haines A, McMichael AJ, Epstein PR. Environment and health: 2. Global climate change and health. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 2000;**163**(6):729-34
10. Braga AL, Zanobetti A, Schwartz J. The time course of weather-related deaths. Epidemiology 2001;**12**(6):662-7
11. Braga AL, Zanobetti A, Schwartz J. The effect of weather on respiratory and cardiovascular deaths in 12 U.S. cities. Environmental health perspectives 2002;**110**(9):859-63
12. Farajzadeh M, Darand M. Analyzing the Influence of Air Temperature on the Cardiovascular, Respiratory and Stroke Mortality in Tehran. Iran J Environ Healt 2009;**6**(4):261-70
13. Liu L, Breitner S, Pan X, et al. Associations between air temperature and

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cardio-respiratory mortality in the urban area of Beijing, China: a time-series analysis. Environmental Health 2011;**10**(1):51

14. Huynen MM, Martens P, Schram D, Weijenberg MP, Kunst AE. The impact of heat waves and cold spells on mortality rates in the Dutch population. Environmental health perspectives 2001;**109**(5):463-70
15. Ye Y, Zulu E, Mutisya M, Orindi B, Emina J, Kyobutungi C. Seasonal pattern of pneumonia mortality among under-five children in Nairobi's informal settlements. The American journal of tropical medicine and hygiene 2009;**81**(5):770-5 doi: 10.4269/ajtmh.2009.09-0070[published Online First: Epub Date]|.
16. Egondi T, Kyobutungi C, Kovats S, Muindi K, Ettarh R, Rocklov J. Time-series analysis of weather and mortality patterns in Nairobi's informal settlements. Global health action 2012;**5**:23-32 doi: 10.3402/gha.v5i0.19065[published Online First: Epub Date]|.
17. Lim YH, Hong YC, Kim H. Effects of diurnal temperature range on cardiovascular and respiratory hospital admissions in Korea. The Science of the total environment 2012;**417-418**:55-60 doi: 10.1016/j.scitotenv.2011.12.048[published Online First: Epub Date]|.
18. Onozuka D, Hashizume M, Hagihara A. Impact of weather factors on Mycoplasma pneumoniae pneumonia. Thorax 2009;**64**(6):507-11 doi: 10.1136/thx.2008.111237[published Online First: Epub Date]|.
19. Zeger SL, Irizarry R, Peng RD. On time series analysis of public health and biomedical data. Annual review of public health 2006;**27**:57-79 doi: 10.1146/annurev.publhealth.26.021304.144517[published Online First: Epub Date]|.
20. Cao J, Li W, Tan J, et al. Association of ambient air pollution with hospital outpatient and emergency room visits in Shanghai, China. The Science of the total environment 2009;**407**(21):5531-6 doi: 10.1016/j.scitotenv.2009.07.021[published Online First: Epub Date]|.
21. Guo Y, Barnett AG, Yu W, et al. A large change in temperature between neighbouring days increases the risk of mortality. PloS one 2011;**6**(2):e16511 doi: 10.1371/journal.pone.0016511[published Online First: Epub Date]|.
22. Kan H, London SJ, Chen H, et al. Diurnal temperature range and daily mortality in Shanghai, China. Environmental research 2007;**103**(3):424-31 doi: 10.1016/j.envres.2006.11.009[published Online First: Epub Date]|.
23. Hastie T, Tibshirani R. Generalized additive models for medical research. Statistical methods in medical research 1995;**4**(3):187-96
24. Kan HD, Jia J, Chen BH. Temperature and daily mortality in Shanghai: a time-series study. Biomedical and environmental sciences : BES 2003;**16**(2):133-9
25. Gouveia N, Hajat S, Armstrong B. Socioeconomic differentials in the temperature-mortality relationship in Sao Paulo, Brazil. International journal of epidemiology 2003;**32**(3):390-7
26. Patz JA, Campbell-Lendrum D, Holloway T, Foley JA. Impact of regional climate

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change on human health. Nature 2005;**438**(7066):310-7 doi: 10.1038/nature04188[published Online First: Epub Date]|.

27. Mo Yun-zheng, Zheng Ya-an, Hui T, et al. Relationship between daily mean temperature and emergency department visits for respiratory diseases: a time-series analysis. (1671-167X (Print))
28. Yusuf S, Piedimonte G, Auais A, et al. The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus. Epidemiology and infection 2007;**135**(7):1077-90 doi: 10.1017/S095026880600776X[published Online First: Epub Date]|.
29. Murdoch DR, Jennings LC. Association of respiratory virus activity and environmental factors with the incidence of invasive pneumococcal disease. The Journal of infection 2009;**58**(1):37-46 doi: 10.1016/j.jinf.2008.10.011[published Online First: Epub Date]|.
30. Lowen Ac Fau - Mubareka S, Mubareka S Fau - Steel J, Steel J Fau - Palese P, Palese P. Influenza virus transmission is dependent on relative humidity and temperature. (1553-7374 (Electronic)) doi: D - NLM: PMC2034399 EDAT- 2007/10/24 09:00 MHDA- 2007/11/14 09:00 CRDT- 2007/10/24 09:00 PHST- 2007/07/11 [received] PHST- 2007/09/05 [accepted] AID - 07-PLPA-RA-0426 [pii] AID - 10.1371/journal.ppat.0030151 [doi] PST - ppublish[published Online First: Epub Date]|.
31. Yu W, Mengersen K, Hu W, Guo Y, Pan X, Tong S. Assessing the relationship between global warming and mortality: Lag effects of temperature fluctuations by age and mortality categories. Environmental pollution 2011;**159**(7):1789-93 doi: http://dx.doi.org/10.1016/j.envpol.2011.03.039[published Online First: Epub Date]|.
32. Donaldson GC, Goldring JJ, Wedzicha JA. Influence of season on exacerbation characteristics in patients with COPD. Chest 2012;**141**(1):94-100 doi: 10.1378/chest.11-0281[published Online First: Epub Date]|.
33. Revich B, Shaposhnikov D. Excess mortality during heat waves and cold spells in Moscow, Russia. Occupational and environmental medicine 2008;**65**(10):691-6 doi: 10.1136/oem.2007.033944[published Online First: Epub Date]|.
34. Kysely J, Pokorna L, Kyncl J, Kriz B. Excess cardiovascular mortality associated with cold spells in the Czech Republic. BMC public health 2009;**9**:19 doi: 10.1186/1471-2458-9-19[published Online First: Epub Date]|.
35. Ma W Fau - Yang C, Yang C Fau - Chu C, Chu C Fau - Li T, Li T Fau - Tan J, Tan J Fau - Kan H, Kan H. The impact of the 2008 cold spell on mortality in Shanghai, China. (1432-1254 (Electronic))
36. Monteiro A Fau - Carvalho V, Carvalho V Fau - Gois J, Gois J Fau - Sousa C, Sousa C. Use of "Cold Spell" indices to quantify excess chronic obstructive pulmonary disease (COPD) morbidity during winter (November to March 2000-2007): case study in Porto. (1432-1254 (Electronic))
37. Ye X, Wolff R, Yu W, Vaneckova P, Pan X, Tong S. Ambient temperature and morbidity: a review of epidemiological evidence. Environmental health

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perspectives 2012;**120**(1):19-28 doi: 10.1289/ehp.1003198[published Online First: Epub Date]|.

38. Yu W, Mengersen K, Wang X, et al. Daily average temperature and mortality among the elderly: a meta-analysis and systematic review of epidemiological evidence. International journal of biometeorology 2012;**56**(4):569-81 doi: 10.1007/s00484-011-0497-3[published Online First: Epub Date]|.
39. Kenney WL, Hodgson JL. Heat Tolerance, Thermoregulation and Aging. Sports Medicine 1987;**4**(6):446-56
40. Armstrong B. Models for the relationship between ambient temperature and daily mortality. Epidemiology 2006;**17**(6):624-31 doi: DOI 10.1097/01.ede.0000239732.50999.8f[published Online First: Epub Date]|.
41. Curriero FC, Heiner KS, Samet JM, Zeger SL, Strug L, Patz JA. Temperature and mortality in 11 cities of the eastern United States. American journal of epidemiology 2002;**155**(1):80-87 doi: Doi 10.1093/Aje/155.1.80[published Online First: Epub Date]|.

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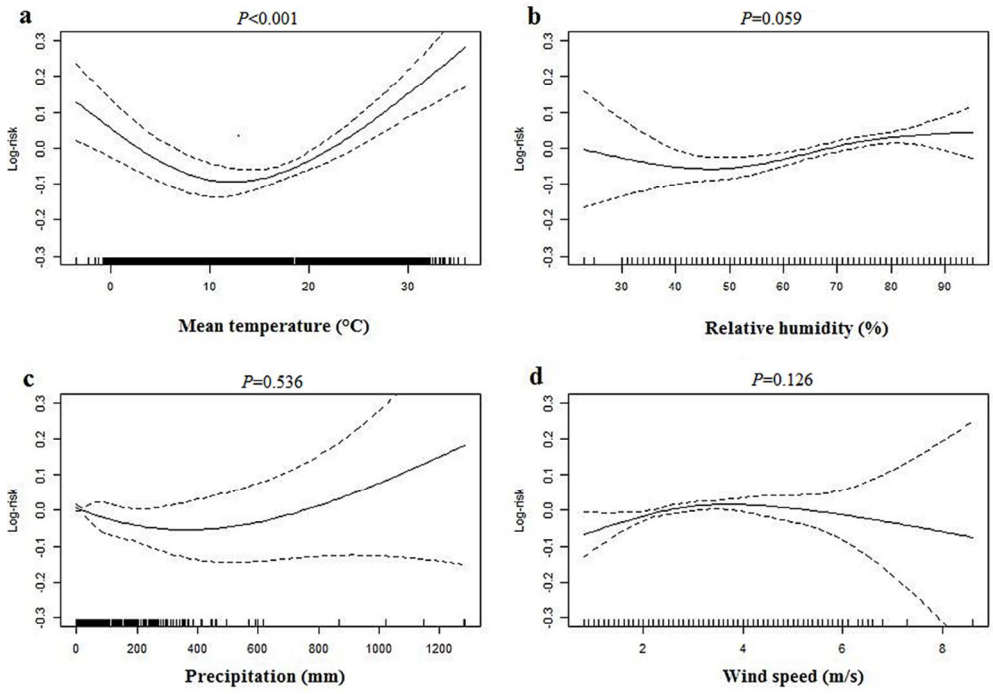

Figure 1 Smoothing plots of meteorological factors against hospital admissions for pneumonia. (a)mean temperature at lag 4; (b) relative humidity at lag 0; (c) precipitation at lag 0; (d) wind speed at lag 0. The solid lines indicate the estimated mean percentage of change in pneumonia hospital admissions, the dotted lines represent 95% confidence interval, and Log-risk represent Log(RR).
90x63mm (300 x 300 DPI)

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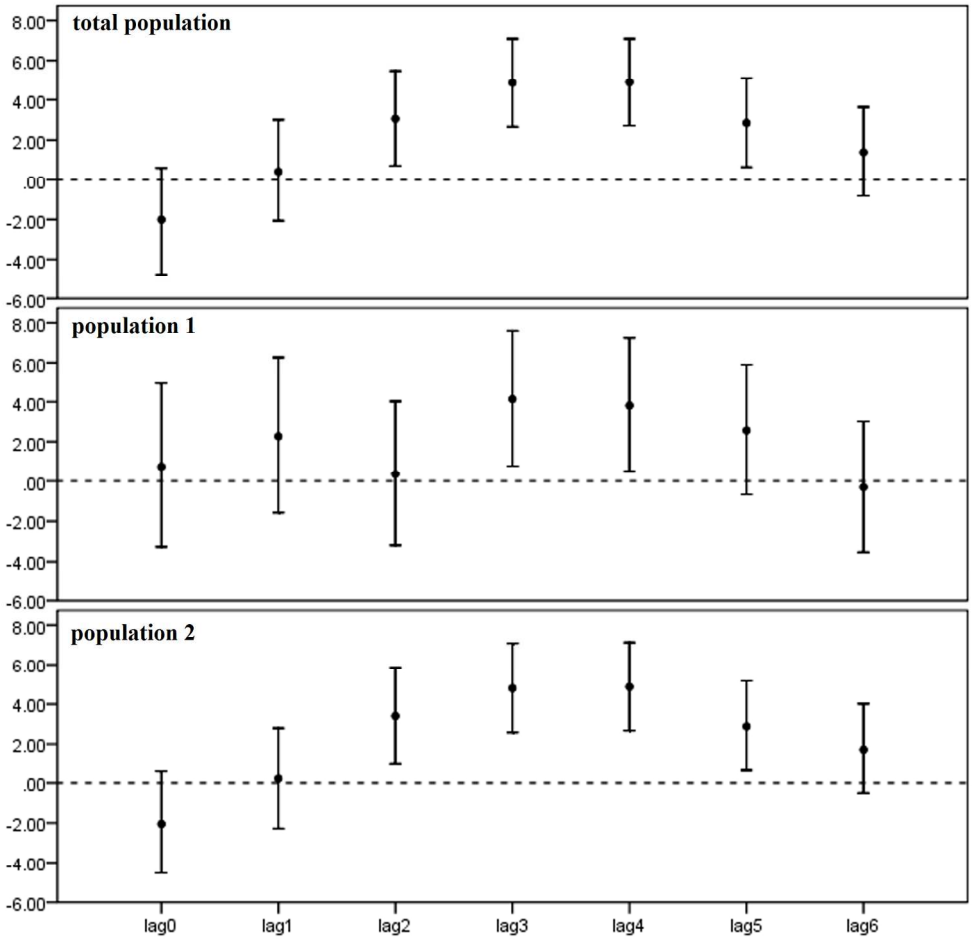

Figure 2 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in cold temperature using single-day lag structure by different sub-population.
173x169mm (300 x 300 DPI)

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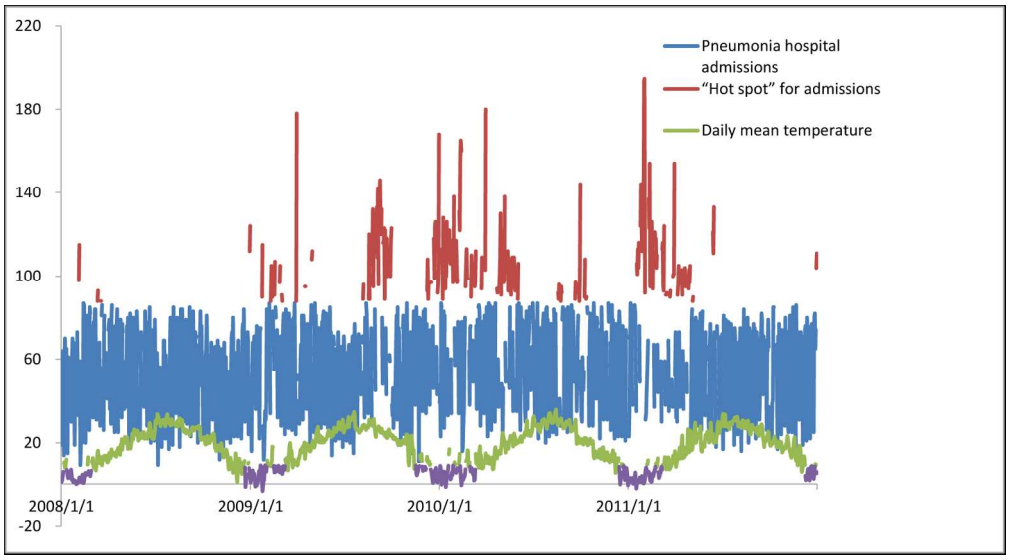

Figure 3 Daily mean temperature and daily pneumonia hospital admissions. Cold period means a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C); "hot spot" for admissions means the day with daily pneumonia hospital admissions larger than the 75th percentile (85).
173x95mm (300 x 300 DPI)

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Supplementary

Table S1 Association between cold period and hot spots

		Cold period[a]	
		0	1
Hot spots[b]	0	948	197
	1	219	97

[a]: a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) of temperature distribution during the study period.

[b]: the day with daily pneumonia hospital admissions larger than the 75th percentile (85.0) of pneumonia hospital admissions.

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Table S2 Pearson's correlations among the meteorological and air pollution variables.

	WS	Precipitation	RH	SO_2	NO_2	PM_{10}
Temperature	0.049**	0.116**	0.207**	-0.468**	-0.402**	-0.197**
WS		0.041**	-0.043**	-0.247**	-0.464**	-0.255**
Precipitation			0.368**	-0.211**	-0.165**	-0.179**
RH				-0.383**	-0.192**	-0.305**
SO_2					0.756**	0.624**
NO_2						0.664**

WS: wind speed; RH: relative humidity.

** P<0.001

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Table S3 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in hot temperature stratified by gender and age.

	No.	OT(°C)	ER[a] (%)						
			Lag0	Lag1	Lag2	Lag3	Lag4	Lag5	Lag6
Gender									
Male	50696	13	0.44	0.07	-0.76	-0.92	-0.14	0.29	0.20
			(-1.41-2.32)	(-1.67-1.84)	(-2.43-0.94)	(-2.55-0.73)	(-1.77-1.51)	(-1.35-1.95)	(-1.45-1.87)
Female	48706	13	1.17	-0.89	-1.18	-0.26	-0.02	-0.52	-1.15
			(-0.77-3.16)	(-2.69-0.93)	(-2.91-0.59)	(-1.96-1.47)	(-1.72-1.71)	(-2.21-1.20)	(-2.84-0.57)
Age									
＜45	9567	13	-1.36	-1.88	-2.37	-3.11*	0.17	0.76	0.54
			(-4.51-1.90)	(-4.84-1.18)	(-5.23-0.59)	(-5.88--0.27)	(-2.65-3.08)	(-2.08-3.69)	(-2.30-3.47)
45-65	25446	14	0.68	-0.35	-1.99	-1.39	-0.61	-0.21	-0.43
			(-1.68-3.11)	(-2.55-1.90)	(-4.09-0.16)	(-3.45-0.71)	(-2.67-1.50)	(-2.28-1.90)	(-2.50-1.69)
65-75	16198	18	0.70	-1.95	-1.48	0.49	0.33	-0.58	-1.43
			(-1.92-3.40)	(-4.36-0.52)	(-3.84-0.93)	(-1.84-2.87)	(-1.98-2.70)	(-2.87-1.77)	(-3.72-0.92)
⩾75	48191	18	1.29	0.37	0.01	-0.08	-0.03	-0.09	-0.39
			(-0.61-3.23)	(-1.41-2.18)	(-1.71-1.76)	(-1.75-1.62)	(-1.70-1.67)	(-1.76-1.60)	(-2.06-1.32)

[a] ER means excess risk, ER= relative risk (RR) – 1.

* P <0.05

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China: a time-series analysis	1
		(b) **Objectives** To explore the association between weather conditions and hospital admissions for pneumonia in Shanghai. **Design** A time-series analysis was performed for a period of 4 years (January 2008-December 2011). Generalized additive model were used to calculate the relative risks. **Conclusions** Cold temperature may be one of the important risk factors for pneumonia hospitalizations.	2
Introduction			
Background/rationale	2	Although pneumonia is recognized to result in substantial morbidity and mortality in some developed countries, the potential patterns of associations in other countries remain unclear	4-5
Objectives	3	pneumonia has been reported to be significantly influenced by meteorological factors.	4-5
Methods			
Study design	4	A time-series analysis	6
Setting	5	Shanghai, China	5
Participants	6	All daily hospital admissions for pneumonia were obtained from the Shanghai health insurance system from January 1, 2008 to December 31, 2011 (n=99,403).	5
Variables	7	The target population included all registered population living in Shanghai with urban residents' basic medical insurance (hereafter population 1) and urban workers' basic medical insurance (hereafter population 2). we stratified the data by temperature above ("hot temperature") or below ("cold temperature") the optimum temperature (OT). We defined "cold period" as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) of temperature distribution during the study period; the "hot spot" for admissions refers to the days with daily pneumonia hospital admissions larger than the 75th percentile (85) of pneumonia hospital admissions.	5, 9, 13
Data sources/ measurement	8*	Daily hospital admissions for pneumonia incurred by residents of Shanghai from January 1, 2008 to December 31, 2011 were collected from the Shanghai Municipal Medical Insurance System. Daily meteorological data (including mean temperature, relative humidity, precipitation and wind speed) were obtained from the Shanghai Center for Urban	6

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		Environmental Meteorology. The weather data were measured at a fixed meteorological station located in the Xuhui District of Shanghai.	
Bias	9	We controlled the potential confounders such as long-term trend, the day of the week (DOW) and air pollutants.	*6*
Study size	10	The target population included all registered population living in Shanghai with urban residents' basic medical insurance or urban workers' basic medical insurance.	5
Quantitative variables	11	The hospital admissions for pneumonia and meteorological factors were linked by the date and therefore can be analyzed with a time-series model.	6
Statistical methods	12	(a) a Poisson generalized additive model (GAM) approach was used to explore the association between meteorological factors and hospital admissions for pneumonia.	6
		(b) The partial autocorrelation function (PACF) was used to select the degrees of freedom of time trends	7
Results			
Participants	13*	All daily hospital admissions for pneumonia were obtained from the Shanghai health insurance system from January 1, 2008 to December 31, 2011 (n=99,403).	8
Descriptive data	14*	During the study period, totalling 1,461 days, 99,403 hospital admissions for pneumonia were recorded in Shanghai, a daily mean of 68 (range, 9–195). During the same time period, the mean daily temperature was 17.3°C (range, -3.4–35.7°C), reflecting the subtropical climate in Shanghai. The relative humidity, precipitation and wind speed averaged respectively at 69%, 30.9 mm and 2.9 m/s. Meanwhile, the mean daily concentrations of SO2, NO2 and PM10 were 36, 54 and 79 ug/m3, respectively	8
Outcome data	15*	Optimum temperature (OT), excess risk (ER)	9-12
Main results	16	(a) The relationship between mean temperature and pneumonia hospital admissions followed a V-shape curve, with an optimum temperature (OT) at 13°C. When mean temperature was below the OT, a 1°C decrease corresponded to a 4.88% (95% confidence interval [CI]: 2.71%-7.09%) and 5.34% (95% CI: 2.04%-8.74%) increase in pneumonia hospital admissions in lag 4 using single-day lag structure and lag 0-7 using multi-day lag structure. Hospitalization for pneumonia increased 15.99% (95% CI: 0.06%-34.46%) in the cold period.	9, 10, 13
		(b) We defined "cold period" as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) of temperature distribution during the study period; the "hot spot" for admissions refers to the days with daily pneumonia hospital admissions larger than the 75th percentile (85) of pneumonia hospital admissions.	13
Other analyses	17	Cold temperature effects on different types of people were observed. The magnitude of the effects of temperature varied with gender and age.	11, 12
Discussion			
Key results	18	The relationship between mean temperature and pneumonia hospital admissions followed a V-shape curve, with the	13, 14, 15

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		optimum temperature (OT) at 13°C. Cold temperature presented larger and more persistent effects and the magnitude of the effects of temperature varied with gender and age.	
Limitations	19	we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure. This is expected to result in exposure misclassification.	16
Interpretation	20	Cold temperature may be one of the important risk factors for pneumonia hospitalizations.	16
Generalisability	21	The setting of this study was Shanghai, China. Although the results are consistent with the lots of other reported studies, it should be careful of generalizability to other populations.	
Other information			
Funding	22	This study was funded by the Global Environment Change Research in Fudan University (Grant No. EZH1829007/003), and the program of Key Discipline Development of Public Health of Shanghai (Grant No. 12GWZX0101).	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China: a time-series analysis

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Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China: a time-series analysis

Yuan Liu[1], Haidong Kan[1,2], Jianming Xu[3,4], David Rogers[5], Li Peng[3,4], Xiaofang Ye[3,4], Renjie Chen[1], Yue Zhang[1], and Weibing Wang [1,2]

Running Title: Weather conditions and pneumonia hospitalization

[1]School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education), Fudan University, Shanghai, China

[2]Fudan Tyndall Centre, Shanghai, China

[3]Shanghai Center for Urban Environmental Meteorology, Shanghai, China

[4]Shanghai Key Laboratory of Meteorology and Health, Shanghai, China

[5]Health and Climate Foundation, USA

Correspondence: Weibing Wang, Department of Epidemiology, School of Public Health, and Fudan Tyndall Centre, Fudan University, 138 Yi Xue Yuan Road, Shanghai 200032, China; Tel: +86 21 54237811; Fax: +86 21 54237710; E-mail: wwb@fudan.edu.cn

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Abstract

Objectives To explore the association between weather conditions and hospital admissions for pneumonia in Shanghai.

Design A time-series analysis was performed for a period of 4 years (January 2008-December 2011). Generalized additive model were used to calculate the relative risks.

Setting Shanghai, China.

Participants All daily hospital admissions for pneumonia were obtained from the Shanghai health insurance system between January 1, 2008 and December 31, 2011 (n=99,403).

Results The relationship between mean temperature and pneumonia hospital admissions followed a V-shaped curve, with an optimum temperature (OT) at 13°C. When mean temperature was below the OT, a 1°C decrease corresponded to a 4.88% (95% confidence interval [CI]: 2.71%-7.09%) and 5.34% (95% CI: 2.04%-8.74%) increase in pneumonia hospital admissions in lag 4 using single-day lag structure and lag 0-7 using multi-day lag structure. When mean temperature ≥ OT, no adverse effects from temperature on pneumonia hospital admissions were found. The magnitude of the effects of temperature varied across gender and age groups. Hospitalizations for pneumonia increased by 15.99% (95% CI: 0.06%-34.46%) in the cold period.

Conclusions Cold temperature may be one of the important risk factors for pneumonia hospitalizations. Prevention programs are needed to reduce the impact of

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cold temperature on pneumonia hospitalizations such as developing a weather warning system within a wide public health context.

Article summary

Article focus

- Pneumonia has been reported to be influenced by meteorological factors
- The potential patterns of associations between weather conditions and pneumonia remain unclear in lots of countries especially in developing countries such as China.
- The study estimates the acute effects and time pattern of meteorological factors on hospital admissions for pneumonia.

Key messages

- The relationship between mean temperature and pneumonia hospital admissions followed a V-shaped curve, with an optimum temperature (OT) at 13°C.
- Cold temperature caused larger and more persistent adverse effects and the magnitude of these effects of temperature varied with gender and age.

Strengths and limitations of this study

- Generalized additive models and two different lag structures were developed to explore the possible interaction between meteorological factors and hospital admissions for pneumonia.
- we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure. This is expected to result in exposure misclassification.

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Background

Despite the availability of safe and effective antibiotics and vaccines for treatment and prevention, pneumonia is still a leading cause of death worldwide [1 2]. Pneumonia, in general lower respiratory tract infections, accounts for 6.6% of all deaths globally [3]. In adults, the incidences varied between 1.6 and 11 per 1,000 adults in different countries, with hospitalization proportions ranging from 40% to 60% [4]. China is estimated to have 2.5 million pneumonia cases annually, of which 5% die from pneumonia-related diseases [5 6].

Climate change is potentially the largest global threat to human health [7]. In recent years, the association between meteorological factors and respiratory diseases has been observed extensively. Temperature has been reported to lead not only to direct deaths and illnesses but also to the aggravation of respiratory diseases [8 9]. Several studies have emphasized the relationships between temperature and daily respiratory deaths [10 11]. Generally, the curves between temperature and daily respiratory deaths were V- or J-shaped [12 13]. In addition, time series studies on respiratory mortality have suggested that temperature has lag effects up to 3 weeks after exposure [14]. As one of the major disease of respiratory diseases, pneumonia has been reported to be influenced by meteorological factors [11 15-17]. However, the relationships varied across areas with different weather patterns and latitudes. In Japan, for example, case number of *Mycoplasma pneumoniae* pneumonia increased with increased average temperature and relative humidity [18]. Contrarily, neither hot nor cold temperatures had much effect on pneumonia death in hot cities in the USA

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[11].

Although pneumonia is recognized to result in substantial morbidity and mortality in some developed countries, the potential patterns of associations in other countries remain unclear. Whereas the populations of source limited countries may be more sensitive to changes in weather conditions because of their poorer public health infrastructure and vulnerability of the populations. We therefore performed a time-series analysis to estimate the acute effects and time pattern of meteorological factors on hospital admissions for pneumonia. Better understanding of the possible interaction will provide relevant information for developing public health plans and risk assessments in ambient environment.

Materials and methods

Data collection

Shanghai is the most populous city in China, located at the eastern tip of the Yangtze River Delta, at latitude 31°14'N and longitude 121°29'E. The city comprises of 19 urban/suburban districts and counties, with a total area of 6341 square kilometers, and had a population of over 23 million people by the end of 2010, of which 14 million are registered residents. The city features a moderate subtropical climate, with four distinct seasons and abundant rainfall.

For this analysis, the target population included all registered population living in Shanghai with urban residents' basic medical insurance (hereafter population 1) and urban workers' basic medical insurance (hereafter population 2). Population 1 included children, students and non-employed adults excluding those with new rural

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cooperative medical insurance. Population 2 included employees, retirees and other insuranced participants. Daily hospital admissions for pneumonia incurred by the two populations of Shanghai from January 1, 2008 to December 31, 2011 were collected from the Shanghai Municipal Medical Insurance System. All forms of pneumonia coded J12-J18 according to the International Classification of Diseases, the tenth version (ICD-10) were included for the analysis. Daily meteorological data (including mean temperature, relative humidity, precipitation and wind speed) were obtained from the Shanghai Center for Urban Environmental Meteorology. The weather data were measured at a fixed meteorological station located in the Xuhui District of Shanghai. Due to the probable confounding effects that air pollution and suspended particles may have on temperature and pneumonia, air pollution data (sulfur dioxide (SO2), nitrogen dioxide (NO2) and particulate matter with particle size below 10 microns (PM10)) were also obtained from the Shanghai Center for Urban Environmental Meteorology.

Patient records/information was de-identified prior to analysis; daily aggregated counts for hospitalizations were calculated and used to implement the final analysis. The authors did not access to individual patient information prior to data anonymization and aggregation, and therefore there was no individual interaction with patients in this study.

Statistical methods

The hospital admissions for pneumonia and meteorological factors were linked

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by the date and therefore can be analyzed with a time-series model [19]. As the number of daily hospital admissions is a type of low probability event and follows a Poisson distribution [20], a Poisson generalized additive model (GAM) approach was used to explore the association between meteorological factors and hospital admissions for pneumonia.

In order to examine the effect of meteorological factors on hospital admissions for pneumonia, we controlled the potential confounders such as long-term trend, the day of the week (DOW) and air pollutants. We first fitted nonparametric smoothing terms for trend on days and dummy variable for DOW. Thereafter, four meteorological factors were introduced into the model to explore the relationship between meteorological factors and hospital admissions for pneumonia. The independent model is described below:

$$\log E(Yt) = \alpha + s(\text{temperature}, df) + s(\text{relative humidity}, df) + s(\text{precipitation}, df) + s(\text{wind speed}, df) + s(\text{time}, df) + DOW + Z_t$$

where E (Yt) denotes the estimated daily hospital admissions for pneumonia counted on day t; α is the intercept; s() denotes a regression spline function for nonlinear variables [21]; time is the number of calendar days on day t; Z_t indicates the pollutant concentrations on day t; df is the degrees of freedom. The partial autocorrelation function (PACF) [22] was used to select the degrees of freedom of time trends until the absolute values of the sum of PACF for lags up to 30 reached a minimum. Sensitivity analyses were performed to check whether the results were robust to the specification of parameters in the model. We found that the effects were stable when

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using 4 or 5 degrees of freedom per year for time. In addition, we modified degrees of freedom of the smoothing spline (4-5 df) for the meteorological factors, and the estimates were not changed substantially. These sensitivity analyses resulted in the selection of 4 df per year to control for time trend and 4 df for meteorological factors. For meteorological factors, the selection of degrees of freedom was based on minimizing Akaike's Information Criterion (AIC) [23].

Additionally, we fitted linear terms for the mean temperature in the GAM to explore the log-risk of daily hospital admissions for pneumonia associated with a unit increase of mean temperature. In examination of the lag effects of meteorological factors on hospital admissions for pneumonia, we developed two different lag structures: single-day lag and multi-day average starting from lag 0. For example, lag 0-1 stands for the 2-day moving average of current and previous day values. Relative risk (RR) refers to the ratio of the probability of an event occurring, while excess risk (ER) is the change in risk of a given activity. We used ER to evaluate the association between daily hospital admissions for pneumonia and a unit change of mean temperature. The value of ER is equal to the value of RR minus one.

We defined "cold period" as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) and "hot spot" for admissions as the days with daily pneumonia hospital admissions larger than the 75th percentile (85).

Data preparation and analysis were carried out using EXCEL 2010, whereas regression models were fitted using the statistical software R version 3.0.1 by using the mgcv package.

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Results

Data description

Table 1 summarizes the basic statistics for our study. During the study period, totaling 1,461 days, 99,403 hospital admissions for pneumonia were recorded in Shanghai with a mean of 68 (range, 9–195) per day. During the same time period, the mean daily temperature was 17.3°C (range, -3.4–35.7°C), reflecting the subtropical climate in Shanghai. A correlation matrix table for the meteorological and air pollution variables was provided in the Supplementary Table S2.

Table 1 Summary statistics of daily hospital admissions for pneumonia and meteorological factors in Shanghai, 2008-2011

	Mean	SD	Min	P25	P75	Max
PHA[a]	68	27	9	50	85	195
Weather condition						
Mean temperature(°C)	17.3	9.2	-3.4	9.3	25.1	35.7
Relative humidity (%)	69	13	23	61	79	95
Precipitation(mm)	30.9	94.5	0.0	0.0	12.0	1284.0
Wind speed(m/s)	2.9	1.0	0.8	2.2	3.5	7.3
Air pollution						
SO_2(ug/m^3)	36	20	11	22	43	147
NO_2(ug/m^3)	54	21	12	39	65	142
PM_{10}(ug/m^3)	79	53	12	45	100	599

[a] PHA: pneumonia hospital admissions.

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Daily hospital admissions and meteorological factors

Figure 1 shows the exposure-response (E-R) relationships between daily hospital admissions for pneumonia, and mean temperature, relative humidity, precipitation and wind speed, after adjusting for long-term trend, DOW and the air pollutants in the GAM. The relationship between mean temperature and pneumonia hospital admissions followed a V-shape (*P<0.001*) (Figure 1a). The optimum temperature (OT), corresponding to the lowest point in the E-R curve, was about 13°C. Below the OT, as temperatures increased, the risk of hospital admissions for pneumonia decreased and then reversed the trend above the OT. In addition, relative humidity, precipitation, and wind speed had no effects on pneumonia hospital admissions.

Lag effects of temperature on daily hospital admissions

As there was a V-shaped relationship between mean temperature and hospital admissions for pneumonia, we stratified the data by temperature above ("hot temperature") or below ("cold temperature") the OT. Then linear terms for the daily mean temperature were fitted in GAMs (Table 2). In single-day lag structures, associations (*P<0.01*) between cold temperature and hospital admissions for pneumonia were found at lag 2 to lag 5. Effect from cold temperature appears larger than that from hot temperature. The multi-day metrics of mean temperature exposure also showed a larger effect of cold temperature than that of hot temperature. The effects by cold temperature peaked at lag 0-6. At lag 0-6, a 1°C decrease in the 7-day moving average of mean temperature corresponded to a 5.34% (95%CI: 2.04%-8.74%) increase in hospital admissions for pneumonia. However, no adverse

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effects of hot temperature were found either in single-day or multi-day lag structures.

Table 2 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C change in mean temperature using alternative lags

Lag(d)[a]	OT(°C)	Cold temperature		Hot temperature	
		ER[b](%)	95%CI	ER(%)	95%CI
Single-day	13				
0		-2.05	-4.78–0.61	0.80	-0.90–2.51
1		0.43	-2.07–3.01	0.41	-1.26–2.11
2		3.06*	0.72–5.47	0.04	-1.62–1.74
3		4.85**	2.65–7.09	0.37	-1.28–2.04
4		4.88**	2.71–7.09	1.28	-0.36–2.96
5		2.85*	0.65–5.10	1.16	-0.48–2.83
6		1.39	-0.81–3.64	1.21	-0.41–2.86
Multi-day	13				
0-1		0.03	-2.62–2.75	0.13	-1.66–1.96
0-2		1.57	-1.26–4.48	-0.08	-1.96–1.83
0-3		3.67*	0.84–6.59	-0.38	-2.39–1.67
0-4		4.88**	1.89–7.95	-0.42	-2.53–1.75
0-5		5.21**	2.14–8.36	-0.62	-2.93–1.75
0-6		5.34**	2.04–8.74	-0.94	-3.42–1.60
0-7		5.10**	1.53–8.79	-0.48	-3.22–2.33
0-8		4.48*	0.72–8.37	-0.67	-3.47–2.21

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0-9	4.01*	0.03–8.15	0.15	-2.81–3.20
0-10	1.43	-0.26–3.16	1.02	-0.52–2.59

[a] Lag 0 to lag 6: single-day lag from 0 to 6; lag 0-1 to lag 0-10: multi-day average of mean temperature (lag 0-1 means 2-day moving average of current and previous day values).

[b] ER means excess risk, ER= relative risk (RR) – 1.

* P <0.05. ** P <0.01.

Effects of cold temperature on different types of people

Since no adverse effects of hot temperature in hospital admissions for pneumonia were found, we focused further analysis on the association between cold temperature and hospital admissions for pneumonia. The association between hot temperature and hospital admissions for pneumonia was showed in Supplementary Table S3. Table 3 shows the different single-day lag effects of cold temperature on different sub-populations. We found the adverse effects of cold temperature in both males and females. The effects increased from lag 0, with peaks in lag 3 for male and in lag 4 for female, and then declined. In age-specific analysis, cold temperature was positively associated with pneumonia hospital admissions and has adverse effects in the categories over age 45. The OT for people who aged above 65 was 18°C, which was larger than that for those younger than 65.

Table 3 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in cold temperature stratified by gender and age.

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	No.	OT(°C)	ER[a] (%)						
			Lag0	Lag1	Lag2	Lag3	Lag4	Lag5	Lag6
Gender									
Male	50696	13	-1.78	0.48	2.51*	3.95**	3.77**	1.88**	0.57
			(-4.49-1.00)	(-2.14-3.18)	(0.07,5.02)	(1.64,6.31)	(1.50-6.09)	(-0.42-4.24)	(-1.70-2.89)
Female	48706	13	-2.25	0.38	3.62*	5.76**	6.01**	3.83**	2.22
			(-5.05-0.64)	(-2.38-3.23)	(0.99-6.31)	(3.34-8.24)	(3.62-8.46)	(1.41-6.32)	(-0.23-4.73)
Age									
＜45	9567	13	-1.36	-0.43	2.23	2.49	3.47	3.26	1.46
			(-5.71-3.19)	(-4.68-4.01)	(-1.83-6.12)	(-1.45-6.50)	(-0.28-7.35)	(-0.52-6.99)	(-2.26-5.32)
45-65	25446	14	-2.81	-1.23	2.32	4.42**	4.88**	3.61*	2.52
			(-6.09-0.59)	(-4.44-2.09)	(-0.75-5.49)	(1.54-7.37)	(2.06-7.79)	(0.75-6.54)	(-0.39-5.51)
65-75	16198	18	-1.34	0.26	2.83	5.35**	5.51**	2.61	0.35
			(-4.98-2.43)	(-3.26-3.90)	(-0.54-6.31)	(2.20-8.60)	(2.42-8.68)	(-0.44-5.74)	(-2.62-3.41)
⩾75	48191	18	-1.95	1.53	3.19*	4.47**	4.64**	2.41	1.10
			(-4.77-0.95)	(-1.26-4.41)	(0.62-5.83)	(2.09-6.91)	(2.26-7.08)	(-0.01-4.88)	(-1.28-3.53)

[a] ER means excess risk, ER= relative risk (RR) – 1.

* P <0.05. ** P <0.01.

Figure 2 shows the single-day lag effects of cold temperature on different sub-population. The effects reached maximum in the lag 3 on population 1 while in the lag 4 on population 2. A 1°C decrease of cold temperature corresponded to a 4.87% (95%CI: 2.67%-7.12%) increase in hospital admissions for pneumonia on population

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2 in lag 4 while it was 4.13% (95%CI: 0.77%-7.60%) on population 1 in lag 3. The effects on population 2 appear larger and more persistent than that on population 1.

Effect of cold period on pneumonia hospital admissions

Since cold temperature had large and persistent effects on pneumonia hospital admissions, we conducted a further analysis of cold temperature effects.

Figure 3 shows pneumonia hospital admissions varied with daily mean temperature, while cold period is related to hot spots for pneumonia hospital admissions. A 2 by 2 table to show the association between cold period and hot spots was provided in the Supplementary Table S1. We used cold period as a binary classification variable and fitted it in the GAM. The result showed that hospital admissions for pneumonia increased by 15.99% (95%CI: 0.06%-34.46%) in the cold period.

Discussion

This time-series analysis showed that ambient temperature was associated with hospital admissions for pneumonia, while relative humidity, precipitation and wind speed did not show the same. To our knowledge, this is the first to report the effects of meteorological factors on hospital admissions for pneumonia in China.

Generally, temperature appears V-, U-, or J-shaped variations with mortality or morbidity, with OT corresponding to the lowest point in temperature mortality curve [8 24]. The present study showed a V-shaped curve in the relationship between mean temperature and hospital admissions for pneumonia. Although the observation is

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consistent with the reported studies, we observed a different OT (13°C) in Shanghai, in comparison with 20°C in St. Paul [25], 16.5°C in Netherlands and 19°C in London [26]. Similar to the Beijing study [27], we found cold temperature presented larger effects. Other studies report that the peaks of respiratory syncytial virus and invasive pneumococcal disease were inversely correlated with temperature [28 29] and cold temperature was favorable to the spread of influenza virus [30], which might partly explain the association between cold temperature and hospital admissions for pneumonia.

We developed two different lag structures to examine the health effect of temperature. Adverse effects in both single-day and multi-day lag effects models for cold temperature were observed, while neither single-day nor multi-day lag effects were found from hot temperature. These findings were slightly different from other studies on morbidity. For example, Braga et al. [11] described that the effect of cold temperatures persisted for days, whereas the effect of high temperatures was restricted to the day or the day before. Yu et al. [31] demonstrated that cold temperature had a lag time of 21 days, while hot temperature appears to exhibit short-term, acute effects.

Given the established importance of seasonal variation in mortality and morbidity excesses of respiratory diseases [32], several research studies have reported particularly on the relationship between extremely cold climatic episodes and mortality and morbidity, noting the tendency for a winter mortality increased after the occurrence of cold spells [33]. However, there is neither a uniform and agreed

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definition of a cold spell [34] nor a precise definition of the period for which such events should be studied. Our criterion for identifying cold period was to combine time and temperature thresholds, which is similar to other studies [35 36]. We found that there was a 15.99% increase of pneumonia hospital admissions in the cold period. Further studies are needed to explore if the cold temperature effects on pneumonia are from cold temperature itself, or from other factors.

The effects of cold temperature on different populations were observed. The effect of cold temperature on population 2 was larger and more persistent than that on population 1. Adverse effects of pneumonia hospitalizations of population 2 were larger (ER increased by 0.67% and 1.06% in lag 3 and lag 4 respectively) than that of population 1. The population 2 included employees and retirees while population 1 was mostly non-employed adults and students. The employees have more work pressure and have fewer opportunities to exercise, which might weaken their immunity; the elderly people are usually more susceptible to heat- or cold-related health risks [37 38]. The magnitude of the effects of temperature varied with gender and age. The OT for $\geqslant$65 age groups was higher than that for $<$65 age groups, indicating that elderly people had increased vulnerability to cold weather for pneumonia. Cold temperature only showed its effect on people older than 45. For residents in this age group, the ability to regulate body temperatures is reduced, and sweating thresholds are generally elevated in comparison with younger people [39].

Influenza epidemics, which generally occurs in the cold weather, have been accounted for as confounders in some studies[40]. Due to lack of reliable data, we

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didn't include the influenza epidemics as a control factor. However, the smooth function of time should have eliminated most such residual secular effects and there is no reason to expect an association of influenza with temperature (after controlling for time trend). In addition, many other studies have not included influenza as a confounder [12 41].

Our study has several limitations. First, we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure. This was expected to result in exposure misclassification. Secondly, our study only contained hospitalizations for pneumonia, but excluded less severe cases. Therefore, meteorological factors' effects on hospital admissions of pneumonia we observed may not be applied to the effects on the overall situation of pneumonia. Thirdly, the findings of this study should be treated cautiously when generalized to other locations, particularly for places with different climates. In addition, the influence of ozone was not controlled for, because the data of ozone was not available.

CONCLUSION

We observed associations between meteorological factors and daily pneumonia hospital admissions in Shanghai. Cold temperature presented larger and more persistent effects and the magnitude of these effects of temperature varied with gender and age. Cold period had adverse effects on pneumonia hospital admissions. Prevention programs may be needed to reduce the impact of cold temperature such as developing a weather warning system within a wide public health context.

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Authors' contributions JX, LP and XY provided and organized data; YL, YZ and RC conducted the study, performed data analysis, and LY drafted the manuscript; WW, HK and DR reviewed and edited the manuscript, and WW conceived the study and contributed to the study design. All authors read and approved the final manuscript.

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References

1. World Health Organization (2008) The top 10 causes of death. Available: http://www.who.int/mediacentre/factsheets/fs310/en/ Accessed 19 Jan 2010
2. Rudan I, O'Brien KL, Nair H, et al. Epidemiology and etiology of childhood pneumonia in 2010: estimates of incidence, severe morbidity, mortality, underlying risk factors and causative pathogens for 192 countries. Journal of global health 2013;**3**(1):10401 doi: 10.7189/jogh.03.010401[published Online First: Epub Date]|.
3. Mathers C BC, and Moesgaard Iburg K. WHO. Global Burden of Disease in 2002: data sources, methods and results. Ref Type: Generic.
4. Polverino E Fau - Torres Marti A, Torres Marti A. Community-acquired pneumonia. (1827-1596 (Electronic))
5. Guan X, Silk BJ, Li W, et al. Pneumonia incidence and mortality in Mainland China: systematic review of Chinese and English literature, 1985-2008. PloS one 2010;**5**(7):e11721 doi: 10.1371/journal.pone.0011721[published Online First: Epub Date]|.
6. Li-xian HE, Xue-hua C. Contentions on the pathogenic spectrum of community-acquired pneumonia and the first experimental application of antibiotic agents. Chinese Journal of Practical Internal Medicine 2007;**27**(2):110-13 doi: 10.3969/j.issn.1005-2194.2007.02.012[published Online First: Epub Date]|.
7. Shea KM, Truckner RT, Weber RW, et al. Climate change and allergic disease. The Journal of allergy and clinical immunology 2008;**122**(3):443-53; quiz 54-5 doi: 10.1016/j.jaci.2008.06.032[published Online First: Epub Date]|.
8. Curriero FC, Heiner KS, Samet JM, et al. Temperature and mortality in 11 cities of the eastern United States. American journal of epidemiology 2002;**155**(1):80-7
9. Haines A, McMichael AJ, Epstein PR. Environment and health: 2. Global climate change and health. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 2000;**163**(6):729-34
10. Braga AL, Zanobetti A, Schwartz J. The time course of weather-related deaths. Epidemiology 2001;**12**(6):662-7
11. Braga AL, Zanobetti A, Schwartz J. The effect of weather on respiratory and cardiovascular deaths in 12 U.S. cities. Environmental health perspectives 2002;**110**(9):859-63
12. Farajzadeh M, Darand M. Analyzing the Influence of Air Temperature on the Cardiovascular, Respiratory and Stroke Mortality in Tehran. Iran J Environ Healt 2009;**6**(4):261-70
13. Liu L, Breitner S, Pan X, et al. Associations between air temperature and cardio-respiratory mortality in the urban area of Beijing, China: a time-series analysis. Environmental Health 2011;**10**(1):51
14. Huynen MM, Martens P, Schram D, et al. The impact of heat waves and cold

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spells on mortality rates in the Dutch population. Environmental health perspectives 2001;**109**(5):463-70
15. Ye Y, Zulu E, Mutisya M, et al. Seasonal pattern of pneumonia mortality among under-five children in Nairobi's informal settlements. The American journal of tropical medicine and hygiene 2009;**81**(5):770-5 doi: 10.4269/ajtmh.2009.09-0070[published Online First: Epub Date]|.
16. Egondi T, Kyobutungi C, Kovats S, et al. Time-series analysis of weather and mortality patterns in Nairobi's informal settlements. Global health action 2012;**5**:23-32 doi: 10.3402/gha.v5i0.19065[published Online First: Epub Date]|.
17. Lim YH, Hong YC, Kim H. Effects of diurnal temperature range on cardiovascular and respiratory hospital admissions in Korea. The Science of the total environment 2012;**417-418**:55-60 doi: 10.1016/j.scitotenv.2011.12.048[published Online First: Epub Date]|.
18. Onozuka D, Hashizume M, Hagihara A. Impact of weather factors on Mycoplasma pneumoniae pneumonia. Thorax 2009;**64**(6):507-11 doi: 10.1136/thx.2008.111237[published Online First: Epub Date]|.
19. Zeger SL, Irizarry R, Peng RD. On time series analysis of public health and biomedical data. Annual review of public health 2006;**27**:57-79 doi: 10.1146/annurev.publhealth.26.021304.144517[published Online First: Epub Date]|.
20. Cao J, Li W, Tan J, et al. Association of ambient air pollution with hospital outpatient and emergency room visits in Shanghai, China. The Science of the total environment 2009;**407**(21):5531-6 doi: 10.1016/j.scitotenv.2009.07.021[published Online First: Epub Date]|.
21. Guo Y, Barnett AG, Yu W, et al. A large change in temperature between neighbouring days increases the risk of mortality. PloS one 2011;**6**(2):e16511 doi: 10.1371/journal.pone.0016511[published Online First: Epub Date]|.
22. Kan H, London SJ, Chen H, et al. Diurnal temperature range and daily mortality in Shanghai, China. Environmental research 2007;**103**(3):424-31 doi: 10.1016/j.envres.2006.11.009[published Online First: Epub Date]|.
23. Hastie T, Tibshirani R. Generalized additive models for medical research. Statistical methods in medical research 1995;**4**(3):187-96
24. Kan HD, Jia J, Chen BH. Temperature and daily mortality in Shanghai: a time-series study. Biomedical and environmental sciences : BES 2003;**16**(2):133-9
25. Gouveia N, Hajat S, Armstrong B. Socioeconomic differentials in the temperature-mortality relationship in Sao Paulo, Brazil. International journal of epidemiology 2003;**32**(3):390-7
26. Patz JA, Campbell-Lendrum D, Holloway T, et al. Impact of regional climate change on human health. Nature 2005;**438**(7066):310-7 doi: 10.1038/nature04188[published Online First: Epub Date]|.
27. Mo Yun-zheng, Zheng Ya-an, Hui T, et al. Relationship between daily mean temperature and emergency department visits for respiratory diseases: a

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time-series analysis. (1671-167X (Print))
28. Yusuf S, Piedimonte G, Auais A, et al. The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus. Epidemiology and infection 2007;**135**(7):1077-90 doi: 10.1017/S095026880600776X[published Online First: Epub Date]|.
29. Murdoch DR, Jennings LC. Association of respiratory virus activity and environmental factors with the incidence of invasive pneumococcal disease. The Journal of infection 2009;**58**(1):37-46 doi: 10.1016/j.jinf.2008.10.011[published Online First: Epub Date]|.
30. Lowen Ac Fau - Mubareka S, Mubareka S Fau - Steel J, Steel J Fau - Palese P, et al. Influenza virus transmission is dependent on relative humidity and temperature. (1553-7374 (Electronic)) doi: D - NLM: PMC2034399 EDAT- 2007/10/24 09:00 MHDA- 2007/11/14 09:00 CRDT- 2007/10/24 09:00 PHST- 2007/07/11 [received] PHST- 2007/09/05 [accepted] AID - 07-PLPA-RA-0426 [pii] AID - 10.1371/journal.ppat.0030151 [doi] PST - ppublish[published Online First: Epub Date]|.
31. Yu W, Mengersen K, Hu W, et al. Assessing the relationship between global warming and mortality: Lag effects of temperature fluctuations by age and mortality categories. Environmental pollution 2011;**159**(7):1789-93 doi: http://dx.doi.org/10.1016/j.envpol.2011.03.039[published Online First: Epub Date]|.
32. Donaldson GC, Goldring JJ, Wedzicha JA. Influence of season on exacerbation characteristics in patients with COPD. Chest 2012;**141**(1):94-100 doi: 10.1378/chest.11-0281[published Online First: Epub Date]|.
33. Revich B, Shaposhnikov D. Excess mortality during heat waves and cold spells in Moscow, Russia. Occupational and environmental medicine 2008;**65**(10):691-6 doi: 10.1136/oem.2007.033944[published Online First: Epub Date]|.
34. Kysely J, Pokorna L, Kyncl J, et al. Excess cardiovascular mortality associated with cold spells in the Czech Republic. BMC public health 2009;**9**:19 doi: 10.1186/1471-2458-9-19[published Online First: Epub Date]|.
35. Ma W Fau - Yang C, Yang C Fau - Chu C, Chu C Fau - Li T, et al. The impact of the 2008 cold spell on mortality in Shanghai, China. (1432-1254 (Electronic))
36. Monteiro A Fau - Carvalho V, Carvalho V Fau - Gois J, Gois J Fau - Sousa C, et al. Use of "Cold Spell" indices to quantify excess chronic obstructive pulmonary disease (COPD) morbidity during winter (November to March 2000-2007): case study in Porto. (1432-1254 (Electronic))
37. Ye X, Wolff R, Yu W, et al. Ambient temperature and morbidity: a review of epidemiological evidence. Environmental health perspectives 2012;**120**(1):19-28 doi: 10.1289/ehp.1003198[published Online First: Epub Date]|.
38. Yu W, Mengersen K, Wang X, et al. Daily average temperature and mortality among the elderly: a meta-analysis and systematic review of epidemiological evidence. International journal of biometeorology 2012;**56**(4):569-81 doi:

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10.1007/s00484-011-0497-3[published Online First: Epub Date]|.
39. Kenney WL, Hodgson JL. Heat Tolerance, Thermoregulation and Aging. Sports Medicine 1987;**4**(6):446-56
40. Armstrong B. Models for the relationship between ambient temperature and daily mortality. Epidemiology 2006;**17**(6):624-31 doi: DOI 10.1097/01.ede.0000239732.50999.8f[published Online First: Epub Date]|.
41. Curriero FC, Heiner KS, Samet JM, et al. Temperature and mortality in 11 cities of the eastern United States. American journal of epidemiology 2002;**155**(1):80-87 doi: Doi 10.1093/Aje/155.1.80[published Online First: Epub Date]|.

FIGURE LEGENDS

Figure 1 Smoothing plots of meteorological factors against hospital admissions for pneumonia.

(a) mean temperature at lag 4; (b) relative humidity at lag 0; (c) precipitation at lag 0; (d) wind speed at lag 0. The solid lines indicate the estimated mean percentage of change in pneumonia hospital admissions, the dotted lines represent 95% confidence interval, and Log-risk represent Log(RR).

Figure 2 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in cold temperature using single-day lag structure by different sub-population.

Figure 3 Daily mean temperature and daily pneumonia hospital admissions. Cold period means a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C); “hot spot” for admissions means the day with daily pneumonia hospital admissions larger than the 75th percentile (85).

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Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China: a time-series analysis

Yuan Liu[1], Haidong Kan[1,2], Jianming Xu[3,4], David Rogers[5], Li Peng[3,4], Xiaofang Ye[3,4], Renjie Chen[1], Yue Zhang[1], and Weibing Wang [1,2]

Running Title: Weather conditions and pneumonia hospitalization

[1]School of Public Health and Key Laboratory of Public Health Safety (Ministry of Education), Fudan University, Shanghai, China

[2]Fudan Tyndall Centre, Shanghai, China

[3]Shanghai Center for Urban Environmental Meteorology, Shanghai, China

[4]Shanghai Key Laboratory of Meteorology and Health, Shanghai, China

[5]Health and Climate Foundation, USA

Correspondence: Weibing Wang, Department of Epidemiology, School of Public Health, and Fudan Tyndall Centre, Fudan University, 138 Yi Xue Yuan Road, Shanghai 200032, China; Tel: +86 21 54237811; Fax: +86 21 54237710; E-mail: wwb@fudan.edu.cn

Keywords: pneumonia, temperature, time-series, generalized additive model

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Abstract

Objectives To explore the association between weather conditions and hospital admissions for pneumonia in Shanghai.

Design A time-series analysis was performed for a period of 4 years (January 2008-December 2011). Generalized additive model were used to calculate the relative risks.

Setting Shanghai, China.

Participants All daily hospital admissions for pneumonia were obtained from the Shanghai health insurance system between January 1, 2008 and December 31, 2011 (n=99,403).

Results The relationship between mean temperature and pneumonia hospital admissions followed a V-shaped curve, with an optimum temperature (OT) at 13°C. When mean temperature was below the OT, a 1°C decrease corresponded to a 4.88% (95% confidence interval [CI]: 2.71%-7.09%) and 5.34% (95% CI: 2.04%-8.74%) increase in pneumonia hospital admissions in lag 4 using single-day lag structure and lag 0-7 using multi-day lag structure. When mean temperature ≥ OT, no adverse effects ~~significant associations between~~ from temperature ~~and~~ on pneumonia hospital admissions were found. The magnitude of the effects of temperature varied across gender and age groups. Hospitalizations for pneumonia increased by 15.99% (95% CI: 0.06%-34.46%) in the cold period.

Conclusions Cold temperature may be one of the important risk factors for pneumonia hospitalizations. Prevention programs are needed to reduce the impact of

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cold temperature on pneumonia hospitalizations such as developing a weather warning system within a wide public health context.

Article summary

Article focus

- Pneumonia has been reported to be ~~significantly~~ influenced by meteorological factors
- The potential patterns of associations between weather conditions and pneumonia remain unclear in lots of countries especially in developing countries such as China.
- The study estimates the acute effects and time pattern of meteorological factors on hospital admissions for pneumonia.

Key messages

- The relationship between mean temperature and pneumonia hospital admissions followed a V-shaped curve, with an optimum temperature (OT) at 13°C.
- Cold temperature caused larger and more persistent adverse effects and the magnitude of these effects of temperature varied with gender and age.

Strengths and limitations of this study

- Generalized additive models and two different lag structures were developed to explore the possible interaction between meteorological factors and hospital admissions for pneumonia.
- we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure.

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This is expected to result in exposure misclassification.

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Background

Despite the availability of safe and effective antibiotics and vaccines for treatment and prevention, pneumonia is still a leading cause of death worldwide [1 2]. Pneumonia, in general lower respiratory tract infections, accounts for 6.6% of all deaths globally [3]. In adults, the incidences varied between 1.6 and 11 per 1,000 adults in different countries, with hospitalization proportions ranging from 40% to 60% [4]. China is estimated to have 2.5 million pneumonia cases annually, of which 5% die from pneumonia-related diseases [5 6].

Climate change is potentially the largest global threat to human health [7]. In recent years, the association between meteorological factors and respiratory diseases has been observed extensively. Temperature has been reported to lead not only to direct deaths and illnesses but also to the aggravation of respiratory diseases [8 9]. Several studies have emphasized the relationships between temperature and daily respiratory deaths [10 11]. Generally, the curves between temperature and daily respiratory deaths were V- or J-shaped [12 13]. In addition, time series studies on respiratory mortality have suggested that temperature has lag effects up to 3 weeks after exposure [14]. As one of the major disease of respiratory diseases, pneumonia has been reported to be ~~significantly~~ influenced by meteorological factors [11 15-17]. However, the relationships varied across areas with different weather patterns and latitudes. In Japan, for example, case number of *Mycoplasma pneumoniae* pneumonia increased ~~significantly~~ with increased average temperature and relative humidity [18]. Contrarily, neither hot nor cold temperatures had much effect on

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pneumonia death in hot cities in the USA [11].

Although pneumonia is recognized to result in substantial morbidity and mortality in some developed countries, the potential patterns of associations in other countries remain unclear. Whereas the populations of source limited countries may be more sensitive to changes in weather conditions because of their poorer public health infrastructure and vulnerability of the populations. We therefore performed a time-series analysis to estimate the acute effects and time pattern of meteorological factors on hospital admissions for pneumonia. Better understanding of the possible interaction will provide relevant information for developing public health plans and risk assessments in ambient environment.

Materials and methods

Data collection

Shanghai is the most populous city in China, located at the eastern tip of the Yangtze River Delta, at latitude 31°14'N and longitude 121°29'E. The city comprises of 19 urban/suburban districts and counties, with a total area of 6341 square kilometers, and had a population of over 23 million people by the end of 2010, of which 14 million are registered residents. The city features a moderate subtropical climate, with four distinct seasons and abundant rainfall.

For this analysis, the target population included all registered population living in Shanghai with urban residents' basic medical insurance (hereafter population 1) and urban workers' basic medical insurance (hereafter population 2). Population 1 included children, students and non-employed adults excluding those with new rural

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cooperative medical insurance. Population 2 included employees, retirees and other insuranced participants. Daily hospital admissions for pneumonia incurred by the two populations of Shanghai from January 1, 2008 to December 31, 2011 were collected from the Shanghai Municipal Medical Insurance System. All forms of pneumonia coded J12-J18 according to the International Classification of Diseases, the tenth version (ICD-10) were included for the analysis. Daily meteorological data (including mean temperature, relative humidity, precipitation and wind speed) were obtained from the Shanghai Center for Urban Environmental Meteorology. The weather data were measured at a fixed meteorological station located in the Xuhui District of Shanghai. Due to the probable confounding effects that air pollution and suspended particles may have on temperature and pneumonia, air pollution data (sulfur dioxide (SO2), nitrogen dioxide (NO2) and particulate matter with particle size below 10 microns (PM10)) were also obtained from the Shanghai Center for Urban Environmental Meteorology.

Patient records/information was de-identified prior to analysis; daily aggregated counts for hospitalizations were calculated and used to implement the final analysis. The authors did not access to individual patient information prior to data anonymization and aggregation, and therefore there was no individual interaction with patients in this study.

Statistical methods

The hospital admissions for pneumonia and meteorological factors were linked

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by the date and therefore can be analyzed with a time-series model [19]. As the number of daily hospital admissions is a type of low probability event and follows a Poisson distribution [20], a Poisson generalized additive model (GAM) approach was used to explore the association between meteorological factors and hospital admissions for pneumonia.

In order to examine the effect of meteorological factors on hospital admissions for pneumonia, we controlled the potential confounders such as long-term trend, the day of the week (DOW) and air pollutants. We first fitted nonparametric smoothing terms for trend on days and dummy variable for DOW. Thereafter, four meteorological factors were introduced into the model to explore the relationship between meteorological factors and hospital admissions for pneumonia. The independent model is described below:

$$\log E(Yt) = \alpha + s(\text{temperature}, df) + s(\text{relative humidity}, df) + s(\text{precipitation}, df) + s(\text{wind speed}, df) + s(\text{time}, df) + DOW + Z_t$$

where E (Yt) denotes the estimated daily hospital admissions for pneumonia counted on day t; α is the intercept; s() denotes a regression spline function for nonlinear variables [21]; time is the number of calendar days on day t; Z_t indicates the pollutant concentrations on day t; df is the degrees of freedom. The partial autocorrelation function (PACF) [22] was used to select the degrees of freedom of time trends until the absolute values of the sum of PACF for lags up to 30 reached a minimum. Sensitivity analyses were performed to check whether the results were robust to the specification of parameters in the model. We found that the effects were stable when

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using 4 or 5 degrees of freedom per year for time. In addition, we modified degrees of freedom of the smoothing spline (4-5 df) for the meteorological factors, and the estimates were not changed substantially. These sensitivity analyses resulted in the selection of 4 df per year to control for time trend and 4 df for meteorological factors. For meteorological factors, the selection of degrees of freedom was based on minimizing Akaike's Information Criterion (AIC) [23].

Additionally, we fitted linear terms for the mean temperature in the GAM to explore the log-risk of daily hospital admissions for pneumonia associated with a unit increase of mean temperature. In examination of the lag effects of meteorological factors on hospital admissions for pneumonia, we developed two different lag structures: single-day lag and multi-day average starting from lag 0. For example, lag 0-1 stands for the 2-day moving average of current and previous day values. Relative risk (RR) refers to the ratio of the probability of an event occurring, while excess risk (ER) is the change in risk of a given activity. We used ER to evaluate the association between daily hospital admissions for pneumonia and a unit change of mean temperature. The value of ER is equal to the value of RR minus one.

We defined "cold period" as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) and "hot spot" for admissions as the days with daily pneumonia hospital admissions larger than the 75th percentile (85).

Data preparation and analysis were carried out using EXCEL 2010, whereas regression models were fitted using the statistical software R version 3.0.1 by using the mgcv package.

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Results

Data description

Table 1 summarizes the basic statistics for our study. During the study period, totaling 1,461 days, 99,403 hospital admissions for pneumonia were recorded in Shanghai with a mean of 68 (range, 9–195) per day. During the same time period, the mean daily temperature was 17.3°C (range, -3.4–35.7°C), reflecting the subtropical climate in Shanghai. A correlation matrix table for the meteorological and air pollution variables was provided in the Supplementary Table S2.

Table 1 Summary statistics of daily hospital admissions for pneumonia and meteorological factors in Shanghai, 2008-2011

	Mean	SD	Min	P25	P75	Max
PHA[a]	68	27	9	50	85	195
Weather condition						
Mean temperature(°C)	17.3	9.2	-3.4	9.3	25.1	35.7
Relative humidity (%)	69	13	23	61	79	95
Precipitation(mm)	30.9	94.5	0.0	0.0	12.0	1284.0
Wind speed(m/s)	2.9	1.0	0.8	2.2	3.5	7.3
Air pollution						
SO_2(ug/m^3)	36	20	11	22	43	147
NO_2(ug/m^3)	54	21	12	39	65	142
PM_{10}(ug/m^3)	79	53	12	45	100	599

[a] PHA: pneumonia hospital admissions.

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Daily hospital admissions and meteorological factors

Figure 1 shows the exposure-response (E-R) relationships between daily hospital admissions for pneumonia, and mean temperature, relative humidity, precipitation and wind speed, after adjusting for long-term trend, DOW and the air pollutants in the GAM. The relationship between mean temperature and pneumonia hospital admissions followed a V-shape ~~with a significant association~~ (*P<0.001*) (Figure 1a). The optimum temperature (OT), corresponding to the lowest point in the E-R curve, was about 13°C. Below the OT, as temperatures increased, the risk of hospital admissions for pneumonia decreased~~–~~ and then reversed the trend above the OT. In addition, ~~GAM did not find effects of~~ relative humidity, precipitation, ~~wind~~and wind speed had no effects on~~in~~ pneumonia hospital admissions.

Lag effects of temperature on daily hospital admissions

As there was a V-shaped relationship between mean temperature and hospital admissions for pneumonia, we stratified the data by temperature above ("hot temperature") or below ("cold temperature") the OT. Then linear terms for the daily mean temperature were fitted in GAMs (Table 2). In single-day lag structures, ~~significant~~ associations (*P<0.01*) between cold temperature and hospital admissions for pneumonia were found at lag 2 to lag 5. Effect from cold temperature appears larger than that from hot temperature. The multi-day metrics of mean temperature exposure also showed a larger effect of cold temperature than that of hot temperature. The effects by cold temperature peaked at lag 0-6~~, with statistical significance in lag 0-3 to lag 0-9~~. At lag 0-6, a 1°C decrease in the 7-day moving average of mean

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temperature corresponded to a 5.34% (95%CI: 2.04%-8.74%) increase in hospital admissions for pneumonia. However, no adverse effects of hot temperature were found either in single-day or multi-day lag structures.

Table 2 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C change in mean temperature using alternative lags

Lag(d)[a]	OT(°C)	Cold temperature		Hot temperature	
		ER[b](%)	95%CI	ER(%)	95%CI
Single-day	13				
0		-2.05	-4.78–0.61	0.80	-0.90–2.51
1		0.43	-2.07–3.01	0.41	-1.26–2.11
2		3.06*	0.72–5.47	0.04	-1.62–1.74
3		4.85**	2.65–7.09	0.37	-1.28–2.04
4		4.88**	2.71–7.09	1.28	-0.36–2.96
5		2.85*	0.65–5.10	1.16	-0.48–2.83
6		1.39	-0.81–3.64	1.21	-0.41–2.86
Multi-day	13				
0-1		0.03	-2.62–2.75	0.13	-1.66–1.96
0-2		1.57	-1.26–4.48	-0.08	-1.96–1.83
0-3		3.67*	0.84–6.59	-0.38	-2.39–1.67
0-4		4.88**	1.89–7.95	-0.42	-2.53–1.75
0-5		5.21**	2.14–8.36	-0.62	-2.93–1.75
0-6		5.34**	2.04–8.74	-0.94	-3.42–1.60

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0-7	5.10**	1.53–8.79	-0.48	-3.22–2.33
0-8	4.48*	0.72–8.37	-0.67	-3.47–2.21
0-9	4.01*	0.03–8.15	0.15	-2.81–3.20
0-10	1.43	-0.26–3.16	1.02	-0.52–2.59

[a] Lag 0 to lag 6: single-day lag from 0 to 6; lag 0-1 to lag 0-10: multi-day average of mean temperature (lag 0-1 means 2-day moving average of current and previous day values).

[b] ER means excess risk, ER= relative risk (RR) – 1.

* P <0.05. ** P <0.01.

Effects of cold temperature on different types of people

Since no ~~significant~~ adverse effects of hot temperature in hospital admissions for pneumonia were found, we focused further analysis on the association between cold temperature and hospital admissions for pneumonia. The association between hot temperature and hospital admissions for pneumonia was showed in Supplementary Table S3. Table 3 shows the different single-day lag effects of cold temperature on different sub-populations. We found the adverse effects of cold temperature in both males and females ~~without a statistically significant difference by gender~~. The effects increased from lag 0, with peaks in lag 3 for male and in lag 4 for female, and then declined. In age-specific analysis, cold temperature was positively associated with pneumonia hospital admissions and has adverse effects ~~was statistically significant~~ in the categories over age 45. The OT for people who aged above 65 was 18°C, which was larger than that for those younger than 65.

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Table 3 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in cold temperature stratified by gender and age.

	No.	OT(°C)	ER[a] (%)						
			Lag0	Lag1	Lag2	Lag3	Lag4	Lag5	Lag6
Gender									
Male	50696	13	-1.78	0.48	2.51*	3.95**	3.77**	1.88**	0.57
			(-4.49-1.00)	(-2.14-3.18)	(0.07,5.02)	(1.64,6.31)	(1.50-6.09)	(-0.42-4.24)	(-1.70-2.89)
Female	48706	13	-2.25	0.38	3.62*	5.76**	6.01**	3.83**	2.22
			(-5.05-0.64)	(-2.38-3.23)	(0.99-6.31)	(3.34-8.24)	(3.62-8.46)	(1.41-6.32)	(-0.23-4.73)
Age									
＜45	9567	13	-1.36	-0.43	2.23	2.49	3.47	3.26	1.46
			(-5.71-3.19)	(-4.68-4.01)	(-1.83-6.12)	(-1.45-6.50)	(-0.28-7.35)	(-0.52-6.99)	(-2.26-5.32)
45-65	25446	14	-2.81	-1.23	2.32	4.42**	4.88**	3.61*	2.52
			(-6.09-0.59)	(-4.44-2.09)	(-0.75-5.49)	(1.54-7.37)	(2.06-7.79)	(0.75-6.54)	(-0.39-5.51)
65-75	16198	18	-1.34	0.26	2.83	5.35**	5.51**	2.61	0.35
			(-4.98-2.43)	(-3.26-3.90)	(-0.54-6.31)	(2.20-8.60)	(2.42-8.68)	(-0.44-5.74)	(-2.62-3.41)
⩾75	48191	18	-1.95	1.53	3.19*	4.47**	4.64**	2.41	1.10
			(-4.77-0.95)	(-1.26-4.41)	(0.62-5.83)	(2.09-6.91)	(2.26-7.08)	(-0.01-4.88)	(-1.28-3.53)

[a] ER means excess risk, ER= relative risk (RR) – 1.

* P <0.05. ** P <0.01.

Figure 2 shows the single-day lag effects of cold temperature on different

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sub-population. The effects reached maximum in the lag 3 on population 1 while in the lag 4 on population 2. A 1°C decrease of cold temperature corresponded to a 4.87% (95%CI: 2.67%-7.12%) increase in hospital admissions for pneumonia on population 2 in lag 4 while it was 4.13% (95%CI: 0.77%-7.60%) on population 1 in lag 3. The effects on population 2 appear larger and more persistent than that on population 1.

Effect of cold period on pneumonia hospital admissions

Since cold temperature had large and persistent effects on pneumonia hospital admissions, we conducted a further analysis of cold temperature effects.

Figure 3 shows pneumonia hospital admissions varied with daily mean temperature, while cold period is related to hot spots for pneumonia hospital admissions. A 2 by 2 table to show the association between cold period and hot spots was provided in the Supplementary Table S1. We used cold period as a binary classification variable and fitted it in the GAM. The result showed that hospital admissions for pneumonia increased by 15.99% (95%CI: 0.06%-34.46%) in the cold period.

Discussion

This time-series analysis showed that ambient temperature was ~~significantly~~ associated with hospital admissions for pneumonia, while relative humidity, precipitation and wind speed did not show the same. To our knowledge, this is the first to report the effects of meteorological factors on hospital admissions for pneumonia in China.

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Generally, temperature appears V-, U-, or J-shaped variations with mortality or morbidity, with OT corresponding to the lowest point in temperature mortality curve [8 24]. The present study showed a V-shaped curve in the relationship between mean temperature and hospital admissions for pneumonia. Although the observation is consistent with the reported studies, we observed a different OT (13°C) in Shanghai, in comparison with 20°C in St. Paul [25], 16.5°C in Netherlands and 19°C in London [26]. Similar to the Beijing study [27], we found cold temperature presented larger effects. Other studies report that the peaks of respiratory syncytial virus and invasive pneumococcal disease were inversely correlated with temperature [28 29] and cold temperature was favorable to the spread of influenza virus [30], which might partly explain the association between cold temperature and hospital admissions for pneumonia.

We developed two different lag structures to examine the health effect of temperature. ~~Statistically significant associations~~Adverse effects in both single-day and multi-day lag effects models for cold temperature were observed, while neither single-day nor multi-day lag effects were~~as~~ found from hot temperature. These findings were slightly different from other studies on morbidity. For example, Braga et al.– [11] described that the effect of cold temperatures persisted for days, whereas the effect of high temperatures was restricted to the day or the day before. Yu et al. [31] demonstrated that cold temperature had a lag time of 21 days, while hot temperature appears to exhibit short-term, acute effects.

Given the established importance of seasonal variation in mortality and morbidity

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excesses of respiratory diseases [32], several research studies have reported particularly on the relationship between extremely cold climatic episodes and mortality and morbidity, noting the tendency for a winter mortality increased after the occurrence of cold spells [33]. However, there is neither a uniform and agreed definition of a cold spell [34] nor a precise definition of the period for which such events should be studied. Our criterion~~a~~ for identifying cold period was to combine time and temperature thresholds, which is similar to other studies [35 36]. We found that there was a 15.99% increase of pneumonia hospital admissions in the cold period. Further studies are needed to explore if the cold temperature effects on pneumonia are from cold temperature itself, or from other factors.

The effects of cold temperature on different populations were observed. The effect of cold temperature on population 2 was larger and more persistent than that on population 1. Adverse effects of pneumonia hospitalizations of population 2 were larger (ER increased by 0.67% and 1.06% in lag 3 and lag 4 respectively) than that of population 1. The population 2 included employees and retirees while population 1 was~~ere~~ mostly non-employed adults and students. The employees have more work pressure and have fewer opportunities to exercise, which might weaken their immunity; the elderly people are usually more susceptible to heat- or cold-related health risks [37 38]. The magnitude of the effects of temperature varied with gender and age. The OT for $\geqslant$65 age groups was higher than that for $<$65 age groups, indicating that elderly people had increased vulnerability to cold weather for pneumonia. Cold temperature only showed its effect on people older than 45. For

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residents in this age group, the ability to regulate body temperatures is reduced, and sweating thresholds are generally elevated in comparison with younger people [39].

Influenza epidemics, which generally occurs in the cold weather, have been accounted for as confounders in some studies[40]. Due to lack of reliable data, we didn't include the influenza epidemics as a control factor. However, the smooth function of time should have eliminated most such residual secular effects and there is no reason to expect an ~~significant~~ association of influenza with temperature (after controlling for time trend). In addition, many other studies have not included influenza as a confounder [12 41].

Our study has several limitations. First, we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure. This was expected to result in exposure misclassification. Secondly, our study only contained hospitalizations for pneumonia, but excluded less severe cases. Therefore, meteorological factors' effects on hospital admissions of pneumonia we observed may not be applied to the effects on the overall situation of pneumonia. Thirdly, the findings of this study should be treated cautiously when ~~to~~ generalized to other locations, particularly for places with different climates. In addition, the influence of ozone was not controlled for, because the data of ozone was not available.

CONCLUSION

We observed ~~significant~~ associations between meteorological factors and daily pneumonia hospital admissions in Shanghai. Cold temperature presented larger and

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more persistent effects and the magnitude of these effects of temperature varied with gender and age. Cold period had adverse effects on pneumonia hospital admissions. Prevention programs may be needed to reduce the impact of cold temperature such as developing a weather warning system within a wide public health context.

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Authors' contributions JX, LP and XY provided and organized data; YL, YZ and RC conducted the study, performed data analysis, and LY drafted the manuscript; WW, HK and DR reviewed and edited the manuscript, and WW conceived the study and contributed to the study design. All authors read and approved the final manuscript.

Competing interests The authors declare that they have no competing interests.

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Figure 1 Smoothing plots of meteorological factors against hospital admissions for pneumonia.

(a) mean temperature at lag 4; (b) relative humidity at lag 0; (c) precipitation at lag 0; (d) wind speed at lag 0. The solid lines indicate the estimated mean percentage of change in pneumonia hospital admissions, the dotted lines represent 95% confidence interval, and Log-risk represent Log(RR).

Figure 2 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in cold temperature using single-day lag structure by different sub-population.

Figure 3 Daily mean temperature and daily pneumonia hospital admissions. Cold period means a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C); "hot spot" for admissions means the day with daily pneumonia hospital admissions larger than the 75th percentile (85).

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References

1. World Health Organization (2008) The top 10 causes of death. Available: http://www.who.int/mediacentre/factsheets/fs310/en/ Accessed 19 Jan 2010
2. Rudan I, O'Brien KL, Nair H, et al. Epidemiology and etiology of childhood pneumonia in 2010: estimates of incidence, severe morbidity, mortality, underlying risk factors and causative pathogens for 192 countries. Journal of global health 2013;**3**(1):10401 doi: 10.7189/jogh.03.010401[published Online First: Epub Date]|.
3. Mathers C BC, and Moesgaard Iburg K. WHO. Global Burden of Disease in 2002: data sources, methods and results. Ref Type: Generic.
4. Polverino E Fau - Torres Marti A, Torres Marti A. Community-acquired pneumonia. (1827-1596 (Electronic))
5. Guan X, Silk BJ, Li W, et al. Pneumonia incidence and mortality in Mainland China: systematic review of Chinese and English literature, 1985-2008. PloS one 2010;**5**(7):e11721 doi: 10.1371/journal.pone.0011721[published Online First: Epub Date]|.
6. Li-xian HE, Xue-hua C. Contentions on the pathogenic spectrum of community-acquired pneumonia and the first experimental application of antibiotic agents. Chinese Journal of Practical Internal Medicine 2007;**27**(2):110-13 doi: 10.3969/j.issn.1005-2194.2007.02.012[published Online First: Epub Date]|.
7. Shea KM, Truckner RT, Weber RW, et al. Climate change and allergic disease. The Journal of allergy and clinical immunology 2008;**122**(3):443-53; quiz 54-5 doi: 10.1016/j.jaci.2008.06.032[published Online First: Epub Date]|.
8. Curriero FC, Heiner KS, Samet JM, et al. Temperature and mortality in 11 cities of the eastern United States. American journal of epidemiology 2002;**155**(1):80-7
9. Haines A, McMichael AJ, Epstein PR. Environment and health: 2. Global climate change and health. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 2000;**163**(6):729-34
10. Braga AL, Zanobetti A, Schwartz J. The time course of weather-related deaths. Epidemiology 2001;**12**(6):662-7
11. Braga AL, Zanobetti A, Schwartz J. The effect of weather on respiratory and cardiovascular deaths in 12 U.S. cities. Environmental health perspectives 2002;**110**(9):859-63
12. Farajzadeh M, Darand M. Analyzing the Influence of Air Temperature on the Cardiovascular, Respiratory and Stroke Mortality in Tehran. Iran J Environ Healt 2009;**6**(4):261-70
13. Liu L, Breitner S, Pan X, et al. Associations between air temperature and cardio-respiratory mortality in the urban area of Beijing, China: a time-series analysis. Environmental Health 2011;**10**(1):51
14. Huynen MM, Martens P, Schram D, et al. The impact of heat waves and cold

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spells on mortality rates in the Dutch population. Environmental health perspectives 2001;**109**(5):463-70
15. Ye Y, Zulu E, Mutisya M, et al. Seasonal pattern of pneumonia mortality among under-five children in Nairobi's informal settlements. The American journal of tropical medicine and hygiene 2009;**81**(5):770-5 doi: 10.4269/ajtmh.2009.09-0070[published Online First: Epub Date]|.
16. Egondi T, Kyobutungi C, Kovats S, et al. Time-series analysis of weather and mortality patterns in Nairobi's informal settlements. Global health action 2012;**5**:23-32 doi: 10.3402/gha.v5i0.19065[published Online First: Epub Date]|.
17. Lim YH, Hong YC, Kim H. Effects of diurnal temperature range on cardiovascular and respiratory hospital admissions in Korea. The Science of the total environment 2012;**417-418**:55-60 doi: 10.1016/j.scitotenv.2011.12.048[published Online First: Epub Date]|.
18. Onozuka D, Hashizume M, Hagihara A. Impact of weather factors on Mycoplasma pneumoniae pneumonia. Thorax 2009;**64**(6):507-11 doi: 10.1136/thx.2008.111237[published Online First: Epub Date]|.
19. Zeger SL, Irizarry R, Peng RD. On time series analysis of public health and biomedical data. Annual review of public health 2006;**27**:57-79 doi: 10.1146/annurev.publhealth.26.021304.144517[published Online First: Epub Date]|.
20. Cao J, Li W, Tan J, et al. Association of ambient air pollution with hospital outpatient and emergency room visits in Shanghai, China. The Science of the total environment 2009;**407**(21):5531-6 doi: 10.1016/j.scitotenv.2009.07.021[published Online First: Epub Date]|.
21. Guo Y, Barnett AG, Yu W, et al. A large change in temperature between neighbouring days increases the risk of mortality. PloS one 2011;**6**(2):e16511 doi: 10.1371/journal.pone.0016511[published Online First: Epub Date]|.
22. Kan H, London SJ, Chen H, et al. Diurnal temperature range and daily mortality in Shanghai, China. Environmental research 2007;**103**(3):424-31 doi: 10.1016/j.envres.2006.11.009[published Online First: Epub Date]|.
23. Hastie T, Tibshirani R. Generalized additive models for medical research. Statistical methods in medical research 1995;**4**(3):187-96
24. Kan HD, Jia J, Chen BH. Temperature and daily mortality in Shanghai: a time-series study. Biomedical and environmental sciences : BES 2003;**16**(2):133-9
25. Gouveia N, Hajat S, Armstrong B. Socioeconomic differentials in the temperature-mortality relationship in Sao Paulo, Brazil. International journal of epidemiology 2003;**32**(3):390-7
26. Patz JA, Campbell-Lendrum D, Holloway T, et al. Impact of regional climate change on human health. Nature 2005;**438**(7066):310-7 doi: 10.1038/nature04188[published Online First: Epub Date]|.
27. Mo Yun-zheng, Zheng Ya-an, Hui T, et al. Relationship between daily mean temperature and emergency department visits for respiratory diseases: a

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time-series analysis. (1671-167X (Print))
28. Yusuf S, Piedimonte G, Auais A, et al. The relationship of meteorological conditions to the epidemic activity of respiratory syncytial virus. Epidemiology and infection 2007;**135**(7):1077-90 doi: 10.1017/S095026880600776X[published Online First: Epub Date]|.
29. Murdoch DR, Jennings LC. Association of respiratory virus activity and environmental factors with the incidence of invasive pneumococcal disease. The Journal of infection 2009;**58**(1):37-46 doi: 10.1016/j.jinf.2008.10.011[published Online First: Epub Date]|.
30. Lowen Ac Fau - Mubareka S, Mubareka S Fau - Steel J, Steel J Fau - Palese P, et al. Influenza virus transmission is dependent on relative humidity and temperature. (1553-7374 (Electronic)) doi: D - NLM: PMC2034399 EDAT- 2007/10/24 09:00 MHDA- 2007/11/14 09:00 CRDT- 2007/10/24 09:00 PHST- 2007/07/11 [received] PHST- 2007/09/05 [accepted] AID - 07-PLPA-RA-0426 [pii] AID - 10.1371/journal.ppat.0030151 [doi] PST - ppublish[published Online First: Epub Date]|.
31. Yu W, Mengersen K, Hu W, et al. Assessing the relationship between global warming and mortality: Lag effects of temperature fluctuations by age and mortality categories. Environmental pollution 2011;**159**(7):1789-93 doi: http://dx.doi.org/10.1016/j.envpol.2011.03.039[published Online First: Epub Date]|.
32. Donaldson GC, Goldring JJ, Wedzicha JA. Influence of season on exacerbation characteristics in patients with COPD. Chest 2012;**141**(1):94-100 doi: 10.1378/chest.11-0281[published Online First: Epub Date]|.
33. Revich B, Shaposhnikov D. Excess mortality during heat waves and cold spells in Moscow, Russia. Occupational and environmental medicine 2008;**65**(10):691-6 doi: 10.1136/oem.2007.033944[published Online First: Epub Date]|.
34. Kysely J, Pokorna L, Kyncl J, et al. Excess cardiovascular mortality associated with cold spells in the Czech Republic. BMC public health 2009;**9**:19 doi: 10.1186/1471-2458-9-19[published Online First: Epub Date]|.
35. Ma W Fau - Yang C, Yang C Fau - Chu C, Chu C Fau - Li T, et al. The impact of the 2008 cold spell on mortality in Shanghai, China. (1432-1254 (Electronic))
36. Monteiro A Fau - Carvalho V, Carvalho V Fau - Gois J, Gois J Fau - Sousa C, et al. Use of "Cold Spell" indices to quantify excess chronic obstructive pulmonary disease (COPD) morbidity during winter (November to March 2000-2007): case study in Porto. (1432-1254 (Electronic))
37. Ye X, Wolff R, Yu W, et al. Ambient temperature and morbidity: a review of epidemiological evidence. Environmental health perspectives 2012;**120**(1):19-28 doi: 10.1289/ehp.1003198[published Online First: Epub Date]|.
38. Yu W, Mengersen K, Wang X, et al. Daily average temperature and mortality among the elderly: a meta-analysis and systematic review of epidemiological evidence. International journal of biometeorology 2012;**56**(4):569-81 doi:

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10.1007/s00484-011-0497-3[published Online First: Epub Date]|.

39. Kenney WL, Hodgson JL. Heat Tolerance, Thermoregulation and Aging. Sports Medicine 1987;**4**(6):446-56
40. Armstrong B. Models for the relationship between ambient temperature and daily mortality. Epidemiology 2006;**17**(6):624-31 doi: DOI 10.1097/01.ede.0000239732.50999.8f[published Online First: Epub Date]|.
41. Curriero FC, Heiner KS, Samet JM, et al. Temperature and mortality in 11 cities of the eastern United States. American journal of epidemiology 2002;**155**(1):80-87 doi: Doi 10.1093/Aje/155.1.80[published Online First: Epub Date]|.

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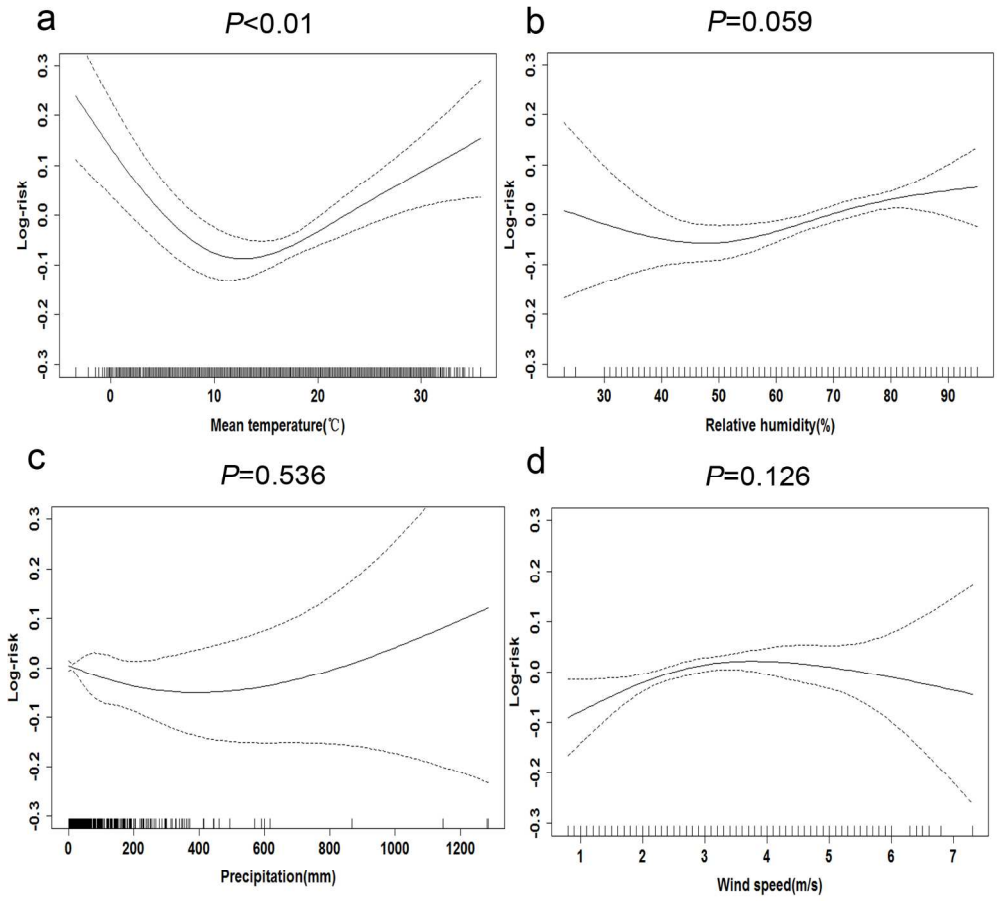

Smoothing plots of meteorological factors against hospital admissions for pneumonia. (a) mean temperature at lag 4; (b) relative humidity at lag 0; (c) precipitation at lag 0; (d) wind speed at lag 0. The solid lines indicate the estimated mean percentage of change in ED visits, and the dotted lines represent twice the standard error
173x169mm (300 x 300 DPI)

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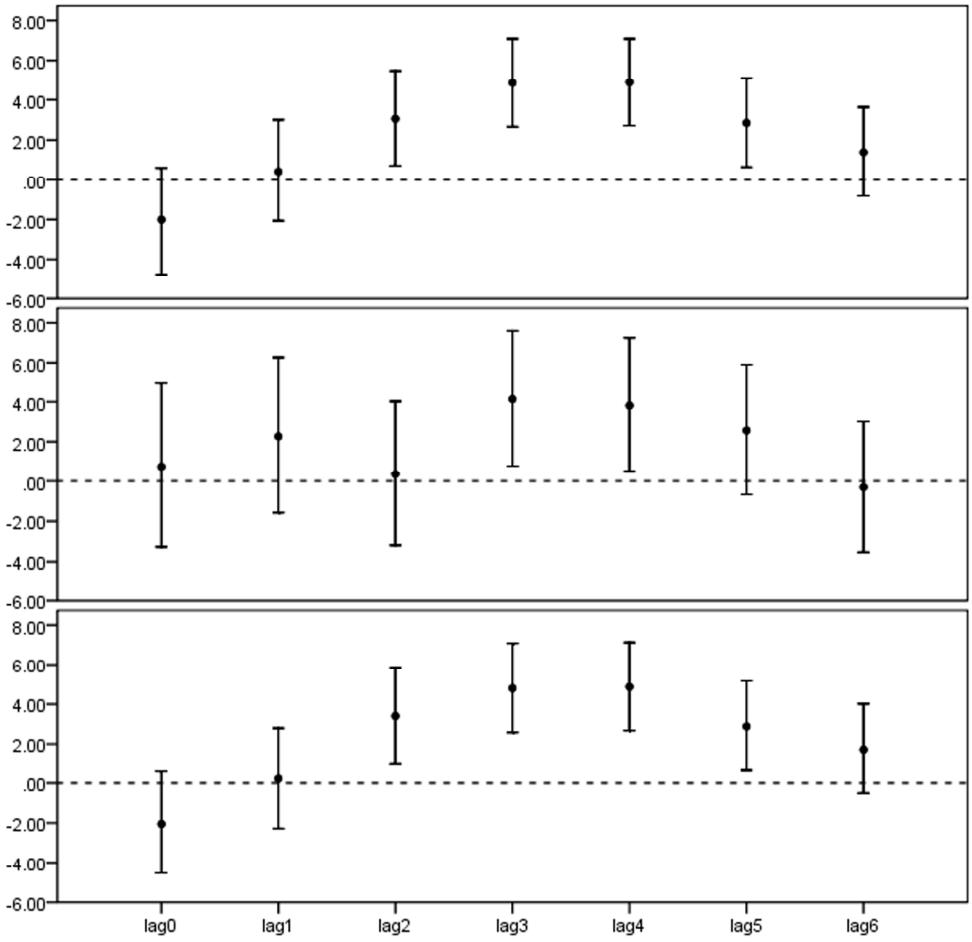

Figure 2 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in cold temperature using single-day lag structure by different sub-population.
173x169mm (300 x 300 DPI)

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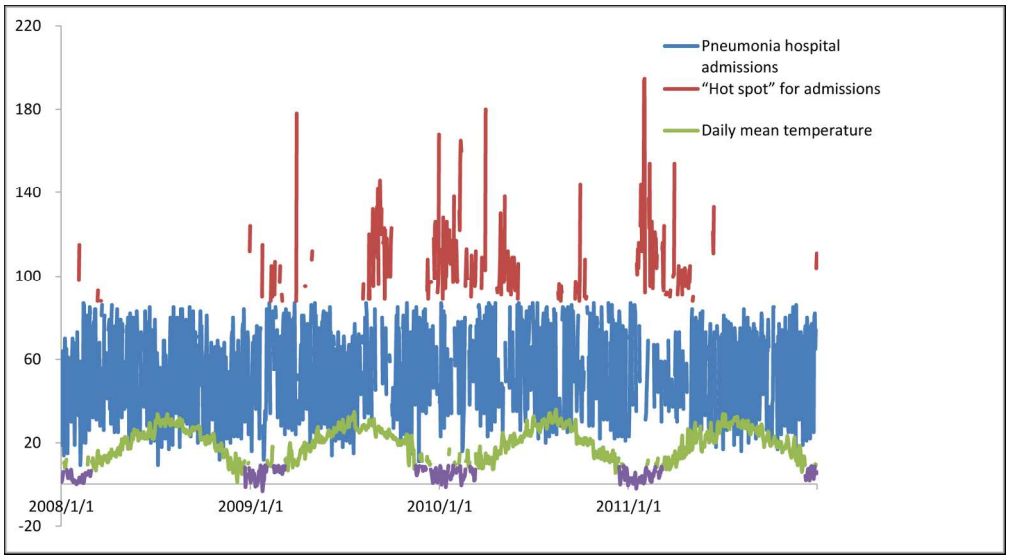

Figure 3 Daily mean temperature and daily pneumonia hospital admissions. Cold period means a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C); "hot spot" for admissions means the day with daily pneumonia hospital admissions larger than the 75th percentile (85).

173x95mm (300 x 300 DPI)

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Supplementary

Table S1 Association between cold period and hot spots

		Cold period[a]	
		0	1
Hot spots[b]	0	948	197
	1	219	97

[a]: a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) of temperature distribution during the study period.

[b]: the day with daily pneumonia hospital admissions larger than the 75th percentile (85.0) of pneumonia hospital admissions.

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Table S2 Pearson's correlations among the meteorological and air pollution variables.

	WS	Precipitation	RH	SO_2	NO_2	PM_{10}
Temperature	0.049**	0.116**	0.207**	-0.468**	-0.402**	-0.197**
WS		0.041**	-0.043**	-0.247**	-0.464**	-0.255**
Precipitation			0.368**	-0.211**	-0.165**	-0.179**
RH				-0.383**	-0.192**	-0.305**
SO_2					0.756**	0.624**
NO_2						0.664**

WS: wind speed; RH: relative humidity.

** P<0.001

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Table S3 Percent change in daily hospital admissions for pneumonia and 95% confidence intervals (CI) per 1°C decrease in hot temperature stratified by gender and age.

	No.	OT(°C)	ER[a] (%)						
			Lag0	Lag1	Lag2	Lag3	Lag4	Lag5	Lag6
Gender									
Male	50696	13	0.44 (-1.41-2.32)	0.07 (-1.67-1.84)	-0.76 (-2.43-0.94)	-0.92 (-2.55-0.73)	-0.14 (-1.77-1.51)	0.29 (-1.35-1.95)	0.20 (-1.45-1.87)
Female	48706	13	1.17 (-0.77-3.16)	-0.89 (-2.69-0.93)	-1.18 (-2.91-0.59)	-0.26 (-1.96-1.47)	-0.02 (-1.72-1.71)	-0.52 (-2.21-1.20)	-1.15 (-2.84-0.57)
Age									
＜45	9567	13	-1.36 (-4.51-1.90)	-1.88 (-4.84-1.18)	-2.37 (-5.23-0.59)	-3.11* (-5.88--0.27)	0.17 (-2.65-3.08)	0.76 (-2.08-3.69)	0.54 (-2.30-3.47)
45-65	25446	14	0.68 (-1.68-3.11)	-0.35 (-2.55-1.90)	-1.99 (-4.09-0.16)	-1.39 (-3.45-0.71)	-0.61 (-2.67-1.50)	-0.21 (-2.28-1.90)	-0.43 (-2.50-1.69)
65-75	16198	18	0.70 (-1.92-3.40)	-1.95 (-4.36-0.52)	-1.48 (-3.84-0.93)	0.49 (-1.84-2.87)	0.33 (-1.98-2.70)	-0.58 (-2.87-1.77)	-1.43 (-3.72-0.92)
⩾75	48191	18	1.29 (-0.61-3.23)	0.37 (-1.41-2.18)	0.01 (-1.71-1.76)	-0.08 (-1.75-1.62)	-0.03 (-1.70-1.67)	-0.09 (-1.76-1.60)	-0.39 (-2.06-1.32)

[a] ER means excess risk, ER= relative risk (RR) – 1.

* *P* <0.05

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China: a time-series analysis	1
		(b) **Objectives** To explore the association between weather conditions and hospital admissions for pneumonia in Shanghai. **Design** A time-series analysis was performed for a period of 4 years (January 2008-December 2011). Generalized additive model were used to calculate the relative risks. **Conclusions** Cold temperature may be one of the important risk factors for pneumonia hospitalizations.	2
Introduction			
Background/rationale	2	Although pneumonia is recognized to result in substantial morbidity and mortality in some developed countries, the potential patterns of associations in other countries remain unclear	4-5
Objectives	3	pneumonia has been reported to be significantly influenced by meteorological factors.	4-5
Methods			
Study design	4	A time-series analysis	6
Setting	5	Shanghai, China	5
Participants	6	All daily hospital admissions for pneumonia were obtained from the Shanghai health insurance system from January 1, 2008 to December 31, 2011 (n=99,403).	5
Variables	7	The target population included all registered population living in Shanghai with urban residents' basic medical insurance (hereafter population 1) and urban workers' basic medical insurance (hereafter population 2). we stratified the data by temperature above ("hot temperature") or below ("cold temperature") the optimum temperature (OT). We defined "cold period" as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) of temperature distribution during the study period; the "hot spot" for admissions refers to the days with daily pneumonia hospital admissions larger than the 75th percentile (85) of pneumonia hospital admissions.	5, 9, 13
Data sources/ measurement	8*	Daily hospital admissions for pneumonia incurred by residents of Shanghai from January 1, 2008 to December 31, 2011 were collected from the Shanghai Municipal Medical Insurance System. Daily meteorological data (including mean temperature, relative humidity, precipitation and wind speed) were obtained from the Shanghai Center for Urban	6

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		Environmental Meteorology. The weather data were measured at a fixed meteorological station located in the Xuhui District of Shanghai.	
Bias	9	We controlled the potential confounders such as long-term trend, the day of the week (DOW) and air pollutants.	*6*
Study size	10	The target population included all registered population living in Shanghai with urban residents' basic medical insurance or urban workers' basic medical insurance.	5
Quantitative variables	11	The hospital admissions for pneumonia and meteorological factors were linked by the date and therefore can be analyzed with a time-series model.	6
Statistical methods	12	(a) a Poisson generalized additive model (GAM) approach was used to explore the association between meteorological factors and hospital admissions for pneumonia.	6
		(b) The partial autocorrelation function (PACF) was used to select the degrees of freedom of time trends	7
Results			
Participants	13*	All daily hospital admissions for pneumonia were obtained from the Shanghai health insurance system from January 1, 2008 to December 31, 2011 (n=99,403).	8
Descriptive data	14*	During the study period, totalling 1,461 days, 99,403 hospital admissions for pneumonia were recorded in Shanghai, a daily mean of 68 (range, 9–195). During the same time period, the mean daily temperature was 17.3°C (range, -3.4–35.7°C), reflecting the subtropical climate in Shanghai. The relative humidity, precipitation and wind speed averaged respectively at 69%, 30.9 mm and 2.9 m/s. Meanwhile, the mean daily concentrations of SO2, NO2 and PM10 were 36, 54 and 79 ug/m3, respectively	8
Outcome data	15*	Optimum temperature (OT), excess risk (ER)	9-12
Main results	16	(a) The relationship between mean temperature and pneumonia hospital admissions followed a V-shape curve, with an optimum temperature (OT) at 13°C. When mean temperature was below the OT, a 1°C decrease corresponded to a 4.88% (95% confidence interval [CI]: 2.71%-7.09%) and 5.34% (95% CI: 2.04%-8.74%) increase in pneumonia hospital admissions in lag 4 using single-day lag structure and lag 0-7 using multi-day lag structure. Hospitalization for pneumonia increased 15.99% (95% CI: 0.06%-34.46%) in the cold period.	9, 10, 13
		(b) We defined "cold period" as a period of at least 5 consecutive days with daily mean temperature below the 25th percentile (9.2°C) of temperature distribution during the study period; the "hot spot" for admissions refers to the days with daily pneumonia hospital admissions larger than the 75th percentile (85) of pneumonia hospital admissions.	13
Other analyses	17	Cold temperature effects on different types of people were observed. The magnitude of the effects of temperature varied with gender and age.	11, 12
Discussion			
Key results	18	The relationship between mean temperature and pneumonia hospital admissions followed a V-shape curve, with the	13, 14, 15

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		optimum temperature (OT) at 13°C. Cold temperature presented larger and more persistent effects and the magnitude of the effects of temperature varied with gender and age.	
Limitations	19	we used available outdoor monitoring data of ambient meteorological factors derived from a monitoring station rather than measures of personal exposure. This is expected to result in exposure misclassification.	16
Interpretation	20	Cold temperature may be one of the important risk factors for pneumonia hospitalizations.	16
Generalisability	21	The setting of this study was Shanghai, China. Although the results are consistent with the lots of other reported studies, it should be careful of generalizability to other populations.	
Other information			
Funding	22	This study was funded by the Global Environment Change Research in Fudan University (Grant No. EZH1829007/003), and the program of Key Discipline Development of Public Health of Shanghai (Grant No. 12GWZX0101).	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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