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Original Contribution

Pneumonia Hospitalization Risk in the Elderly Attributable to Cold and Hot Temperatures in Hong Kong, China

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The growth of pathogens potentially relevant to respiratory tract infection may be triggered by changes in ambient temperature. Few studies have examined the association between ambient temperature and pneumonia incidence, and no studies have focused on the susceptible elderly population. We aimed to examine the short-term association between ambient temperature and geriatric pneumonia and to assess the disease burden attributable to cold and hot temperatures in Hong Kong, China. Daily time-series data on emergency hospital admissions for geriatric pneumonia, mean temperature, relative humidity, and air pollution concentrations between January 2005 and December 2012 were collected. Distributed-lag nonlinear modeling integrated in quasi-Poisson regression was used to examine the exposure-lag-response relationship between temperature and pneumonia hospitalization. Measures of the risk attributable to nonoptimal temperature were calculated to summarize the disease burden. Subgroup analyses were conducted to examine the sex difference. We observed significant nonlinear and delayed associations of both cold and hot temperatures with pneumonia in the elderly, with cold temperatures having stronger effect estimates. Among the 10.7% of temperature-related pneumonia hospitalizations, 8.7% and 2.0% were attributed to cold and hot temperatures, respectively. Most of the temperature-related burden for pneumonia hospitalizations in Hong Kong was attributable to cold temperatures, and elderly men had greater susceptibility.

aged; attributable risk; distributed-lag nonlinear model; emergency hospital admission; geriatric illness; pneumonia; relative risk; time series

Abbreviations: CI, confidence interval; PM_{10}, particulate matter with an aerodynamic diameter less than or equal to 10 µm.

Pneumonia, a lower respiratory tract infection that affects lung tissue, is the second leading cause of death worldwide. Pneumonia affects approximately 450 million people globally per year (7% of the population) and results in about 4 million deaths (1). While most deaths are recorded in developing countries, it was the second leading cause of death in Hong Kong, China, between 2012 and 2014. Increasing trends in the number of pneumonia-related deaths and death rates have been observed since 2001. The number of deaths due to pneumonia in 2014 was 7,502, accounting for 16.4% of total registered deaths in Hong Kong (2). Males had higher death rates than females (110.8 and 81.4 per 100,000 population, respectively, in 2013), and the age-specific death rates increased markedly at or above age 65 years. The number of inpatient discharges due to pneumonia has also continued to rise gradually in recent years (3). Low socioeconomic status; inadequate nutrition; exposure to tobacco smoke, air pollution, and extreme weather; and not receiving immunizations may be predisposing factors for lower respiratory tract infection in older people (4).

Thus far, only a few studies have examined the association between weather factors and pneumonia incidence (5–11), with most focused on pneumonia in children (5–9). Researchers have found positive associations between pneumonia-related hospitalizations or emergency room visits and increases in weekly mean temperature (9), daily mean temperature (6, 10), and the temperature change between 2 neighboring days (5). In a Japanese study, the weekly number of cases of *Mycoplasma pneumoniae* infection increased by 16.9% (95% confidence interval (CI): 11.3, 22.8) for every 1°C increase in the average temperature (9); and in Suzhou, China, rates of *M. pneumoniae* infection among hospitalized children showed a strong correlation ($r = 0.825$) with monthly mean temperature (7). However, few studies have accounted for possible nonlinear and delayed associations between temperature and pneumonia (6, 10), and none (to our knowledge) have targeted the elderly population.

Older persons are usually more susceptible to health risks related to cold and hot temperatures (10, 12, 13). Possible causal pathways may include reduced thermoregulatory capacity and increased vulnerability to infection. In this study, we aimed to conduct a time-series analysis to examine the association between ambient temperature and emergency hospital admissions for geriatric pneumonia in Hong Kong and to assess the disease burden attributable to cold and hot temperatures under its complex exposure-lag-response relationships. Identifying the role of ambient temperature in the risk of geriatric pneumonia will help to guide public health policy-makers in planning interventions and prevention measures for temperature-related pneumonia in the vulnerable elderly population.

METHODS

Data collection

Emergency hospital admission data. The daily number of emergency hospital admissions for pneumonia (as the principal diagnosis; *International Classification of Diseases, Ninth Revision*, codes 480–486) was obtained from the Hospital Authority Corporate Data Warehouse. The Hospital Authority is the statutory body running all public hospitals in Hong Kong. Records of admission were taken from the publicly funded hospitals, which provide 24-hour accident and emergency care and which cover 90% of all hospital beds for local residents in Hong Kong (14). For the study period of 2005–2012, the Hospital Authority provided us with daily counts of emergency hospital admissions aggregated over age, sex, admission date, and principal diagnosis upon discharge. We abstracted data on overall daily pneumonia emergency admissions, admissions of elderly subjects (i.e., persons aged ≥65 years), and admissions in different sexes as the health outcomes. Results of separate analyses carried out for childhood pneumonia (children aged <15 years) and adult pneumonia (persons aged 15–64 years) are also included in the accompanying Web material (cited below) for a more complete picture. Daily numbers of admissions for influenza (*International Classification of Diseases, Ninth Revision*, code 487) were used to identify influenza epidemics, which were then treated as a potential confounder in the data analysis (15). Ethical approval and consent from individual subjects were not required by our institution, as we used only aggregated data in this study, not any individualized data.

Temperature and air pollution data. The daily mean temperature and relative humidity for each day from January 1, 2005, to December 31, 2012, were obtained from the Hong Kong Observatory. Extreme cold weather was defined as a daily mean temperature at or lower than the first percentile of the distribution of daily mean temperatures during the study period, while moderate cold was defined as a daily mean temperature between the first percentile and the optimal temperature. Extremely hot and moderately hot weather were defined using the 99th percentile as the cutoff point accordingly (16, 17).

Air pollution concentrations in the same period were obtained from the Hong Kong Environmental Protection Department. We calculated the daily 24-hour mean concentrations of particulate matter with an aerodynamic diameter less than or equal to 10 μm (PM_{10}) and nitrogen dioxide, as well as daytime 8-hour (10:00–18:00 or 10:00 a.m. to 6:00 p.m.) mean ozone concentrations, for each pollutant monitoring site and then averaged them across the 10 monitoring stations (18). Air pollutants were considered potential confounders in the data analysis.

Statistical modeling

The relative risk of emergency hospital admission for pneumonia according to temperature exposure, overall and in each subgroup, was estimated in a standard time-series quasi-Poisson regression. The association with temperature was modeled using a distributed-lag nonlinear model, where temperature was included in the model as a *cross-basis* function to flexibly account for the potentially lagged and nonlinear association between temperature and pneumonia hospitalization (19). This distributed-lag nonlinear model had the advantage of estimating the associations with cumulative temperature exposure over multiple days while adjusting for the collinearity of temperature on neighboring days (20).

Specifically, we modeled the exposure-response relationship with a natural cubic spline for temperature and the lag-response relationship with a natural cubic spline for lag days, using the median value of temperature as the preliminary reference. Spline knots were placed at equal spaces in the temperature range to allow enough flexibility at the two ends of the temperature distribution, and they were placed at equally spaced values on the log scale to allow more flexible lag effects at shorter delays. The knots for temperature and lag, with a range of 1–5, were tested and chosen by the minimum Akaike's Information Criterion value for quasi-Poisson models (19, 21). In the current study, for examination of the association between ambient temperature and pneumonia hospitalizations in the elderly, 2 knots for temperature and 4 knots for lag produced the best model fit. We extended the lag period to 21 days in order to capture the long delay in cold-related risk and adequately assessed heat-related risk after excluding emergency hospitalizations advanced by only a few days (the harvesting effect) (22). The short lags could not adequately be used to assess the heat-related risks, as the harvesting effects are ignored (21).

We included a natural cubic spline of time with 8 degrees of freedom per year to control for seasonal and long-term trends, a natural cubic spline of relative humidity with 3 degrees of freedom, and dummy variables for day of the week, public holidays, and influenza epidemics, to control for these time-varying confounders (23). We included air pollutants (PM_{10}, nitrogen dioxide, and ozone) in the model as cross-basis functions with a natural cubic spline of 2 knots and a maximum lag of 3 days for pollutant concentrations, and we included a natural cubic spline for lags with 2 knots in the model to control for their distributed-lagged confounding effects on pneumonia hospitalizations (16).

We determined the optimal temperature, corresponding to a minimum number of emergency hospitalizations for pneumonia in the elderly, from the threshold model by setting the threshold between 18°C and 30°C (in 0.1°C gaps) and identified the model with minimized residual deviance (21). We then defined the threshold value as the reference temperature (centering value) to fit the exposure-lag-response relationship between temperature and pneumonia hospitalizations. The overall risk associated with temperature was cumulated over the lag period. Because previous studies indicated that the associations with hot temperatures were generally more short-term than those from cold temperatures while including some harvesting a few days later, besides the cumulative risk over 0–21 lag days, we also estimated the associations with temperature over the following lag periods: 0–1 days, 2–6 days, and 7–21 days, to represent the acute, delayed, and long-lasting risks, respectively (24). Because the temperature-mortality or temperature-morbidity relationship was generally U- or J-shaped, we calculated the relative risks for cold and hot temperatures, respectively. Specifically, we calculated the relative risks of pneumonia hospitalization at extremely cold (first percentile of temperature distribution) and moderately cold (10th percentile) temperatures and at extremely hot (99th percentile) and moderately hot (90th percentile) temperatures, compared with the optimal temperature in Hong Kong. We also conducted subgroup analyses by sex to capture the sex difference.

Computation of attributable risk

We also considered the optimal temperature as the reference to compute the attributable risk by centering the natural cubic spline that modeled the exposure-response relationship. For each day of the series for a pneumonia subgroup, the overall cumulative relative risk corresponding to each day's temperature was used to compute the attributable number and attributable fraction in the next 21 days, using a backward approach previously described by Gasparrini and Leone (25) that summarized the current burden due to the past exposures.

The total attributable number of hospitalizations due to nonoptimal temperatures was given by the sum of the contributions from all of the days in the series, and its ratio with the total number of hospitalizations provided the total attributable fraction. We computed the components attributable to cold and hot weather by summing the subsets corresponding to days with temperatures lower or higher than the optimum, respectively. We further separated the components into moderate and extreme contributions by defining extreme cold and heat as the temperatures lower than the first percentile and higher than the 99th percentile, respectively, while moderate temperatures were defined as the range between the optimal temperature and the cutoff (25, 26).

Table 1. Daily Numbers of Emergency Hospital Admissions for Pneumonia, Weather Conditions, and Air Pollution Concentrations in Hong Kong, China, 2005–2012 (2,922 days)

Variable	Mean (SD)	Percentile				
		Minimum	25th	50th	75th	Maximum
Daily no. of emergency hospital admissions for pneumonia						
Total	91.5 (21.8)	42	76	88	103	184
Age group, years						
<15	11.6 (6.1)	0	7	11	15	48
15–64	12.3 (4.9)	2	9	12	15	40
≥65	67.5 (17.0)	24	55	65	77	135
Elderly women	32.2 (9.5)	10	25	31	37	67
Elderly men	35.4 (9.6)	12	29	34	41	78
Weather conditions						
Mean temperature, °C	23.4 (5.2)	8.7	19.1	24.7	27.9	31.8
Relative humidity, %	78.4 (10.5)	31.0	74.0	79.0	85.8	99.0
Pollution concentration, μg/m^3						
PM_{10}	50.5 (28.8)	7.6	28.2	45.1	68.1	573.0
Nitrogen dioxide	55.9 (19.3)	13.0	41.7	53.1	66.9	153.0
Ozone	47.1 (30.2)	4.8	23.2	39.7	64.9	203.2

Abbreviations: PM_{10}, particulate matter with an aerodynamic diameter less than or equal to 10 μm; SD, standard deviation.

Empirical confidence intervals were obtained by means of Monte Carlo simulations assuming a multivariate normal distribution of the reduced coefficients of the cumulative effect estimate (25). We derived empirical confidence intervals for backward total attributable number and attributable fraction, computed overall and for separate components, by simulating 5,000 samples from the assumed distribution.

All analyses were conducted in R, version 3.1.3 (R Development Core Team, Vienna, Austria, 2014). We used the "dlnm" package (20) to fit the distributed-lag nonlinear model for estimation of the association with temperature.

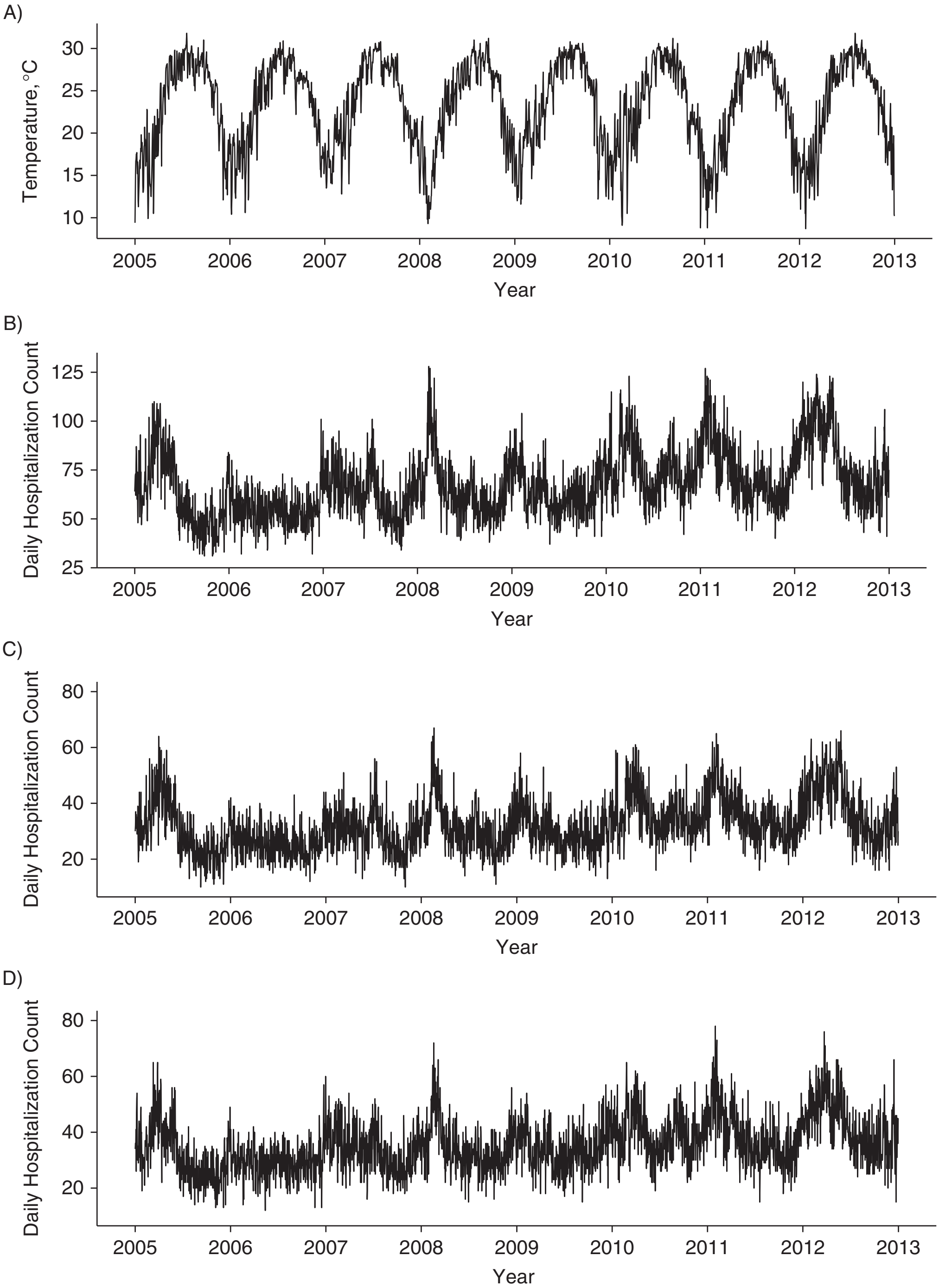

Figure 1. Time-series plots of the associations between ambient temperature and emergency hospital admissions for pneumonia in Hong Kong, China, during 2005–2012. A) Daily mean temperature; B–D) daily numbers of emergency hospital admissions for pneumonia in the elderly (ages ≥65 years) (B), women (C), and men (D).

The attributable risk measures (attributable fraction and attributable number) were calculated using the function "attrdl" provided by Gasparrini (27).

RESULTS

Data description

During the study period, a total of 197,316 emergency hospital admissions for pneumonia in subjects aged ≥65 years were recorded, which accounted for 73.8% of the total number of pneumonia cases. On average, there were 67 emergency pneumonia hospitalizations (32 female and 35 male) in the elderly population per day. The median of the daily mean air temperatures was 24.7°C, with a range between 8.7°C and 31.8°C, and the relative humidity was 79%. The daily 24-hour mean concentration of air pollutants was 50.5 μg/m^3 for PM_{10} and 55.9 μg/m^3 for nitrogen dioxide, while the daytime 8-hour mean concentration of ozone was 47.1 μg/m^3 (Table 1). The time-series plot shows the variation of daily mean temperature and emergency hospital admissions for pneumonia in the elderly and by sex (Figure 1).

Relative risk of cold/hot temperature

The exposure-lag-response surface shows the distributed-lag nonlinear relationship between ambient temperature and emergency hospitalizations for geriatric pneumonia (see Web Figure 1, available at http://aje.oxfordjournals.org/). Figure 2 shows the association with cumulative temperature exposure over the range of 0–21 lag days, using a natural cubic spline distributed-lag nonlinear model with 2 equally spaced knots for temperature and 4 knots for lag. The temperature-hospitalization relationship was reverse J-shaped, with significantly higher risks at both low and high temperatures. Temperature-specific risks of geriatric emergency pneumonia hospitalization at the first, 10th, 90th, and 99th percentiles (relative to the optimal temperature of 25.0°C) over the range of 0–21 lag days revealed that the risk associated with significant cold appeared at a lag of 1–2 days and lasted for 2–3 weeks, whereas the risk associated with heat occurred acutely within a lag of 0–1 days, followed by some harvesting on lag days 2–6, and remained relatively low over the longer lags (Table 2). The exposure-response relationship between relative humidity and pneumonia hospitalizations in the elderly is shown in Web Figure 2. Although there was no statistical significance, a slightly positive association between pneumonia hospitalizations and same-day relative humidity was found.

As indicated in Table 2, the associations with temperature varied by lag period. The overall relative risks for cold temperatures were nonsignificant on lag days 0–1; increased relative risks started to appear on lag day 2, and the risk elevation generally lasted for 3 weeks. Compared with the optimal temperature of 25°C, the cumulative relative risk of geriatric pneumonia hospitalization over lag days 0–21 was 1.61 (95% CI: 1.43, 1.81) for extreme cold (first percentile, 11.2°C) and 1.35 (95% CI: 1.22, 1.49) for moderate cold (10th percentile, 15.8°C), both higher than the effect estimates from the general whole population. The cold-associated risks were significantly stronger for men than for women. Hot temperatures showed acute effect estimates for geriatric pneumonia at a lag of 0–1 days; the cumulative relative risk over the range of 0–21 lag days was 1.13 (95% CI: 1.03, 1.23) for extreme heat (99th percentile, 30.6°C) and 1.08 (95% CI: 1.01, 1.16) for moderate heat (90th percentile, 29.4°C), compared with the optimal temperature (Table 2). The heat-related risks did not show much difference between the sexes. The exposure-response curves showed consistent associations between cold/hot temperatures and pneumonia hospitalizations in the elderly and by sex (Figure 3).

We also explored the associations in different age groups, including pneumonia hospitalizations among children, adults, and the elderly, respectively. As shown in Web Figure 3, childhood pneumonia was not associated with cold temperatures; adult pneumonia was not associated with either hot or cold temperatures. Note, however, that only 12.7% and 13.5% of total pneumonia cases were in children and adults, respectively. The relatively smaller

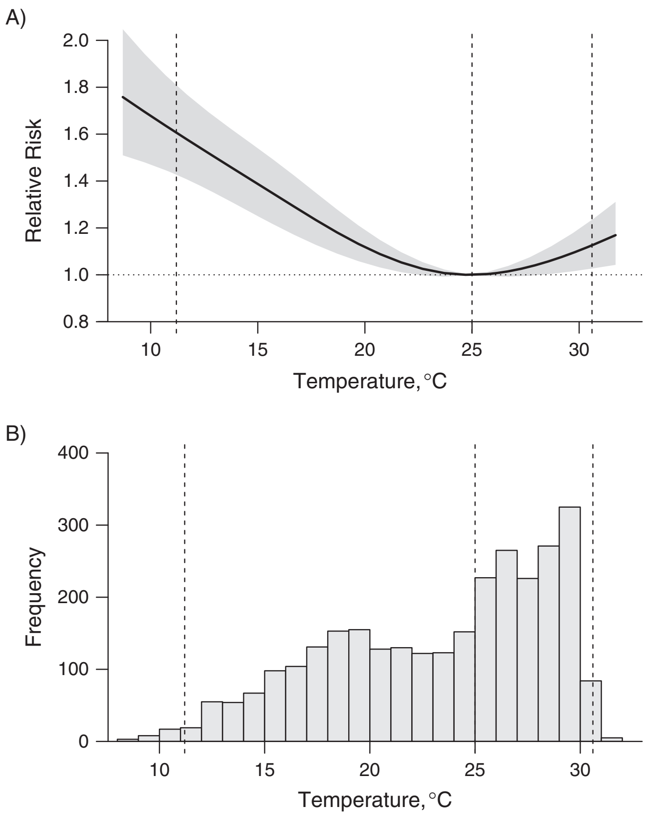

Figure 2. A) Association between cumulative temperature exposures over 0–21 lag days and emergency hospitalizations for pneumonia in the elderly (ages ≥65 years), Hong Kong, China, 2005–2012. Shaded area, 95% confidence interval. B) Temperature distribution in Hong Kong during 2005–2012. The 3 vertical dashed lines show the first percentile of ambient temperature, the optimum of 25.0°C, and the 99th percentile, respectively.

Table 2. Relative Risk of Emergency Hospitalization for Pneumonia Associated With Cold and Hot Ambient Temperatures in the Elderly (Ages ≥65 Years) Population Over Multiple Lag Days, Overall and by Sex, Hong Kong, China, 2005–2012

Disease Category and No. of Lag Days	Temperature Category[a]							
	Extreme Cold[b]		Moderate Cold[c]		Moderate Heat[d]		Extreme Heat[e]	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Total pneumonia								
0–1	0.79	0.76, 0.82	0.83	0.81, 0.86	1.09	1.06, 1.11	1.11	1.07, 1.15
2–6	1.20	1.15, 1.26	1.15	1.11, 1.20	0.97	0.95, 1.00	0.97	0.93, 1.01
7–21	1.48	1.37, 1.60	1.29	1.21, 1.38	1.05	1.01, 1.10	1.08	1.02, 1.15
0–21	1.41	1.27, 1.56	1.24	1.13, 1.36	1.11	1.05, 1.18	1.16	1.07, 1.26
Pneumonia in the elderly (ages ≥65 years)								
0–1	0.80	0.76, 0.83	0.83	0.80, 0.86	1.11	1.07, 1.14	1.14	1.09, 1.18
2–6	1.31	1.24, 1.38	1.21	1.16, 1.27	0.96	0.93, 0.99	0.96	0.92, 1.00
7–21	1.54	1.41, 1.68	1.34	1.24, 1.44	1.02	0.97, 1.07	1.04	0.97, 1.11
0–21	1.61	1.43, 1.81	1.35	1.22, 1.49	1.08	1.01, 1.16	1.13	1.03, 1.23
Elderly women								
0–1	0.77	0.73, 0.82	0.83	0.79, 0.87	1.12	1.08, 1.16	1.16	1.10, 1.22
2–6	1.30	1.21, 1.40	1.18	1.11, 1.26	0.94	0.90, 0.98	0.93	0.87, 0.98
7–21	1.35	1.19, 1.52	1.16	1.05, 1.29	1.01	0.94, 1.09	1.02	0.93, 1.12
0–21	1.35	1.15, 1.60	1.14	0.99, 1.31	1.07	0.97, 1.17	1.10	0.96, 1.25
Elderly men								
0–1	0.82	0.77, 0.87	0.83	0.79, 0.87	1.09	1.05, 1.13	1.12	1.06, 1.18
2–6	1.32	1.23, 1.41	1.24	1.17, 1.32	0.98	0.94, 1.02	0.99	0.93, 1.04
7–21	1.74	1.55, 1.96	1.52	1.37, 1.68	1.02	0.95, 1.09	1.05	0.96, 1.15
0–21	1.89	1.61, 2.22	1.57	1.37, 1.80	1.10	1.00, 1.20	1.15	1.02, 1.31

Abbreviations: CI, confidence interval; RR, relative risk.
[a] All temperatures were compared with the optimal temperature of 25.0°C.
[b] The first percentile of temperature (11.2°C).
[c] The 10th percentile of temperature (15.8°C).
[d] The 90th percentile of temperature (29.4°C).
[e] The 99th percentile of temperature (30.6°C).

sample size could have reduced our statistical power to examine the relationships in these two groups.

Attributable risk of cold/hot temperature

The optimal temperature corresponding to the minimum number of emergency hospitalizations for geriatric pneumonia identified in Hong Kong was 25.0°C. It was used as the reference point for computing the attributable risk measures. Table 3 shows estimates of the attributable fraction and attributable number for geriatric pneumonia hospitalizations attributed to nonoptimal temperature, by temperature category. Cold weather was responsible for most of the burden, while the fraction of hospitalizations due to heat was more limited. Of all emergency hospitalizations for geriatric pneumonia, 10.7% were attributed to nonoptimal temperatures, of which 8.7% and 2.0% were due to cold and hot weather, respectively, totaling 17,102 and 3,981 cases during the 8-year study period. Elderly men showed a significantly higher fraction of cases attributable to cold than did women (12.5% vs. 3.9%); however, not much difference in the attributable fraction was found between the sexes for hot weather (2.2% vs. 1.8%).

We further separated the contributions made by cold and hot weather into moderate and extreme temperatures. Results showed that the moderate temperatures accounted for the vast majority of the pneumonia hospitalizations attributable to nonoptimal temperature. Among the 8.7% of geriatric pneumonia hospitalizations attributed to cold weather, 8.1% were from moderate cold (11.2°C–25.0°C), while of the 2.0% of geriatric hospitalizations attributable to hot weather, 1.9% were from moderate heat (25.0°C–30.6°C). This phenomenon was similar for both sexes.

DISCUSSION

In this study, we examined the association between ambient temperature and emergency hospitalizations for pneumonia in the elderly population of Hong Kong. We observed significant nonlinear and delayed risks for

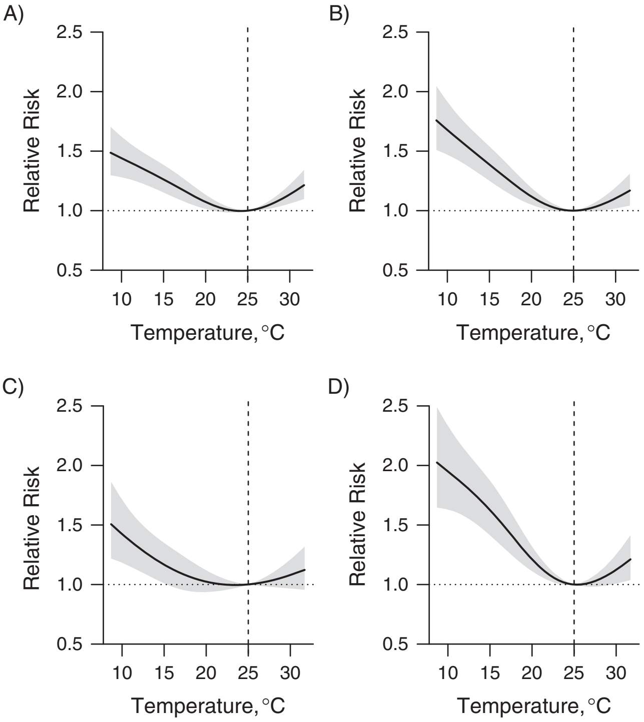

Figure 3. Association between cumulative temperature exposures over 0–21 lag days and emergency hospitalizations for pneumonia in the elderly (ages ≥65 years) in Hong Kong, China, during 2005–2012, overall and by sex, centering at 25.0°C (dashed line). A) Total pneumonia (all ages); B) elderly pneumonia (identical to Figure 2A); C) elderly pneumonia in women; D) elderly pneumonia in men. Shaded areas, 95% confidence intervals.

both cold and hot temperatures in geriatric pneumonia. Cold temperatures showed considerably higher risk for pneumonia incidence than hot temperatures. Although the relative risks were greater for extreme temperatures, the majority of the hospital admissions were attributed to moderately cold weather. Sex differences were also observed—elderly men showed significantly greater susceptibility to the cold than women.

Although the associations between weather-related factors, including sunshine, temperature, and humidity, and clinical pneumonia have been established in the literature (8, 9, 28), few studies have examined the short-term association between ambient temperature and pneumonia incidence (6, 10). In a study conducted in Shanghai, China, Liu et al. (10) observed a V-shaped relationship between daily mean temperature and pneumonia hospitalizations, with an optimum temperature at 18°C for subjects aged 65 years or older. In that study, a 5% increase in daily pneumonia hospitalizations per 1°C decrease in temperature at a lag of 4 days below the optimum was recorded; however, the distributed-lag effect was not considered, which may have produced underestimation of the true association. In another study conducted in Brisbane, Australia, Xu et al. (6) used temperature estimated from satellite remote sensing and a distributed-lag nonlinear model to examine risks associated with emergency

Table 3. Numbers and Fractions of Emergency Pneumonia Hospitalizations Attributable to Ambient Temperature in the Elderly (Ages ≥65 Years), Overall and by Sex and Temperature Category, Hong Kong, China, 2005–2012

Temperature Category	Total (*n* = 197,316)				Women (*n* = 93,964)				Men (*n* = 103,352)			
	AN[a]	95% CI	AF, %	95% CI	AN[a]	95% CI	AF, %	95% CI	AN[a]	95% CI	AF, %	95% CI
Overall	21,058	15,554, 26,347	10.67	7.79, 13.47	5,340	1,065, 9,511	5.68	1.31, 9.86	15,224	11,394, 18,596	14.73	11.08, 18.18
Cold[b]	17,102	11,174, 22,510	8.67	5.40, 11.69	3,667	−973, 7,773	3.90	−1.08, 8.13	12,964	8,910, 16,554	12.54	8.86, 15.91
Extreme cold[c]	1,258	907, 1,565	0.64	0.46, 0.81	424	180, 641	0.45	0.21, 0.69	822	593, 1,055	0.80	0.57, 1.01
Moderate cold[d]	15,964	9,468, 21,135	8.09	4.89, 10.73	3,224	−1,386, 7,293	3.43	−1.48, 7.55	12,304	8,761, 15,243	11.90	8.39, 15.38
Heat[b]	3,981	385, 7,527	2.02	−0.15, 3.78	1,681	−789, 4,048	1.79	−1.02, 4.02	2,276	−316, 4,638	2.20	−0.37, 4.53
Extreme heat[c]	168	34, 294	0.09	0.02, 0.15	65	−27, 148	0.07	−0.02, 0.16	103	15, 196	0.10	0.01, 0.18
Moderate heat[d]	3,801	140, 7,541	1.93	0.23, 3.71	1,607	−913, 3,791	1.71	−0.92, 3.94	2,169	−127, 4,561	2.10	−0.50, 4.36

Abbreviations: AF, attributable fraction; AN, attributable number; CI, confidence interval.
[a] The values in subgroups do not sum to the total because of approximation during calculation. The cumulative relative risks over the range of 0–21 lag days were used to compute the AN and the AF.
[b] Components attributable to cold and heat were computed with temperatures lower or higher than the optimal temperature (25°C), respectively.
[c] Extreme cold/heat was defined as ambient temperature lower than the first percentile or higher than the 99th percentile.
[d] Moderate cold/heat was defined as ambient temperature ranging between the first/99th percentiles and the optimal temperature (25°C).

department visits for childhood pneumonia. Those authors reported an optimum temperature of 23°C and found that both low and high temperatures were associated with increased risk of childhood pneumonia onset. However, associations with pneumonia in the elderly were not reported. In the current study, we observed significant positive estimated effects on geriatric pneumonia hospitalization for both cold and hot temperatures over 0–21 lag days. To our knowledge, this was the first study to explore the nonlinear and delayed associations between ambient temperature and pneumonia hospitalizations in the elderly.

Biological plausibility for the association and the sex difference

Several underlying mechanisms have been proposed in explaining increased pneumonia risk associated with exposure to cold and hot temperatures. It was suggested that cold weather would induce bronchoconstriction and suppress mucociliary defenses and other immunological reactions, resulting in local inflammation and increased risk of respiratory infection (29). Exposure to hot weather may trigger acute reactions when the body exceeds its thermoregulatory threshold. Meanwhile, in Hong Kong, hot weather is always accompanied by high humidity in the summertime. Hot and humid conditions provide suitable environments for the spread of fungal spores, bacteria, and viruses, which may be inhaled and subsequently lead to clinical disease in susceptible individuals (8, 9). The elderly population generally also has a lower thermoregulatory capacity and relatively weak immunological defenses, which increase their vulnerability to respiratory tract infection due to hot and cold weather.

The biological plausibility of a sex difference has been explored. Previous studies have indicated that men with pneumonia tend to be notably sicker than women and that they have more complications and worse vital signs (30). This may be explained by patterns of inflammatory, coagulation, and fibrinolysis biomarkers among men (31). A sex difference in immune system response to infection has also been suggested, with investigations into the role of X chromosomes, which encode genes for several important immune system mediators (32). In addition, smoking is associated with several diseases of the respiratory tract that predispose people to infections, and it activates a process that destroys the epithelium of the upper airways, which eliminates the normal washout of potential pathogens (32). A higher prevalence of smoking in men than in women in Hong Kong (19.9% vs. 3.0% in 2010) (33) may partly explain the vulnerability of Hong Kong men to cold exposure.

Higher risk attributable to cold temperature

The optimum temperature corresponding to the minimum level of geriatric pneumonia identified in Hong Kong was 25°C, which was very close to the median ambient temperature (24.7°C) during the study period. Using the optimum temperature as the reference, we calculated the overall disease burden of geriatric pneumonia attributable to temperature and computed the components attributable to cold and heat, with temperature below or above the optimum, respectively. We followed the approach proposed by Gasparrini and Leone (25), which accounted for the complex temporal patterns in exposure-lag-response relationships, and provided more appropriate estimations of attributable risk measures. The advantage of this approach was the provision of estimates for separate components of attributable risk (i.e., the risks attributable to cold and hot temperatures), allowing further examination of the associations for extreme and moderate temperatures with different exposure ranges. Most of the temperature-related geriatric pneumonia hospitalizations in Hong Kong were in fact attributable to cold, consistent with the exposure-response relationships and the temperature distribution, as illustrated in Figure 2. Among the 10.7% of nonoptimal temperature-related emergency hospitalizations for geriatric pneumonia, 8.7% and 2.0% were due to cold and hot weather, inducing 17,102 and 3,981 cases, respectively. As for the overwhelming majority of the attributable risk occurring in the moderate temperature range in spite of its relatively low relative risks, one explanation may be that moderate temperatures included the majority of the days in the series.

The limitations of this study should also be noted. Firstly, as in all other monitor-based time-series studies, personal exposure data were not available. The use of ambient temperature monitoring data to represent the population's exposure may have led to exposure misclassification. Hong Kong is a subtropical city with a very high prevalence of air conditioning use in the summer, which is hot and humid, but a low prevalence of house heating in the winter, which is a more temperate season. Thus, the outdoor fixed-site measurement of ambient temperature may have represented average population exposure better in the cool season than in the hot season. Secondly, we only included emergency hospital admissions for pneumonia, which reflects the associations of acute cases with environmental risk factors. However, the less severe cases were not captured. Therefore, the association with temperature examined in this study may not be applicable to the overall incidence of pneumonia in elderly subjects. Finally, caution is warranted when the findings of this single-city study are generalized to other places with different climates and population characteristics.

In conclusion, we observed significant nonlinear and delayed associations between both cold and hot ambient temperatures and geriatric pneumonia. Cold temperatures exhibited much higher risk for pneumonia incidence than hot temperatures. The majority of the temperature-related burden for pneumonia hospitalizations was attributable to cold weather. Results suggested that elderly males had greater susceptibility to cold weather than females. This study will help to inform public health policies in the planning of mitigation and intervention measures (such as central heating in winter) to prevent temperature-related pneumonia in vulnerable elderly populations.

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REFERENCES

1. World Health Organization. *Global Health Risks: Mortality and Burden of Disease Attributable to Selected Major Risks*. Geneva, Switzerland: World Health Organization; 2009. http://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_full.pdf. Accessed June 10, 2015.
2. Centre for Health Protection, Hong Kong Department of Health. Number of deaths by leading causes of death, 2001–2014. http://www.chp.gov.hk/en/data/4/10/27/380.html. Published 2012. Updated September 29, 2015. Accessed January 12, 2016.
3. HealthyHK, Hong Kong Department of Health. Pneumonia. http://www.healthyhk.gov.hk/phisweb/en/healthy_facts/disease_burden/major_causes_death/pneumonia/. Updated June 7, 2016. Accessed January 12, 2016.
4. Loeb MB. Community-acquired pneumonia in older people: the need for a broader perspective. *J Am Geriatr Soc*. 2003; 51(4):539–543.
5. Xu Z, Hu W, Tong S. Temperature variability and childhood pneumonia: an ecological study. *Environ Heal*. 2014;13:51.
6. Xu Z, Liu Y, Ma Z, et al. Impact of temperature on childhood pneumonia estimated from satellite remote sensing. *Environ Res*. 2014;132:334–341.
7. Chen Z, Ji W, Wang Y, et al. Epidemiology and associations with climatic conditions of *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae* infections among Chinese children hospitalized with acute respiratory infections. *Ital J Pediatr*. 2013;39:34.
8. Paynter S, Weinstein P, Ware RS, et al. Sunshine, rainfall, humidity and child pneumonia in the tropics: time-series analyses. *Epidemiol Infect*. 2013;141(6):1328–1336.
9. Onozuka D, Hashizume M, Hagihara A. Impact of weather factors on *Mycoplasma pneumoniae* pneumonia. *Thorax*. 2009;64(6):507–511.
10. Liu Y, Kan H, Xu J, et al. Temporal relationship between hospital admissions for pneumonia and weather conditions in Shanghai, China: a time-series analysis. *BMJ Open*. 2014; 4(7):e004961.
11. Djawe K, Levin L, Swartzman A, et al. Environmental risk factors for *Pneumocystis* pneumonia hospitalizations in HIV patients. *Clin Infect Dis*. 2013;56(1):74–81.
12. 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. *Int J Biometeorol*. 2012;56(4):569–581.
13. Ye X, Wolff R, Yu W, et al. Ambient temperature and morbidity: a review of epidemiological evidence. *Environ Health Perspect*. 2012;120(1):19–28.
14. Wong TW, Lau TS, Yu TS, et al. Air pollution and hospital admissions for respiratory and cardiovascular diseases in Hong Kong. *Occup Environ Med*. 1999;56(10):679–683.
15. Wong C-M, Atkinson RW, Anderson HR, et al. A tale of two cities: effects of air pollution on hospital admissions in Hong Kong and London compared. *Environ Health Perspect*. 2002; 110(1):67–77.
16. Chen R, Wang C, Meng X, et al. Both low and high temperature may increase the risk of stroke mortality. *Neurology*. 2013;81(12):1064–1070.
17. Yi W, Chan APC. Effects of temperature on mortality in Hong Kong: a time series analysis. *Int J Biometeorol*. 2015; 59(7):927–936.
18. Qiu H, Yu IT-S, Wang X, et al. Cool and dry weather enhances the effects of air pollution on emergency IHD hospital admissions. *Int J Cardiol*. 2013;168(1):500–505.
19. Gasparrini A, Armstrong B, Kenward MG. Distributed lag non-linear models. *Stat Med*. 2010;29(21):2224–2234.
20. Gasparrini A. Distributed lag linear and non-linear models in R: the package dlnm. *J Stat Softw*. 2011;43(8):1–20.
21. Guo Y, Barnett AG, Pan X, et al. The impact of temperature on mortality in Tianjin, China: a case-crossover design with a distributed lag nonlinear model. *Environ Health Perspect*. 2011;119(12):1719–1725.
22. Schwartz J, Samet JM, Patz JA. Hospital admissions for heart disease: the effects of temperature and humidity. *Epidemiology*. 2004;15(6):755–761.
23. Peng RD, Dominici F, Louis TA. Model choice in time series studies of air pollution and mortality. *J R Stat Soc Ser A Stat Soc*. 2006;169(2):179–203.
24. Armstrong B. Models for the relationship between ambient temperature and daily mortality. *Epidemiology*. 2006;17(6): 624–631.
25. Gasparrini A, Leone M. Attributable risk from distributed lag models. *BMC Med Res Methodol*. 2014;14:55.
26. Gasparrini A, Guo Y, Hashizume M, et al. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *Lancet*. 2015;386(9991): 369–375.
27. Gasparrini A. R documentation of "attrdl.Rd": attributable risk from a DLNM. http://www.biomedcentral.com/content/supplementary/1471-2288-14-55-S2.pdf. Published April 16, 2014. Accessed April 16, 2015.
28. Kim PE, Musher DM, Glezen WP, et al. Association of invasive pneumococcal disease with season, atmospheric conditions, air pollution, and the isolation of respiratory viruses. *Clin Infect Dis*. 1996;22(1):100–106.
29. Eccles R. An explanation for the seasonality of acute upper respiratory tract viral infections. *Acta Otolaryngol*. 2002; 122(2):183–191.
30. Choi W-I, Rho BH, Lee M-Y. Male predominance of pneumonia and hospitalization in pandemic influenza A (H1N1) 2009 infection. *BMC Res Notes*. 2011;4:351.
31. Reade MC, Yende S, D'Angelo G, et al. Differences in immune response may explain lower survival among older men with pneumonia. *Crit Care Med*. 2009;37(5): 1655–1662.
32. Falagas ME, Mourtzoukou EG, Vardakas KZ. Sex differences in the incidence and severity of respiratory tract infections. *Respir Med*. 2007;101(9):1845–1863.
33. Centre for Health Protection, Hong Kong Department of Health. Smoking. http://www.chp.gov.hk/en/content/9/25/8806.html. Published 2012. Accessed June 15, 2015.