RESEARCH PAPER

Human Vaccines & Immunotherapeutics 10:8, 2421–2432; August 2014; © 2014 Landes Bioscience

The relationship between meteorological factors and mumps incidence in Guangzhou, China, 2005–2012:

A distributed lag nonlinear time-series analysis

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Keywords: meteorological factor, mumps, relationship, distributed lag non-linear model, China

Abbreviations: CI, confidence interval; MMR, measles-mumps-rubella; MR, measles-mumps; IPCC, Intergovernmental Panel on Climate Change; DLNM, distributed lag non-linear model; Q-AIC, Akaike information criterion for quasi-Poisson; RR, relative risk; DF, degree of freedom; NS, natural cubic spline

Background: Over the past decade, there have been resurgences and large-scale outbreaks of mumps worldwide. Little evidence is available on the relationship between meteorological factors and the incidence of mumps. We aimed to explore the effects of meteorological factors on mumps incidence.

Methods: A Poisson regression model combined with a distributed lag non-linear model (DLNM) was used to evaluate the association between meteorological factors and the mumps incidence in Guangzhou, China, 2005–2012.

Results: Nonlinear relationships between meteorological factors, except sunshine hours, and mumps incidence were observed. The relative risks (RRs) of mean temperature, relative humidity and atmospheric pressure were 1.81 (95% confidence interval (CI), 1.41 to 2.32), 1.28 (95% CI, 1.02 to 1.59), and 0.80 (95% CI, 0.67 to 0.95) comparing the 99th percentile to the median of their own, respectively. For wind velocity, the RR was 0.70 (95%CI, 0.54 to 0.91) comparing the 1st percentile to the median. The hot effect and cold effect were larger in females than in males, and the hot effect increased with age.

Conclusions: Mean temperature, relative humidity, wind velocity and atmospheric pressure might be important predictors of the mumps incidence. Tropical cyclone caused a higher increase in mumps cases. Our findings highlight the need to strengthen the awareness of using protective measures during typhoon days and allocating more attention to the susceptible populations during the summer. The two-dose regimen of mumps vaccine should be included in the National Immunization Program schedule, and the catch-up vaccination campaigns should be promoted among adults.

Introduction

Mumps virus causes an acute febrile illness with a nonspecific prodrome followed by painful swelling of the parotid and less commonly, other salivary glands. The complications of mumps include deafness, mastitis, aseptic meningitis, encephalitis, and, in postpubertal age groups, oophoritis, and orchitis. The incubation period of mumps ranges from 12–25 d (median, 19 d).[1] Mumps is primarily transmitted by direct contact, droplet spread, or contaminated fomites. Although routine vaccination has resulted in a sharp decrease in the number of reported mumps cases,[2] there have been resurgences and large-scale outbreaks of mumps in many countries over the past decade, even in vaccinated population.[3-9] A total of 909087 mumps cases were reported during 2008–2010, and up to 81.8% of the cases were children aged 3–14 y in China, in which mumps is categorized as a class "C" infectious disease.[10]

The international measles-mumps-rubella (MMR) vaccine was introduced in Guangzhou in 1990. Since 1995, domestic live attenuated mumps vaccine has been in use and is provided to children over 8 mo of age.[11] As a part of the national routine vaccination schedule, MMR or MM (measles-mumps) vaccine has been administered to children 18–24 mo of age since 2008. Mumps is still a threat to children and young people in Guangzhou, where 10008 and 7856 mumps cases were reported

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Submitted: 04/21/2014; Revised: 05/09/2014; Accepted: 05/20/2014; Published Online: 06/23/2014
http://dx.doi.org/10.4161/hv.29286

Table 1. Daily weather conditions and the mumps incidence in Guangzhou, southern China, 2005–2012

Variable	Minimm	P25	Median	P75	Maximum	Mean ± SD
Maximum temperature(°C)	6.2	22.8	28.3	32.3	39.0	27.0 ± 6.6
Mean temperature(°C)	5.1	18.0	24.2	27.7	34.2	22.6 ± 6.3
Minimum temperature(°C)	1.8	14.8	21.2	24.8	30.4	19.5 ± 6.4
Relative humidity(%)	20.0	65.0	75.0	83.0	99.0	72.9 ± 13.2
Sunshine hours	0	0.2	3.9	7.7	11.8	4.2 ± 3.6
Wind velocity(m/s)	0.4	1.2	1.5	2.0	9.1	1.7 ± 0.9
Atmospheric pressure(hPa)	987.4	1002.3	1007.1	1012.8	1027.2	1007.5 ± 7.0
Number of mumps case	0	10	14	22	90	17 ± 10.5

P25 and P75 represent the 25th and 75th percentiles, respectively.

in 2011 and 2012, respectively, according to the notifiable communicable disease epidemic report.

According to the Intergovernmental Panel on Climate Change (IPCC) Fourth Assessment Report in 2007, the global average temperature increased by 0.74 °C for 100 y ending in 2005. In the context of global warming, climate change has been occurring and affecting the distribution and the transmission of infectious diseases, especially vector-borne and waterborne infectious diseases.[12] Studies have shown that climatic factors strongly influence the ecology, development, behavior, and survival of mosquitoes and the transmission dynamics of the diseases they transmit.[13] For example, rain and 3 cyclones inundated Mozambique for 6 wk, which resulted in a 5-fold increase in the incidence of malaria in 2000.[14] Temperature and humidity can affect the survival and transmission of airborne viruses.[15,16]

Seasonality in mumps incidence has been observed in some countries. For example, a significant annual pattern was documented in mumps incidence (April peak) in the United States,[17] and in Iowa, the peak of the outbreaks occurred in the spring of 2006 in April.[18] However, in China, the peaks were in winter and spring.[10] Climate change may partly influence the morbidity of mumps, so it is particularly necessary to explore whether climatic variations are one of the risk factors of the increased mumps cases in China. Little literature was found on the relationship between meteorological factors and mumps.[19] To access the effects of meteorological factors on the incidence of mumps and find the vulnerable populations, we performed a distributed lag nonlinear time-series analysis.

Results

There were 49 760 mumps cases reported in Guangzhou during 2005–2012, with a male to female sex ratio of 1.76:1 (31 746:18 014). The largest number of mumps cases (10 008) was found in 2011, and the incidence rate was 78.80/100 000. During 2005–2012, the peak in mumps cases was in summer. The descriptive statistics for the daily weather conditions and the incidence of mumps are shown in **Table 1**. The daily average maximum, mean and minimum temperature were 27.0 °C, 22.6 °C, and 19.5 °C, respectively. The average of the daily weather conditions were as follows: relative humidity, 72.9%; sunshine hours, 4.2 h; wind velocity, 1.7 m/s; and atmospheric pressure, 1007.5hPa.

Based on Spearman's correlation analysis (**Table 2**), the maximum temperature, mean temperature, minimum temperature, relative humidity, wind velocity, and atmospheric pressure were associated with the incidence of mumps. We used the statistically significant variables above for subsequent analyses.

The left 2 graphs of **Figure 1** (**Fig. 1A and B**) showed the patterns of mean temperature and the daily mumps cases over time with the seasonal patterns. The right graphs showed the crude relationship of the daily mumps cases with mean temperature. **Figure 1C** showed one point per day and **Figure 1D** showed data using systematic sampling every 30 cases from the fifth case sorted by mean temperature. Nonlinear relationship between mean temperature and the incidence of mumps was found in **Figure 1C and 1D**.

Table 3 provided the matrix of Spearman's correlation coefficient within the meteorological variables. The 3 temperature measures were strongly correlated with each other and with atmospheric pressure. Our results in **Table 4** indicated that mean temperature was associated with the lowest Q-AIC. We used mean temperature for the subsequent analyses for a better explanation of results and we conducted 2 independent DLNMs using 6 df for time per year for mean temperature and atmospheric pressure. **Table 4** showed that the time-series analysis using a NS with 6

Table 2. Spearman's correlation results between weather conditions and mumps incidence in Guangzhou, southern China, 2005–2012

	Maximum temperature	Mean temperature	Minimum temperature	Relative humidity	Sunshine hours	Wind velocity	Atmospheric pressure
The incidence of mumps	0.305**	0.314**	0.321**	0.207**	0.027	0.215**	–0.460**

**$P < 0.01$

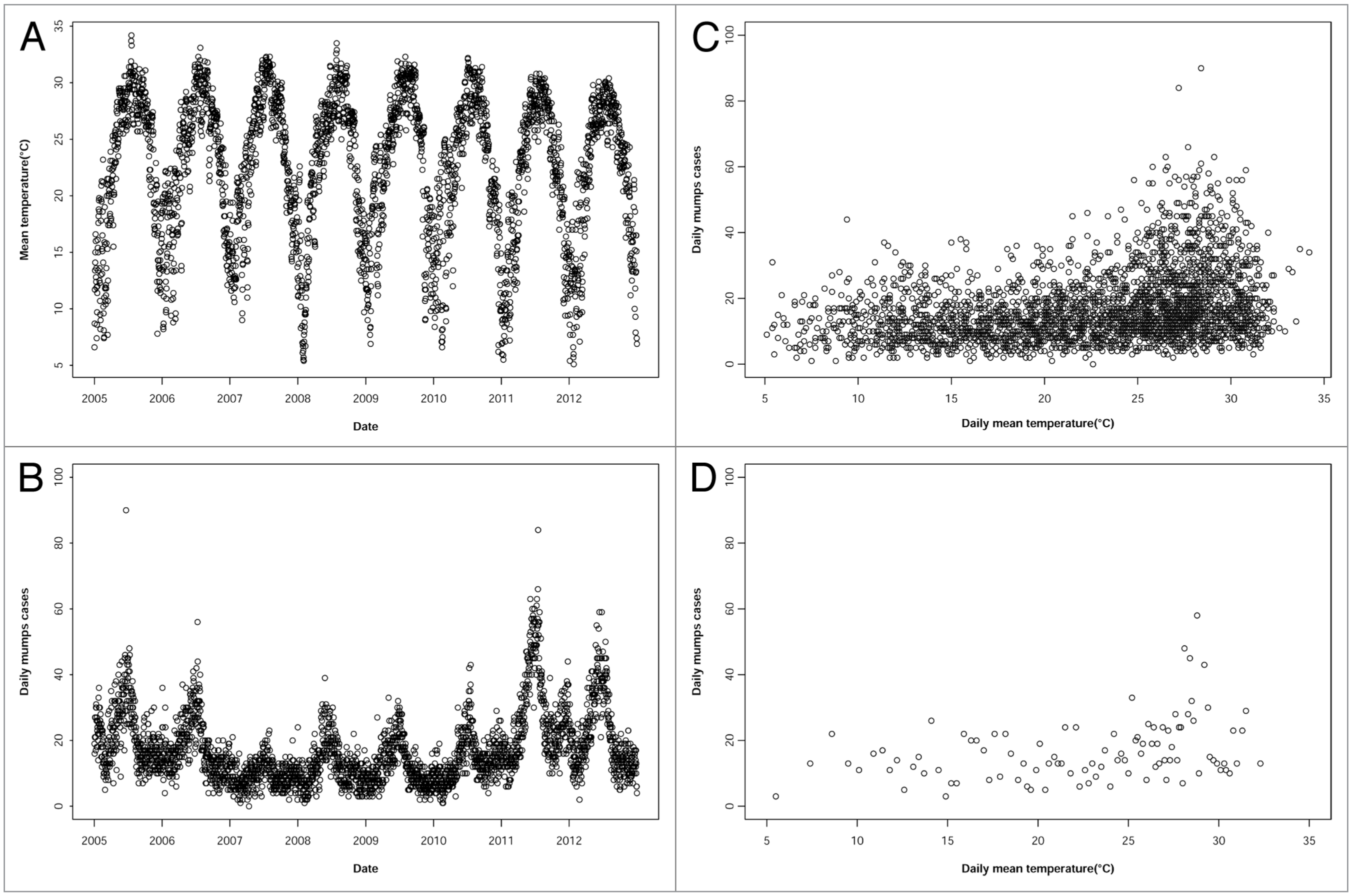

Figure 1. Daily mumps cases and mean temperature (°C) in Guangzhou, 2005–2012: patterns over time and crude association.

df per year for time for our data performed better than the case-crossover design.

The three-dimensional plots of **Figure 2** showed the relationship between the meteorological variables and the incidence of mumps with various lag days. All the relationship curves were nonlinear, whereas the different variables had different characteristics. The risk was the highest when daily mean temperature was 5.1 °C at lag 0 d and the RR was 1.05 (95%CI, 1.02–1.10); when relative humidity was 99% at lag 24 d, the RR was the highest as 1.39 (95%CI, 1.03–1.89); when wind velocity was 9.1m/s at lag 10 d, the RR was the highest as 1.82 (95%CI, 0.98–3.42); and when atmospheric pressure was 987.4 hPa at lag 3 d, the RR was the highest as 1.04 (95%CI, 0.92–1.18).

For better interpretative purpose, we plotted the specific unidimensional summaries of the associations. **Figure 3** summarized the estimated overall effects of the meteorological variables over the corresponding lag days. In general, mean temperature, relative humidity and wind velocity were positively associated with the incidence of mumps, whereas atmospheric pressure was negatively associated with the incidence of mumps. The overall effects of mean temperature and wind velocity were greater than the effects of relative humidity and atmospheric pressure.

To identify the cumulative extreme effects, we plotted the estimated effects of mean temperature, relative humidity, wind velocity, and atmospheric pressure comparing the 1st to their own 10th percentile and the 99th to their own 90th percentile (**Fig.** 4). The significant cold effect, which was protective, occurred within 0–10 d, whereas the significant hot effect was the highest on the current day and appeared within 0–25 d. The dry effect was not significant, and significant wet effect occurred after a 17- day lag. The significant windless effect appeared within 3–15 d, whereas the significant windy effect appeared within 5–12 d. The low-pressure effect was not significant and the significant high-pressure effect occurred within 1–3 d.

We also calculated the cumulative extreme effect of meteorological variables on the incidence of mumps along the lag days (**Table 5**). For mean temperature, the RR was 1.81 (95% CI, 1.41 to 2.32) comparing the 99th percentile to the median, and the RR was 0.61 (95% CI, 0.41 to 0.91) comparing the 1st percentile to the median. For relative humidity, the RR was 1.28 (95% CI: 1.02 to 1.59) comparing the 99th percentile to the median. For wind velocity, the RR was 0.70 (95% CI, 0.54 to 0.91) comparing the 1st percentile to the median. For atmospheric pressure, the RR was 0.80 (95% CI, 0.67to 0.95) comparing the 99th percentile to the median. Generally, the cumulative extreme effects of mean temperature were greater than the extreme effects of relative humidity, wind velocity, and atmospheric pressure.

Because temperature is more familiar to the public than other meteorological variables as well as being easier to determine

Table 3. Spearman's correlation coefficients matrix of meteorological variables in Guangzhou, southern China, 2005–2012

	Maximum temperature	Mean temperature	Minimum temperature	Relative humidity	Wind velocity	Atmospheric pressure
Maximum temperature	1.00					
Mean temperature	0.97**	1.00				
Minimum temperature	0.908**	0.973**	1.00			
Relative humidity	0.003	0.077**	0.178**	1.00		
Wind velocity	–0.108**	–0.085**	–0.058**	–0.004	1.00	
Atmospheric pressure	–0.775**	–0.815**	–0.827**	–0.396**	–0.105**	1.00

**$P < 0.01$

with a thermometer by themselves, and the effects of mean temperature on the incidence of mumps was apparent, we evaluated the effects of mean temperature on the incidence of mumps for the subpopulations (**Table 6**). The hot effect (the RR of the incidence of mumps by comparing the 99th to the 90th percentile of mean temperature) and cold effect (the RR of the incidence of mumps by comparing the 1st to the 10th percentile of mean temperature) were larger in females than in males. In general, the hot effects increased with age, whereas cold effects did not have the similar trend.

Based on the findings that the peak of mumps in Guangzhou was in summer during 2005–2012 and the relationship between the meteorological variables and the incidence of mumps that we obtained above, we hypothesized tropical cyclones affected mumps morbidity and calculated the RRs of the mumps incidence during the case periods vs. the reference periods in 2005–2012 (**Table 7**). There were excess cases between 2 periods of each year. The highest number of excess cases was 129 in 2010, and the least was 5 in 2007. The RRs were higher than 1, and the statistical significance of the RR 95% CIs were (1.04, 1.62), (1.14, 1.88), (1.37, 1.94), (1.06, 1.51), and (1.00, 1.52) in 2006, 2008, 2010, 2011, and 2012, respectively. In general, tropical cyclones caused a higher increase in mumps cases.

The sensitivity analyses showed that changing the df of seasonality and long-term trends caused similar results. Modifying the df for relative humidity, df for wind velocity and the maximum lag from 20 to 30 d for temperature, the results were robust to the alternative models.

Discussion

The relationships between meteorological variables and mumps incidence have been examined in this study. Our results indicated that there were nonlinear relationships between the meteorological variables and mumps incidence, except for sunshine hours. Mean temperature, relative humidity, and wind velocity were positively associated with mumps incidence, whereas atmospheric pressure was inversely associated with mumps incidence. In terms of the effects of extreme weathers on mumps, we detected that the hot effect and cold effect were larger in females than in male, and the hot effect increased with age.

Over the past decade, there have been frequent resurgences and large-scale global outbreaks of mumps, which have attracted an increasing degree of attention.[20-23] Very few studies have explored the relationship between meteorological factors and the incidence of mumps. To the best of our knowledge, this study is the first to apply a DLNM which simultaneously estimates the nonlinear and delayed effects to evaluate the effects of meteorological factors on the mumps incidence in China.

In our study, the relationships between meteorological factors and the incidence of mumps were nonlinear. We found that the RR of the mumps incidence increased with mean temperature and relative humidity, which is consistent with the findings in Fukuoka, Japan.[19] Little literature is available on the effects of wind velocity and atmospheric pressure. We found that the RR of the mumps incidence increased with wind velocity, whereas it decreased with increased atmospheric pressure. Our study shows that there is no significant relationship between sunshine hours and the mumps incidence.

The findings in this study are biologically and physically plausible. Temperature and humidity are the influence factors that affect the reproduction and the growth of virus. Although mumps virus is stable at 4 °C for days,[1] the virus will be inactivated. The temperature in Guangzhou is not high enough to kill the virus rapidly, but with an increase in the temperature, the activity of mumps virus increases. Moreover, an epidemiological study demonstrated that adolescents usually participate in fewer physical activities in colder months than warmer months.[24] This might result in an increase in contact frequency among children, which could increase the risk of mump infection in turn. A review concluded that viruses with lipid envelopes generally tend to survive longer at a lower relative humidity.[25] This finding might apply to mumps virus, which is lipid enveloped. There are always exceptions depending on individual situations, however, the biological effects of mumps virus has not been reported. Mumps virus might survive for a shorter time at higher humidity, however, higher humidity frequently occurs at higher temperature

Table 4. Akaike information criterion for quasi-Poisson(Q-AIC) values for the relationship between temperature measures and mumps incidence by DLNM type

DLNM type	Temperature measure	Q-AIC
Natural cubic spline-natural cubic spline(6df/year)[a]	Maximum temperature	17022.92
	Mean temperature	16984.23
	Minimum temperature	17007.85
Combined with case-crossover design(calendar month)[b]	Maximum temperature	17254.83
	Mean temperature	17252.24
	Minimum temperature	17252.90

[a]Using the natural cubic spline-natural cubic spline DLNM with 5 degrees of freedom for temperature, 3 degrees of freedom for lag and 6 degrees of freedom for controlling seasonality and the long-term trend; [b]Using the natural cubic spline-natural cubic spline DLNM combined with case-crossover design(calendar month) to control seasonality and the long-term trend.

because of an exponential relationship.[26] In Guangzhou, higher temperature and higher relative humidity occur in summer, when more people are likely to spend their time outside in more crowded environments which could promote mumps infection risk. Furthermore, high humidity causes the particulate matter that mumps virus attaches to become heavy, which will influence the concentration of the virus near the source of infections. Wind is of potential importance as a dilution and survival factor in the concentration of microbes. In Guangzhou, most of the time the wind is mild. The faster the wind velocity, the less time there is for mumps viruses to remain at a destination before they die, i.e., the faster the wind velocity, the more the concentration will resemble the source concentration of the infection.[27] When there is low pressure, the atmosphere is neutral or unstable, which is beneficial for the transmission of mumps virus, whereas high pressure hinders the spread of the virus.

The mumps incidence is high in Guangzhou (an incidence rate of 78.80/100100 and 61.61/100000 in 2011 and 2012, respectively). The peak of mumps was in summer in Guangzhou, which was different from the entire country in which the peak was in winter and spring.[10] However, the peak of mumps was also in summer in entire Guangdong Province,[28] and similar seasonal trend was found in Jiangxi and Fujian Province which are nearby Guangzhou city.[29,30] We hypothesized the different peaks might be partially due to the diverse geographical locations and the different temperature profiles in these areas.

The summers in Guangzhou are long, hot and humid. In China, Guangdong is the first of the coastal provinces in which tropical cyclones land, and more than one-half of the tropical cyclones are typhoons.[31] Typhoons usually bring low pressure and a large amount of rainfall.[32,33] High temperature, high relative humidity, high wind velocity and low atmospheric pressure increase the mumps incidence, according to the findings of our study. We hypothesized that tropical cyclones affect the mumps incidence and calculated the RRs of the mumps incidence during the case periods vs. the reference periods. Our results indicated that tropical cyclones generally caused a higher increase in mumps cases. These findings highlight the need to strengthen the awareness of using protective measures during typhoons. Because typhoons are predicable, it might be useful to take protective measures such as wearing breathing masks during typhoons to reduce the mumps incidence.

In this study, we found that the hot effect and cold effect were larger in females than in males. This finding might be attributable to factors such as physiological differences between males and females, the differences in behavior patterns, or confounding by social conditions (e.g., educational attainment, occupation, living alone). For example, an individual who has a higher education might pay more attention to hygiene and might be more likely to take protective measures such as using masks when necessary to, reduce the risk of infections.

Mumps is a common childhood disease and our data showed that mumps virus rarely infects old person. Therefore, we limited our analysis to the mumps cases among people age 0–64 y. We found that the hot effects increased with age, whereas mumps mainly targets children. We hypothesize that this effect might be because of the frequency and degree of hot exposure. High temperature often occurs in summer, and children have summer holidays and they usually are prevented by their parents from going out at the hottest hours of the day. Adults must work regardless of high temperature. Mumps is transmitted by close contact and increased with age, people contact with more and more people because of education, work, or social activities. Some studies indicated one of the most likely cause of mumps outbreaks in small group is intense social exposures.[34-36] We frequently pay more attention to children and men, because children are the target population of mumps virus, and males have the higher rate of complications than female.[7] Our findings highlight the need to strengthen the awareness of avoiding intense social expose and taking protective measures on hot days, especially for female and those who often work outside. Policy makers should pay more attention to susceptible subpopulations, such as providing high temperature holidays or offering necessary protective supplies. We could not find the trend of cold effect by age similar to the hot effect. One possible explanation is that mumps viruses might be inactive in low temperatures.

In this study, we found that mean temperature performed better according to the Q-AIC although maximum, mean, and minimum temperature had similar predictive results, which might be due to their strong correlation.

Many studies exploring the relationship between temperature and mortality selected the effect of relative humidity and atmospheric pressure at the current day, which indicates that they do not have lag effects.[37,38] In our study, we selected a

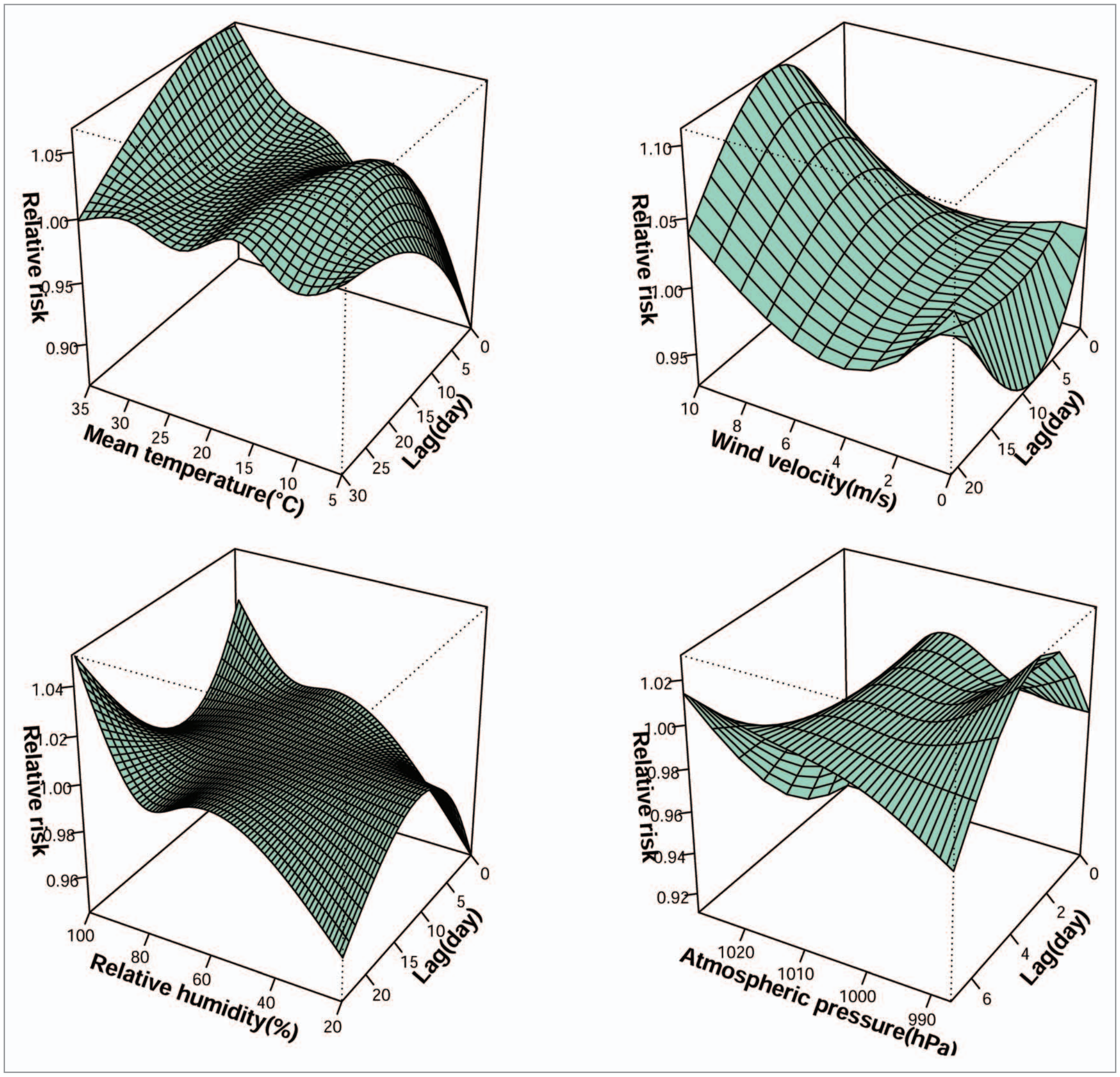

Figure 2. Relative risk of meteorological variables on mumps incidence, including mean temperature, relative humidity, wind velocity, and atmospheric pressure.

maximum lag of 24 d for relative humidity, a maximum lag of 7 d for atmospheric pressure and a maximum lag of 21 d for wind velocity, and we found that mumps activities are better explained. The incubation period of mumps is approximately 15 to 24 d,[18] and as early as 7 d before and until 9 d after onset of clinical symptoms, mumps virus can be isolated from saliva.[39] For this reason, we consider that relative humidity, wind velocity and atmospheric pressure will influence the incidence of mumps a few days later.

The case-crossover design is one of the most commonly used methods to assess the effects of temperature on mortality and morbidity. It controls seasonality and long-term trends by comparing the exposure on a period shortly prior to or after the onset to the reference periods in relatively small time windows (e.g., calendar month).[40-42] We compared the time-series design using a NS with 6 df per year for time and the case-crossover design. In our study, the time-series design using a NS with 6df per year for time performed better than the case-crossover design according to the Q-AIC.

Climate change has a long-term effect on marine and terrestrial ecosystems, which could directly or indirectly affect the survival and/or the spread of pathogens and their vectors. As a result, Climate change influences infectious diseases.[12,13,43] Our study also indicated that meteorological factors are associated with the incidence of mumps. In the context of climate change, it is quite possible that the frequency and the intensity of mumps outbreaks or resurgences will increase.

Mumps remains a threat to public health in Guangzhou. Mumps-containing vaccines were introduced in China in the 1990s, however, until 2008 the MMR or MM vaccine was not included in the National Immunization Program, in which the recommended target vaccination population are children aged 18–24 mo. Most population are not recommended to receive the mumps vaccination to protect themselves from virus infection.

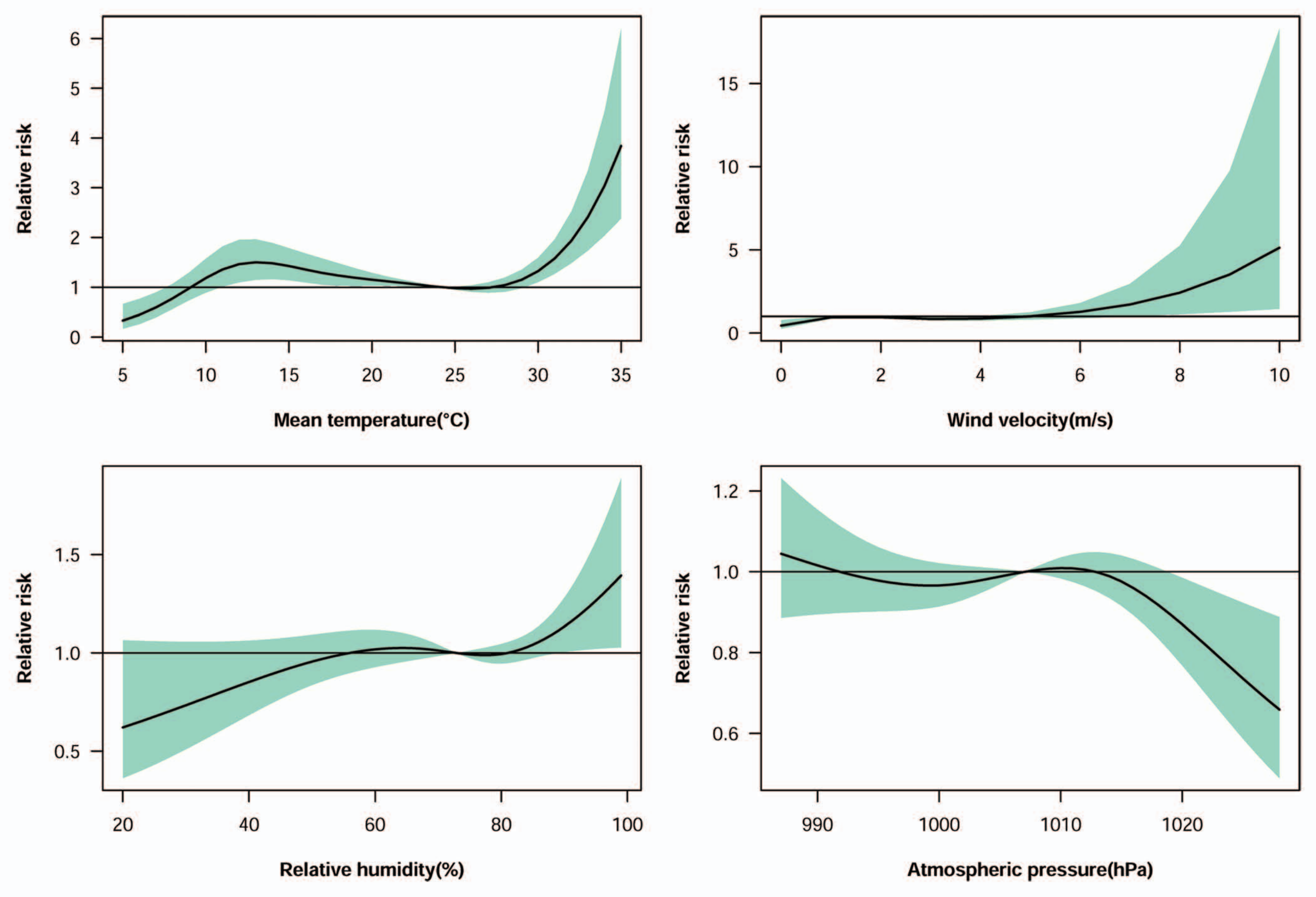

Figure 3. The estimated overall effects of mean temperature, relative humidity, wind velocity, and atmospheric pressure over 30, 24, 21, 7 d, respectively. The black lines represent mean relative risks, and green regions represent 95%CIs.

The mumps vaccines used in China do not provide full protection against mumps and our prior published study showed that the vaccine effectiveness of one dose of the mumps vaccine was 53.6% in Guangzhou in 2006–2012.[44] Moreover, about one half of the population in Guangzhou are floating, and 90% of them were 16 to 45-y-old. The floating population, with lower living standard and education, lack awareness regarding the vaccination for their children and themselves generally. The large floating population might contribute to the transmission of mumps virus. A large floating population, insufficient immunization coverage, unsatisfactory vaccine effectiveness, appropriate climate, and global warming cause the high incidence of mumps in Guangzhou.

In Guangzhou, an increasing mumps incidence has been observed among teenagers and adults in recent years. During the study period, 8967 of all notified mumps cases (18.0%) were >14-y-old. Because they have to pay for the vaccinations by their guardians or themselves, few would like to receive the vaccination for mumps prevention. Teenagers and young adults, who usually have low sero-positive prevalence and have more social contacts than younger children, have a higher risk of mumps.[45] In our study, we also found that adults are more susceptible to hot effect than young children. Besides the moderate vaccine effectiveness of one dose of mumps vaccine, we recommended the two-dose regimen of mumps vaccine should be included in the National Immunization Program schedule, and the catch-up vaccination campaigns should be initiated by using mumps-containing vaccine (for example MMR or MM vaccine) among adults.

To the best of our knowledge, this study is the first to apply DLNM, to estimate the relationship between meteorological factors and the incidence of mumps in China. We fitted a model for each combination of temperature measures to select the best-predicted temperature measures. We compared a time-series analysis using a NS with 6df per year for time to the case-crossover design, one of the most commonly used methods to assess the effects of temperature on mortality and morbidity, to determine which design performed better. We controlled for the day of the week and public holidays. We examined the cold and hot effects by sex and age to explore the susceptible populations and explored the effects of tropical cyclones on mumps incidence.

There are some limitations in the study. First, we only used data from one city to examine the effects of meteorological factors on the incidence of mumps, and it is difficult to generalize to other areas. Second, there are 30–50% silent infections of mumps,[46] which we were unable to report. The silent infections of mumps, as important sources of infection, might partly affect

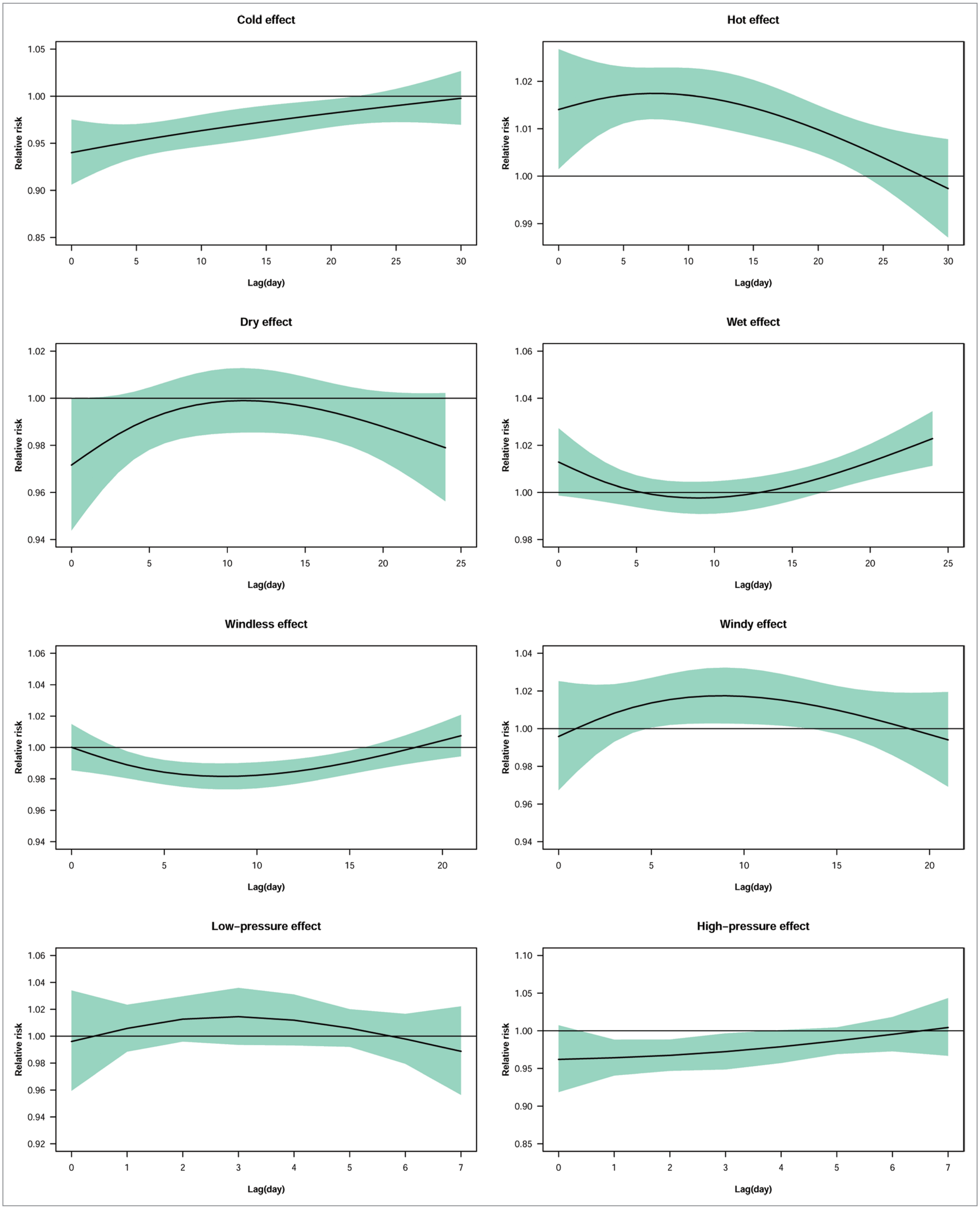

Figure 4. The estimated extreme effects of mean temperature, relative humidity, wind velocity, and atmospheric pressure. The black lines are mean relative risks, and green regions are 95%CIs.

Table 5. The cumulative extreme effects of meteorological variables on mumps incidence along the lag days

Meteorological variables	RR(95%CI)	
	Effect of extremely high value[a]	Effect of extremely low value[b]
Mean temperature	1.81 (1.41, 2.32)	0.61 (0.41, 0.91)
Relative humidity	1.28 (1.02, 1.59)	0.79 (0.59, 1.07)
Wind velocity	0.99 (0.78, 1.27)	0.70 (0.54, 0.91)
Atmospheric pressure	0.80 (0.67, 0.95)	1.00 (0.90, 1.11)

[a]The effects of an extremely high value were presented by the RR of the meteorological variables on the incidence of mumps by comparing the 99th to the 90th percentile of each variable. [b]The effects of an extremely low value were presented by the RR of the meteorological variables on the incidence of mumps by comparing the 1th to the 10th percentile of each variable.

the incidence of mumps. Third, we used the clinical diagnosis of mumps for cases instead of laboratory confirmed cases, which might overestimate the incidence of mumps. However, it is when the incidence of mumps is low that other causes of parotitis should be considered, and without laboratory confirmation of the diagnosis the overestimation of mumps will be likely.[1,47] In Guangzhou, the number of mumps cases was an average of 17 per day in 2005–2012, so we hypothesize that the clinical diagnosis of mumps will be relatively accurate. Fourth, we do not control for wind direction, precipitation, and some air pollutions, because these data were not available. A previous study showed that air pollution might alter early childhood susceptibility to infection,[48] so air pollution might be a confounding factor. Further study is needed to address the issue.

Materials and Methods

Data collection

Guangzhou, locating at 22°26′N to 23°56′N, and 112°57′E to 114°3′E, is the largest metropolis in southern China, covering an area of 7434 km^2 and with the population over 12.75 million in 2012. Traversed the Tropic of Cancer, Guangzhou has a typical subtropical climate with a distinct 4 seasons, in which summers are long, hot, and humid, winters are short, mild, and dry.

Mumps has been a notifiable disease in Guangzhou, and reports of mumps cases were derived from the National Information System for Disease Control and Prevention, a physician-based system for reporting suspected or confirmed cases from 1 January 2005 to 31 December 2012.[49] Because the web-based disease reporting system was initiated on 1 January 2004, the records might not be comprehensive in 2004, we collected the cases from January 2005. A clinical case of mumps was defined as acute onset of unilateral or bilateral tender, self-limited swelling of the parotid or other salivary glands lasting 2 or more days without other apparent cause. Bacterial infection was excluded by the absence of an increase in the white blood cell count.[50] We obtained demographic information for the cases including gender and age (between the date of mumps onset and the date of birth).

The daily meteorological data, including the maximum, mean, minimum temperature, and relative humidity, atmospheric pressure, wind velocity, and duration of sunshine, were obtained from the China Meteorological Administration.

Data analysis

We used Spearman's correlation to examine the relevance between the daily weather conditions and the incidence of mumps. Scatter plots were drawn to observe the patterns of temperature, the patterns of the incidence of mumps over time, and the crude relationship between temperature and the incidence of mumps. Because the scatter plot showed that the temperature-incidence relationships were nonlinear, and many studies have shown that temperature has a lag effect,[51-53] we fitted the distributed lag nonlinear model (DLNM) to assess the association between

Table 6. Relative risk of the mumps incidence associated with the hot and cold effects by gender and age

Variable	RR(95%CI)	
	Hot effect[a]	Cold effect[b]
Gender		
Male	1.35 (1.16, 1.56)	0.39 (0.24, 0.65)
Female	1.55 (1.28, 1.88)	0.43(0.23, 0.81)
Age		
0~4	1.30 (1.05, 1.61)	0.56(0.26, 1.19)
5~9	1.43 (1.17, 1.74)	0.16(0.08, 0.32)
10~14	1.58 (1.16, 2.16)	0.16(0.05, 0.48)
15~29	1.71 (1.22, 2.38)	2.17(0.83, 5.67)
30~64	1.83 (1.19, 2.80)	1.23(0.35, 4.28)

[a]The hot effect was the RR of the incidence of mumps by comparing the 99th to the 90th percentile of mean temperature; [b]The cold effect was the RR of the incidence of mumps by comparing the 1th to the 10th percentile of mean temperature.

Table 7. Relative risks of the mumps incidence during the case periods vs. the reference periods in 2005–2012, Guangzhou, southern China

Case period		Reference period		Excess cases	RR (95%CI)
Date	Number of cases	Date	Number of cases		
2005.7.18–2005.7.26	286	2005.6.27–2005.6.30 and 2005.8.12–2005.8.16	266	20	1.08 (0.91, 1.27)
2006.7.15–2006.7.20	182	2006.6.24–2006.6.26 and 2006.8.8–2006.8.10	140	42	**1.30 (1.04, 1.62)**
2007.9.23–2007.9.28	51	2007.9.2–2007.9.4 and 2007.10.17–2007.10.19	46	5	1.11 (0.74, 1.65)
2008.6.18–2008.6.23	151	2008.5.28–2008.5.30 and 2008.7.12–2008.7.14	103	48	**1.47 (1.14, 1.88)**
2009.6.23–2009.7.1	211	2009.6.2–2009.6.5 and 2009.7.18–2009.7.22	178	33	1.19 (0.99,1,45)
2010.7.15–2010.7.26	334	2010.6.24–2010.6.29 and 2010.8.11–2010.8.16	205	129	**1.63 (1.37, 1.94)**
2011.7.28–2011.8.3	271	2011.7.7–2011.7.9 and 2011.8.21–2011.8.24	214	57	**1.27 (1.06, 1.51)**
2012.7.24–2012.7.29	192	2012.7.3–2012.7.5 and 2012.8.17–2012.8.19	156	36	**1.23 (1.00, 1.52)**

The bold font means statistically significant.

the daily temperature and the daily number of mumps cases. DLNM, proposed and developed in recent years, is a flexible model that simultaneously estimates the nonlinear and delayed effects of exposure-response relationship, especially the effect of temperature (or air pollution) on mortality (or morbidity).[51,54] The DLNM can show the relationship between temperature and the incidence of mumps at specified temperature and lag and can calculate the cumulative effect in the presence of delayed distributions. We used DLNM to assess the relationships between other daily weather conditions and the daily number of mumps cases.

We calculated the Spearman's correlation coefficient matrix within the meteorological variables for a preliminary analysis. Because strong negative correlations were shown between each temperature measure and atmospheric pressure (**Table 3**), the constructed model using the 2 variables contemporaneously might result in colinearity problems. Thus, we conducted 2 separate DLNMs in the analysis as follows: the first DLNM considered the temperatures with no atmospheric pressure, while the second included atmospheric pressure with no temperatures. A Poisson regression with quasi-Poisson function which allows for over-dispersion in the daily number of mumps cases to combine a DLNM, was constructed. The model structure is as follows:

$$Log[E(Y_t)] = \alpha + NS(M,\ df,\ lag,\ df) + \sum NS_i(X_i) + \gamma DOW_t + \delta Holiday_t + NS(Time, 6{*}8)$$

where Y_t is the observed daily number of mumps cases on day t; α is the intercept; NS is a natural cubic spline; M is one of the 2 strongly correlative variable to estimate, including temperature (or atmospheric pressure); X_i is the other explanatory variables of meteorological factors, including relative humidity and wind velocity; DOW_t is day of the week on day t, and γ is vector of coefficients; $Holiday_t$ is a binary variable of which the value is "1" if day t was a public holiday; *Time* represent seasonality and the long-term trend, and we used the Akaike information criterion for quasi-Poisson(Q-AIC) and found that using 6 df/year for controlling seasonality and long-term trend produced the best model fitting.

We used a NS-NS DLNM to explore the effect of the explanatory variables and the lagged effects. On the basis of the biological characteristics of mumps virus, we used the Q-AIC to choose the df for temperature and atmospheric pressure and, the df for lag and the maximum lag. NS with 5df was applied to the daily temperature, and NS with 3df was applied to the lag. NS with 3 df was applied to the daily atmospheric pressure and NS with 3 df was applied to the lag. The knots were placed at equally spaced values in the temperature and atmospheric pressure to allow more flexibility in the 2 ends of the distribution and at equal intervals in the log scale of lags to allow more flexible lag effect for the early stage of delay. A maximum lag of 30 d was used to model the effect of temperature on the incidence of mumps because averaging over 31 d could cause bias in the estimates.[54] The maximum lag was set to 7 d for atmospheric pressure. The reference value was defined as the median value of temperature and atmospheric pressure to calculate the RR. According to the Q-AIC and the prior studies,[38,42,54] we selected NS with 3 df for the daily relative humidity and wind velocity, and NS with 3df for lag. We selected a maximum lag of 24 d for relative humidity and of 21 d for wind velocity.

We fitted a model for each combination of temperature measures (the daily maximum, mean, and minimum temperature) and the incidence of mumps using the above steps to observe which measures of temperature provided the lowest Q-AIC. We used the temperature with the lowest Q-AIC for subsequent analyses. During the study period, 99.7% mumps cases were those of 0- to 64-y-old. We focused on the cases of patients aged 0–64 y and stratified this population into 5 age groups (0–4, 5–9, 10–14, 15–29, and 30–64 y). Because more than 80% cases were children aged 0–14 y, which is the target mumps vaccination population, we divided children 0–14 y into 3 groups as the previous study.[19] We conducted stratified analyses by gender and age group to identify subpopulations that are more susceptible to the effect of cold or hot temperatures.

To further explore the relationship between meteorological factors and the incidence of mumps, we calculated the RRs comparing tropical cyclone periods with non-tropical cyclone periods to determine whether tropical cyclone occurrence is related to the incidence of mumps. During 2005–2012, we selected one tropical cyclone periods of each year that influenced Guangzhou as a case period, and selected the non-tropical cyclone in the same year as the reference period. Considering the possibility of lagged effects of tropical cyclones, we extended the case periods by 3 subsequent days following the tropical cyclone periods. To minimize potential time-varying confounding effects, the reference period was selected as a bidirectional near-term summer period of the dentical duration and with the dentical distribution of the days of the week as the case period. For example, we selected one tropical cyclone period between July 18th and July 23rd (6 d) in 2005 and the case period was July 18th to 26th, 2005 (9 d). The reference periods were the periods of June 27–30, 2005 and August 12–16, 2005. We assumed that the population of Guangzhou changed little during one summer and the reference period had the same length with the case period. Thus, the person-time units in the denominators of the 2 incidences were equivalent for the 2 periods. This result allowed us to calculate the ratios between the numbers of mumps cases as the RRs for each of the 2 periods of 2005–2012. We also calculated the excess cases as the difference in the number of mumps cases in the 2 periods of each year and the 95% confidence intervals (95%CI) of RR.

Some studies[42,55] used the case-crossover design to control for season and secular trends by controlling the case and control days in relatively small time windows (e.g., calendar month). We also compared the case-crossover design and the NS-NS DLNM with 6df/year to determine which model performed better.

All statistical tests were two-sided and $P < 0.05$ was regarded as a statistically significant difference. The analyses were performed using R software (version 3.0.1; R Development Core Team 2013) and the 'dlnm' package was used to create the DLNM.[56]

Sensitivity analysis

Sensitivity analyses were performed by changing the df (5–9 per year) for time to control for seasonality and secular trends, the df (4–7) for relative humidity, the df (4–7) for wind velocity and the maximum lag from 20 to 30 d for temperature.

The data were collated and aggregated at the Guangzhou Center for Disease Control and Prevention (GZCDC), and the study approval was obtained from the GZCDC ethics committee. All data used was anonymized.

Conclusions

Our study has provided evidence of the relationship between meteorological factors and the incidence of mumps. Mean temperature, relative humidity, wind velocity, and atmospheric pressure might be important predictors of the mumps incidence. Tropical cyclones caused a higher increase in mumps cases. Our findings highlight the need to strengthen the awareness of using protective measures during typhoon days and allocating more attention to the susceptible populations during the summer. The two-dose regimen of mumps vaccine should be included in the National Immunization Program schedule, and the catch-up vaccination campaigns should be promoted among adults.

Disclosure of Potential Conflicts of Interest

The author states he has no conflict of interest

Acknowledgments

We highly appreciate the help from the physicians from sentinel surveillance hospitals and Guangzhou CDC for providing data of mumps cases and China Meteorological Administration for providing meteorology data. We also thank the Project For Key Medicine Discipline Construction Of Guangzhou Municipality (2013–2015–07) for their contribution in the study.

Funding

This work was supported by a grant from the Guangdong Provincial Department of Science and Technology (2012B091100045).

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