The association between multiple meteorological factors and seasonal influenza A and B virus transmission in Macau

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Abstract

Background and objectives: Few studies evaluated the influence of meteorological factors on different influenza types activity in subtropical regions. The study aimed to explore the association between meteorological factors and the onset of influenza A (Flu-A) and B (Flu-B) in Macau.

Methods: Daily influenza cases data were collected from Kiang Wu Hospital from January 1st, 2014 to December 31st, 2018 in Macau. Daily meteorological data were obtained from Macau Meteorological Service. The distributed lag non-linear model (DLNM) was used to estimate the effects of meteorological factors on the seasonal influenza outbreak.

Results：Mean temperature had the peaking risks of both types at 4.0°C and 28.0°C. For the diurnal temperature range (DTR), the peaks of the cumulative relative risk (RR) of Flu-A were at 1.0°C and 5.0°C, while the cumulative RR of Flu-B increased as the DTR decreased. The association between influenza and relative humidity were showed a U-shape curve. The risk of influenza increased when the relative humidity was below 50% or above 90%. Both types increased significantly when the sunshine duration was below about 3.5 hours. Taking the median value as the reference, a significant cold effect was observed along 16-24 lag days in Flu-A. The lag effects were found in low-DTR, humid and short sunshine conditions in both types.

Conclusions：This study revealed the complex non-linear association between meteorological factors and the different influenza types activity in Macau. The finding helped to develop an early warning system to improve the response capacity to influenza epidemics.

Introduction

Influenza is considered as powerful and sometimes lethal for humans due to the constant mutations of the viruses, though vaccination can effectively prevent the occurrence of the diseases and treatments have been developed.(1) Around half-a-million people worldwide die from influenza annually, which causes a considerable health burden.(1) Seasonal Flu-A and B viruses lead to the majority of influenza globally.(2) And the prevalence patterns of Flu-A and Flu-B differ from each other and vary across regions.(3, 4) The transmission patterns of seasonal influenza might be influenced by the complex interaction among influenza viruses, meteorological factors, air pollutants, host susceptibility and human activity patterns.(5–7)

Influenza epidemics showed a typical seasonality in the temperate regions which witnessed a peak in winter, while the epidemics might occur at different times of a year or all-year-round in tropical and subtropical regions.(8) The varied prevalence patterns might result from the different characteristics of the climate variables in temperate and subtropical regions. A study conducted in six temperate European countries indicated that the outbreak of influenza was highly associated with low temperature and low UV indexes while lowlily associated was shown with humidity, wind speed and atmospheric pressure.(9) In Japan, lower temperature and lower relative humidity increased the risk of influenza by 65% and 40%.(10) Limited research was conducted in subtropical regions and their results were inconsistent. Hongkong, Guangzhou and Shenzhen are three cities lie on the south coast of China with a subtropical monsoon climate. Rainfall was a significant meteorological factor positive associated with influenza activity in Hong Kong, but the association were not found in Guangzhou nor Shenzhen.(11–13) A moderate wind (2-3m/s) was considered as a risk factor for influenza activity in Shenzhen but no association was shown in Guangzhou.(12, 13) In addition, meteorological factors might have different effects on different influenza types, but the research was limited. A study of 8 temperate regions, 2 subtropical regions and one tropical region showed a U-shaped association between temperature and Flu-A, but not Flu-B.(14) Absolute humidity was negatively correlated with Flu-B virus in temperate regions, whereas absolute humidity was positively correlated with Flu-A and B viruses in subtropical and tropical regions.(14) Another study conducted in Shanghai, a subtropical city on the east coast of China, found that exposure to a large DTR significantly increased the risk of Flu-A transmission while the relationship was contrasted in Flu-B.(5)

Macau is one of the most famous tourism cities with around tourist 320 million a year and the most densely populated area with 20,426 persons/ square kilometers worldwide.(15) It has an oceanic subtropical monsoon climate with abundant heat, sufficient water vapor, high temperature, and rainy climate characteristics. The spring, autumn and winter seasons in Macau are short, while the summer lasts for nearly 6 months with high temperature and humidity. It is usually affected by typhoons in summer and autumn. In addition, the vaccination of seasonal influenza has been included in the immunization programme of the Government of Macao Special Administrative Region. Macau has a moderate influenza vaccination coverage rate at around 24%, which was much higher than other regions of China, where the vaccination rate was 2% in mainland China but lower than the United States with around 50%.(16) Environmental factors have different effects on influenza in populations with different vaccination rates.(17) No relevant studies have been conducted in subtropical regions with the most densely populated and moderate vaccination coverage to explore this issue. Thus, it is necessary to access the association between different influenza types activity and meteorological factors in Macau based on the above unique features. This study aimed to find out the significant meteorological factors which had an impact on each type of seasonal influenza and the extreme effect of meteorological factors on each type in Macau. It was the first study of the impact of meteorological factors on influenza activity in subtropical regions with a moderate vaccination rate. This study could offer the government a foundation for developing an early warning system to improve the response capacity to influenza epidemics, help the public health department to optimize vaccination programmes and healthcare resource allocation.

Material And Methods

Data collection

Daily influenza A and B cases data were collected from Kiang Wu Hospital from January 1st, 2014 to December 31st, 2018 in Macau. Patients with influenza-like symptoms and laboratory-confirmed positive influenza virus test of throat and/or nasal swabs were diagnosed as influenza confirmed cases. Influenza-like symptoms were defined as acute respiratory infection and fever (> 38°C) with a least one respiratory symptom (cough, sore throat, or running or congested nose) and one systemic symptom (headache, muscle ache, sweats or chills, or tiredness).(18) Laboratory-confirmed positive influenza virus test was used the BD Veritor System for rapid detection of Flu A / B reagent. The daily meteorological data including mean temperature, relative humidity, wind velocity, atmospheric pressure and mean sunshine were obtained from Macau Meteorological Service. Further, the daily maximum and minimum temperatures were also collected to calculate DTR (DTR = maximum temperature – minimum temperature).

Statistical analysis

A descriptive analysis was used to describe the characteristic of daily meteorological parameters and influenza cases. The distribution patterns of influenza cases and daily meteorological parameters over time were displayed through scatter plots, respectively. The association of daily influenza cases and meteorological factors was examined by Spearman correlation analysis. To evaluate the potential nonlinear impacts of meteorological factors on seasonal influenza transmission with the lag effects of meteorological factors, DLNM was developed for Flu-A and Flu-B, respectively.(19, 20) Then Spearman correlation coefficients were calculated to explore the multicollinearity between meteorological factors. Only one of the high-correlated meteorological factors ($r > 0.8$) was included in the model. Because of the strong correlation between mean temperature and atmospheric pressure, the latter was eliminated from the model (Table 2). The model structure was stated as follow:

$Log[E(Y_t)] \sim \alpha + cb$ (meteorological variables, lag, df) + $\sum$ ns (X_j, df) + factor (DOW) + factor (holiday) + ns (time, df*5)

Where $E(Y_t)$ is the expected daily count of influenza cases on day t; α is the intercept; cb () represents the cross-basis matrix of meteorological factor; ns () is a natural cubic spline function; day of the week (DOW) is marked by categorical variable and is included in the model to control the day of the week effects; holiday is a binary variable and to minimize the impact of public holidays; time refers to seasonality and long-term trends in influenza and it was found that using a ns with 7 df per year fitted the model best supported by the previous study.(21) X_j represents other meteorological variables excluding the meteorological factors in the cross-basis matrix.

The model was established for each meteorological variable including mean temperature, diurnal temperature range, relative humidity and sunshine, respectively. The maximum lag day was defined as 27 days, which was based on the incubation period of influenza and infectious period of influenza virus from the previous studies.(12, 22) Akaike Information criterion (AIC) was used to select the dfs for meteorological variable in each model and the lowest AIC score was the most fitted model. The AIC values were summarized in Table S1. The effects of mean temperature, diurnal temperature range, relative humidity and sunshine were controlled using 5df, 5df, 4df, and 4df in the Flu-A model, respectively. In the Flu-B model, 5df, 2df, 4df and 3df were selected for these variables. The reference level was defined as the median values of mean temperature, relative humidity, sunshine, and the lowest point in the curve of the fitted association using DLNM of DTR. Further, the extreme effects of meteorological factors on the onset of influenza were estimated by comparing the 97.5th percentiles and 2.5th percentiles to the median values. the RR and 95%CI were calculated. To test the robustness of the model, sensitivity analyses were performed by using 2–5 df for each meteorological variable in the model.

All data analysis were conducted by R studio 3.6.2 and the “dlnm” package was used for the DLNMs. All statistical tests were two-sided with a statistically significant P-value < 0.05.

Results

Descriptive statistics

A total of 17104 influenza cases were confirmed from January 1st, 2014 to December 31st, 2018.

11982 specimens (70.1%) were detected as Flu-A and 5122 (29.9%) were detected as Flu-B. Table 1 showed the daily meteorological conditions and influenza cases. Flu-A had a higher daily incidence than Flu-B with the mean number of cases of 6.6 and 2.8, respectively. And the median of daily Flu-A and Flu-B cases were 3.0 and 0. The median of daily mean temperature, DTR, relative humidity, wind velocity, atmospheric pressure and mean sunshine were 18.4°C, 4.0°C, 77.0%, 2.2m/s, 1008.0hPa and 4.5h, respectively. The time-series distribution of daily Flu-A, Flu-B and meteorological factors were displayed in Fig. 1. For Flu-A, the prevalence in winter was higher than other seasons and there was an obvious outbreak every other year, concentrated in summer. For Flu-B, there was an increasing trend by years and witnessed a seasonal pattern with the peak at spring each year.

Correlation analysis

Table 2 demonstrated the bivariate correlations between influenza types and meteorological factors. Flu-A and Flu-B were both negatively associated with mean temperature, DTR, sunshine and positively associated with relative humidity, atmospheric pressure. No significant association between either type and wind velocity was found. Thus, the statistically significant variables including mean temperature, DTR, relative humidity and sunshine were used for subsequent analysis.

Association between meteorological variables and different seasonal influenza types

Obvious nonlinear cumulative associations were found between meteorological factors and both types when DLNM was applied (Fig. 2). The results of the highest cumulative RR for Flu-A/Flu-B activity and meteorological factors were shown in Table S2. In terms of mean temperature, the cumulative RRs of Flu-A and Flu-B had two common peaks, with the first peak at 4.0°C and the second peak at 28.0°C. At 4.0°C, the cumulative RR of Flu-A was 26.28 (95% CI: 6.52–105.90), and the cumulative RR of Flu-B was 4.57 (95% CI: 1.07–19.43). At 28.0°C, the cumulative RR of Flu-A was 4.74 (95% CI: 2.81-8.00), and the cumulative RR of Flu-B was 3.83 (95% CI: 1.50–9.80). At 20.0°C, another peak was found in Flu-B but not Flu-A with a cumulative RR of 3.53 (95%CI: 1.16–10.78). For DTR, two peaks in the cumulative RR of Flu-A were shown, with the first peak at 1.0°C (RR: 28.60, 95% CI: 5.56-147.16) and the second peak at 5.0°C (RR: 23.09, 95% CI: 8.34–63.93). The cumulative RR of Flu-B increased as the DTR decreased and the peaking risk was at 1.0°C (RR: 7.38, 95% CI: 2.07–26.29). The association between each type and relative humidity were similar and showed a U-shape curve. The first peak of Flu-A and Flu-B was at 35% with the cumulative RR of 15.54 (95% CI: 3.46–69.83) and 8.29 (95% CI: 1.23–55.97), respectively. And the second peak was located at 100% with the cumulative RR of Flu-A 8.52 (95% CI: 4.11–17.66) and Flu-B 3.28 (95% CI: 1.24–8.73). Additionally, both Flu-A and Flu-B increased significantly with shorter sunshine duration when the sunshine duration was below about 3.5 hours. The first peaking risk of Flu-A and Flu-B was at 0.0h, with the cumulative RR of 18.43 (95% CI: 10.60-32.07) and 4.95 (95% CI: 2.63–9.31), separately. As the increasing of the sunshine duration, another peak was observed at 9.0h for both types with the cumulative RR of Flu-A 9.02 (95% CI: 4.75–17.13) and Flu-B 4.28 (95% CI: 2.45–7.48).

The lagged association between meteorological factors at specific values, which were the highest points in Fig. 2, and Flu-A/Flu-B were then analyzed. For mean temperature, the highest risk of Flu-A at 4.0°C was found at the lag of 7-day (RR: 1.24, 95% CI: 1.15–1.33), while the highest risk of Flu-B at 4.0°C was found at the lag of 7-day (RR: 1.14, 95% CI: 1.05–1.23), 21-day (RR: 1.14, 95% CI: 1.05–1.23) and 27-day (RR: 1.14, 95% CI: 1.05–1.23), which the relatively high risk continued from 7-day lag to 27-day lag. In terms of DTR, 1.0°C had the highest risk of Flu-A at 21-day lag (RR: 1.22, 95% CI: 1.13–1.33), but Flu-B at 27-day lag (RR: 1.18, 95% CI: 1.03–1.35). Regarding relative humidity, relative humidity of 35% at 7-day lag had the highest risks for both types, with RRs of 1.17 (95%

CI: 1.08–1.26) for Flu-A and 1.13 (95% CI: 1.03–1.26) for Flu-B. Moreover, the lowest sunshine of 0.0h had the highest risks of Flu-A at 7-day lag (RR: 1.14, 95% CI: 1.10–1.17) and Flu-B at 27-day lag (RR: 1.09, 95% CI: 1.01–1.17). The detailed RRs with 95% CI by time lag were shown in Table 3 and the trends of lag-response curves of each type were displayed in Figure S1.

The trends of lag-response curves of extreme effects of the meteorological factors on Flu-A and Flu-B were displayed in Fig. 3 and Fig. 4. For Flu-A, a significant cold effect was observed along 16–24 lag days, the hot effect was not significant. No extreme effects of mean temperature were found in Flu-B. Only low-DTR effects were found in Flu-A and Flu-B, but no high-DTR effects. The low-DTR effect appeared within 21–27 lag days of Flu-A, and within 2–14 lag days and 24–27 lag days of Flu-B. The humid effect but not the dry effect was significant in both Flu-A and Flu-B. A significant humid effect was found within 6–27 lag days for Flu-A and within 6–13 lag days and 24–27 lag days for Flu-B. Short sunshine was a significant risk factor occurring within 1–27 lag days for Flu-A and 4–27 lag days for Flu-B, while long sunshine was not significant in both types. Table S3 showed the detailed RRs with 95% CI by the time lag of extreme effects of the meteorological factors on Flu-A and Flu-B.

Discussion

This was the first study attempt to reveal the association between meteorological factors and different types of seasonal influenza in Macau, a subtropical climate region with a moderate vaccination coverage and the densest population worldwide. In our study, it was found that mean temperature, DTR, relative humidity and sunshine were significantly associated with Flu-A and Flu-B by different time lags.

Flu-A virus was the dominant type. It might be because of a faster rate of influenza A virus mutation rates ranging from around 1×10^{-3} to 8×10^{-3} substitutions per site per year, which declined the effectiveness of the vaccination.(2, 23) The prevalence of Flu-A was higher in winter and epidemics occurred in summer every other year in Macau. Flu-B witnessed an increasing trend over years and has a typical seasonality with the peak at spring each year. The prevalence pattern of Flu-A in Macau was very similar to that of Flu-A in other subtropical cities in China.(13, 24, 25) Flu-B had a peak in winter in Shanghai, which is a subtropical city at mid-latitudes in China, while the peak was found in spring in Macau.(25) Macau is at low latitudes in China and has shorter winter. The potential explanation was that the latitudes and climate characteristics might have an impact on the transmission of Flu-B.(13)

Cold weather was associated with higher cumulative risks of influenza activity in our study which was consistent with previous studies performed in temperate and subtropical areas.(5, 8, 25) Low temperature was proved to keep the stability of the influenza virus particle by promoting the ordering of lipids on the viral membrane, which was critical for airborne transmission.(26) And the mucociliary clearance reduced at 5°C which allowed the virus remain on the upper respiratory mucosa.(27) Moreover, people prefer to stay indoors which increased the contact rate.(28) Moderative high temperature also favored the influenza activity in both types and the results were similar with studies conducted in subtropical regions like Shanghai and Shenzhen, China.(5, 13) One possible reason was that these cities are all in a subtropical monsoon climate, and the high temperature and rainy summer provide favorable conditions for the spread of the virus. Because in warm, humid climates, water droplets evaporate less water, and virus-carrying droplets could easily deposit on surfaces, increasing the chance of contact transmission.(29) Hypersecretion of mucin production might increase the host sensibility and research found that mucin production increased under 25°C and 40% relative humidity, but not at 37°C, 80% relative humidity.(30) When the temperature exceeded 30°C, no aerosol transmission was observed in any humidity which might explained the lowest cumulative risks of influenza activity over 30°C.(31)

In our study, small DTR was negatively associated with influenza outbreaks including Flu-A and Flu-B. The effect of low-DTR had 3 weeks to 4 weeks lag in Flu-A, while influencing Flu-B during the whole 4 weeks. In Shanghai, the Flu-A risk dramatically increased after exposure to large DTR, whereas Flu-B had a higher risk when exposed to stable temperatures.(5) The mechanism of DTR on influenza was not elucidated. Another possible reason was that large DTR occurred in transition seasons, and the transition seasons were short in Macau which reduced the large DTR effect on the occurrence of influenza.

Both the dry and humid conditions promoted the influenza transmission and the humid effect could persist for up to 27 days, which was consistent with a cross-dimensional study in eight cities in China.(32) Animal transmission studies in the guinea pig model and ferrets model showed that high RH (> 60%) and low RH (< 40%) kept influenza virus active in droplets for longer periods of time, while those at moderate RH (40–60%)), the virus was inactivated.(29, 31) In respiratory fluid and human mucus, influenza virus had high viability when the relative humidity below 50% or near 100%.(33) Inhalation of dry air caused shedding of guinea pig airway epithelial cilia, epithelial cell shedding, and tracheal inflammation, impairing innate antiviral defenses and tissue repair.(34, 35) Disruption of airway epithelial integrity caused by inhalation of dry air might be associated with winter epidemics of certain types of respiratory viral infections.(36) In humid conditions, virus-carrying water droplets were more likely to deposit on surfaces, increasing the chance of contact transmission.(29)

Short sunshine was found to increase the risk of each type. This founding was similar with previous studies.(9, 22) One hypothesis was that the lack of sunshine reduced the synthesis of melatonin and vitamin D in the body, which decreased human immunity.(37) Melatonin could activate intracellular signalling pathways and transcription factors, thereby inhibiting inflammatory activity.(38) Vitamin D reduced the risk of infections by inducing cathelicidins and defensins and reducing concentrations of pro-inflammatory cytokines.(39) Moreover, in our study, we found the risk of being infected increase during the moderative long sunshine (5.0h-9.0h). The mechanism was unknown because of the limited research and it required further study.

There were some strengths in this study. Firstly, this was the first study that explored the complex and delayed relationship between meteorological factors and seasonal influenza in a subtropical climate region with a moderate vaccination coverage and the most dense population worldwide. Secondly, the dominant influenza types were both included in this study, which provided more comprehensive and comparable information of the epidemic characteristics as well as relations to meteorological conditions. Several limitations were noted in this study. Firstly, a previous study figured out that the association had a slight difference among different age groups.(12) To have more accurate results, further work could explore the association between meteorological factors and influenza activity among different subgroups. Secondly, air pollutants were not adjusted in this study which might result in bias. Air pollutants such as PM2.5, PM10, O3 and mean temperature were found that had a significant interaction effect on diseases.(40, 41) Thirdly, Macau is an international tourism city. Influenza cases counted in our study covered both local residents and tourists which might lead to selection bias. However, based on our previous research finding that tourist cases account for a small percentage of total cases (Flu-A: 7.44%, Flu-B: 6.83%), our results were reliable.(42)

Conclusions

This study revealed mean temperature, DTR, relative humidity and sunshine significantly non-linearly associated with Flu-A and Flu-B by different time lags in Macau. The finding provided an in-depth insight into the interaction between influenza activity and meteorological factors, and helped to develop an early warning system to improve the response capacity to influenza epidemics.

Abbreviations

AIC: Akaike Information criterion

DLNM: distributed lag non-linear model

DTR: diurnal temperature range

DOW: day of the week

Flu-A: influenza A

Flu-B: influenza B

RR: relative risk

95% CI: 95% confidence intervals

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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Authors’ contributions

Ng HoiMan, Yusi Li, Teng Zhang, Ni JinLiang and Qi Zhao conceived the study and developed its design. Ng HoiMan and Wong ChioHang were involved in the acquisition of data. Yusi Li, Teng Zhang and Yiping Lu performed the statistical analysis and the interpretation of the data. Ng HoiMan and Yusi Li drafted the manuscript. Ni JinLiang and Qi Zhao revised and approved the final manuscript. All authors revised the manuscript. All authors contributed to the final version and agreed to the submission.

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Tables

Table 1
Statistics of daily meteorological parameters and influenza cases in Macau, 2014–2018

Variables	Mean	SD	Min.	P25	P50	P75	Max.
Flu-A frequency	6.6	9.6	0	1.0	3.0	8.0	85.0
Flu-B frequency	2.8	7.0	0	0	0	2.0	57.0
Mean temperature (°C)	22.9	5.5	3.6	18.4	24.2	27.8	32.6
DTR (°C)	5.4	1.9	0.90	4.0	5.5	6.7	13.0
Relative humidity (%)	82.0	10.7	35.0	77.0	84.0	90.0	100.0
Wind velocity (m/s)	3.0	1.3	0.6	2.2	2.8	3.6	13.3
Atmospheric pressure (hPa)	1013.0	6.7	988.0	1008.0	1013.0	1018.0	1035.0
Mean sunshine (h)	4.7	4.0	0	0.2	4.5	8.7	12.7
DTR: diurnal temperature range							
SD: standard deviation; Min.: minimum; Max.: maximum; P25: the 25th ; percentile; P50: the 50th percentile; P75: the 75th percentile.							

Table 2
Spearman correlation between influenza cases and meteorological factors in Macau, 2014–2018

Variables	Influenza A frequency	Influenza B frequency	Mean temperature (°C)	Diurnal temperature range (°C)	Relative humidity (%)	Wind velocity (m/s)	Atmospheric pressure (hPa)
Flu-A frequency	1						
Flu-B frequency	0.47	1					
Mean temperature (°C)	-0.19*	-0.24*	1				
Diurnal temperature range (°C)	-0.05*	-0.10*	0.08*	1			
Relative humidity (%)	0.06*	0.11*	0.07*	-0.56*	1		
Wind velocity (m/s)	-0.03	-0.03	-0.43*	-0.14*	-0.23*	1	
Atmospheric pressure (hPa)	0.09*	0.15*	-0.86*	0.05*	-0.33*	0.40*	1
Sunshine (h)	-0.09*	-0.12*	0.45*	0.56*	-0.56*	-0.19*	-0.16*
*: $P < 0.05$							

Table 3
The RRs with 95% CI of Flu-A and Flu-B associated with meteorological variables at specific values by different time lags in Macau, from 2014–2018

		RR				
		0-day lag	7-day lag	14-day lag	21-day lag	27-day lag
Mean temperature						
Flu-A	4.0°C vs 24.2°C	0.81 (0.65–1.01)	1.24 (1.15–1.33) *	1.10 (1.02–1.18) *	1.16 (1.08–1.25) *	1.05 (0.87–1.27)
Flu-B	4.0°C vs 24.2°C	0.76 (0.61–0.93)	1.14 (1.05–1.23) *	1.09 (1.01–1.18) *	1.14 (1.05–1.23) *	1.14 (1.05–1.23) *
Diurnal temperature range						
Flu-A	1.0°C vs 10.0°C	1.04 (0.87–1.24)	1.06 (0.98–1.16)	1.11 (1.02–1.21) *	1.22 (1.13–1.33) *	1.20 (1.04–1.40) *
Flu-B	1.0°C vs 13.0°C	1.13 (0.95–1.34)	1.08 (1.01–1.16) *	1.06 (1.00-1.12)	1.03 (0.97–1.10)	1.18 (1.03–1.35) *
Relative humidity						
Flu-A	35.0% vs 84.0%	1.10 (0.93–1.31)	1.17 (1.08–1.26) *	1.14 (1.06–1.23) *	1.00 (0.93–1.08)	1.15 (1.00-1.32) *
Flu-B	35.0% vs 84.0%	0.96 (0.81–1.13)	1.13 (1.03–1.26) *	1.08 (0.99–1.18)	1.06 (0.97–1.15)	1.08 (0.95–1.22)
Sunshine						
Flu-A	0.0h vs 4.5h	1.03 (0.95–1.11)	1.14 (1.10–1.17) *	1.12 (1.08–1.15) *	1.12 (1.08–1.15) *	1.07 (1.00-1.14) *
Flu-B	0.0h vs 4.5h	0.99 (0.90–1.08)	1.05 (1.02–1.09) *	1.06 (1.03–1.10) *	1.08 (1.05–1.12) *	1.09 (1.01–1.17) *
*: P < 0.05						

Figures

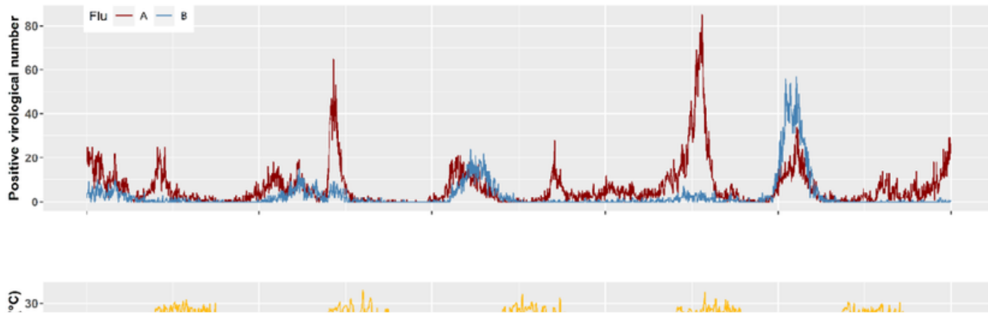

Figure 1

The time series of daily influenza cases and daily meteorological factors in Macau, 2014-2018

Legends: DTR: diurnal temperature range

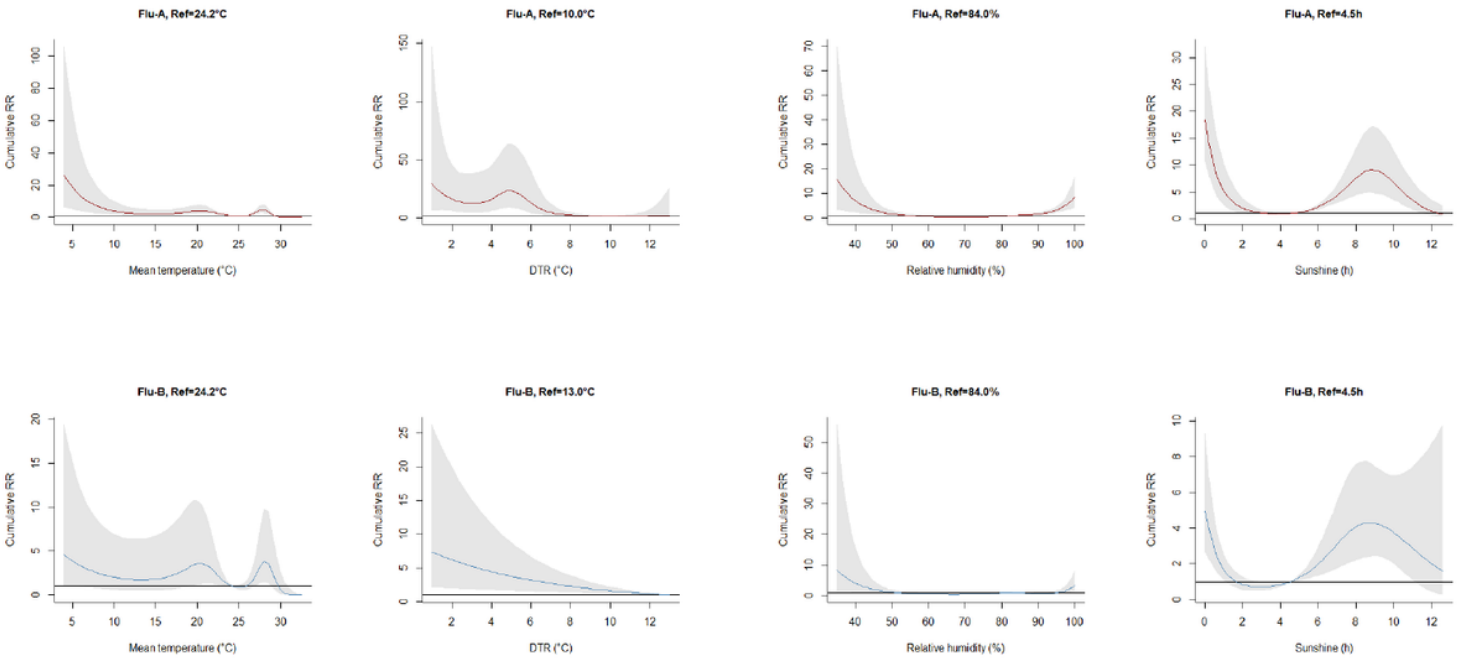

Figure 2

Cumulative associations between meteorological factors with Flu-A and Flu-B in Macau

Legends: DTR: diurnal temperature range; the reference values for mean temperature, relative humidity and sunshine were their medians, and those for DTR were their lowest RR points

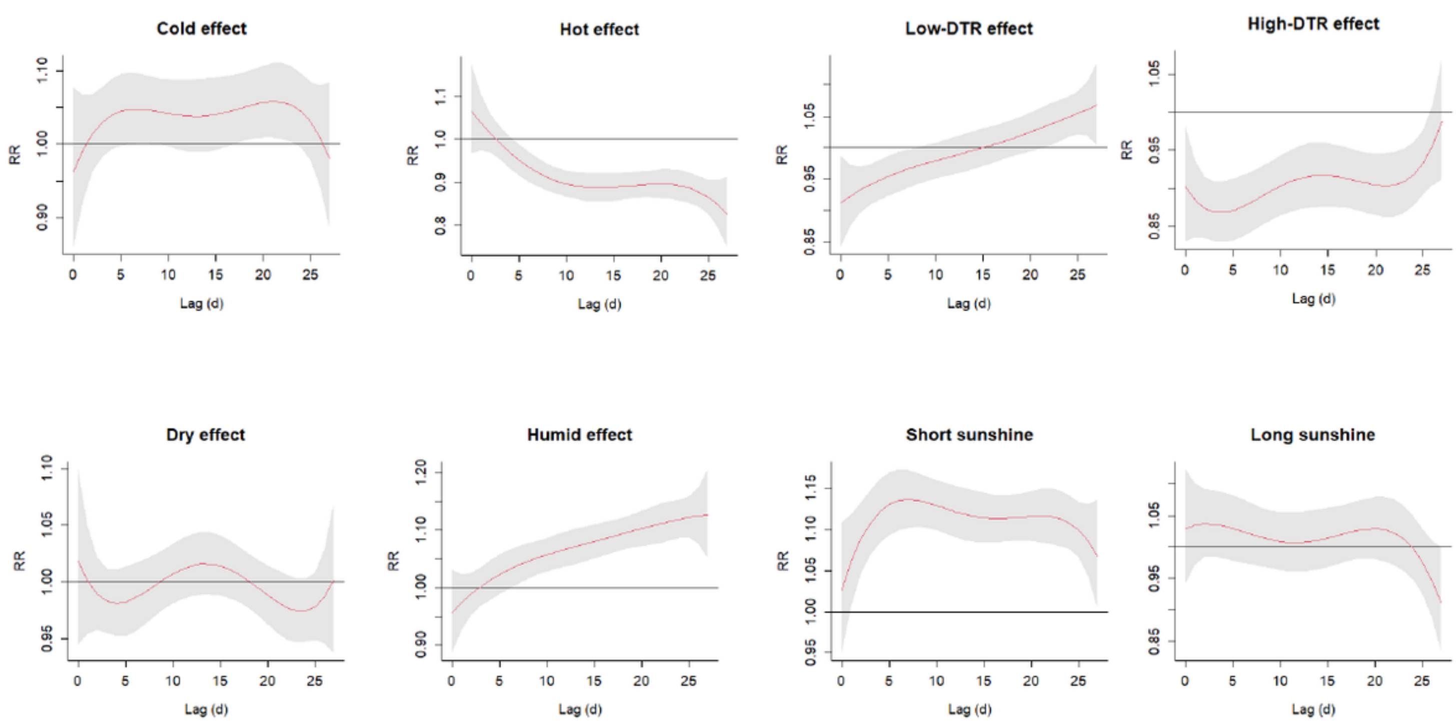

Figure 3

The estimated extreme effects at the 2.5th and the 97.5th percentile of meteorological factors at different lag days on Flu-A in Macau

Legends: DTR: diurnal temperature range; the reference values for mean temperature, DTR, relative humidity and sunshine and were their medians

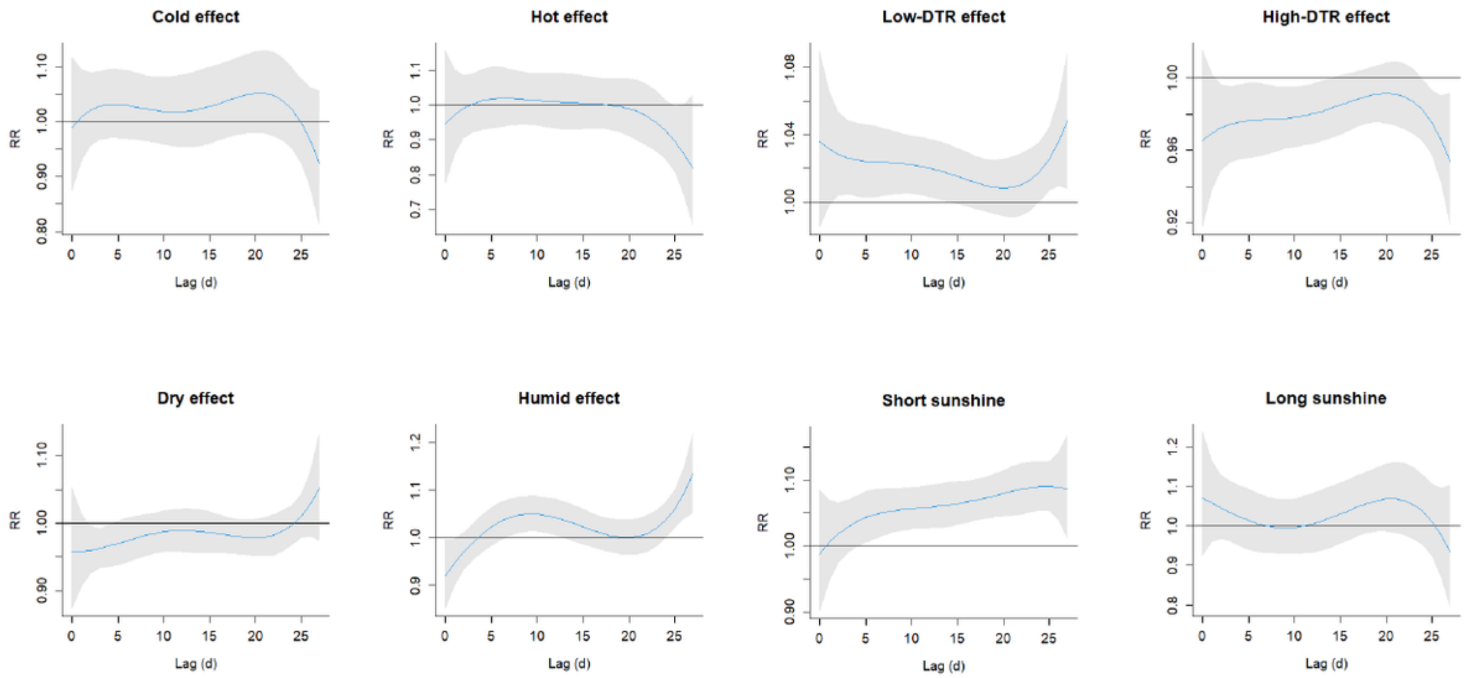

Figure 4

The estimated extreme effects at the 2.5th and the 97.5th percentile of meteorological factors at different lag days on Flu-B in Macau

Legends: DTR: diurnal temperature range; the reference values for mean temperature, DTR, relative humidity and sunshine and were their medians

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile1.pdf
- FigureS1.pdf