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The complex associations of climate variability with seasonal influenza A and B virus transmission in subtropical Shanghai, China

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Abstract

Most previous studies focused on the association between climate variables and seasonal influenza activity in tropical or temperate zones, little is known about the associations in different influenza types in subtropical China. The study aimed to explore the associations of multiple climate variables with influenza A (Flu-A) and B virus (Flu-B) transmissions in Shanghai, China. Weekly influenza virus and climate data (mean temperature (MeanT), diurnal temperature range (DTR), relative humidity (RH) and wind velocity (Wv)) were collected between June 2012 and December 2018. Generalized linear models (GLMs), distributed lag non-linear models (DLNMs) and regression tree models were developed to assess such associations. MeanT exerted the peaking risk of Flu-A at 1.4℃ (2-weeks' cumulative relative risk (RR): 14.88, 95% confidence interval (CI): 8.67-23.31) and 25.8℃ (RR: 12.21, 95%CI: 6.64-19.83), Flu-B had the peak at 1.4℃ (RR: 26.44, 95%CI: 11.52-51.86). The highest RR of Flu-A was 23.05 (95%CI: 5.12-88.45) at DTR of 15.8℃, that of Flu-B was 38.25 (95%CI: 15.82-87.61) at 3.2℃. RH of 51.5% had the highest RR of Flu-A (9.98, 95%CI: 4.03-26.28) and Flu-B (4.63, 95%CI: 1.95-11.27). Wv of 3.5m/s exerted the peaking RR of Flu-A (7.48, 95%CI: 2.73-30.04) and Flu-B (7.87, 95%CI: 5.53-11.91). DTR ≥12℃ and MeanT <22℃ were the key drivers for Flu-A and Flu-B, separately. The study found complex non-linear relationships between climate variability and different influenza types in Shanghai. We suggest the careful use of meteorological variables in influenza prediction in subtropical regions, considering such complex associations, which may facilitate government and health authorities to better minimize the impacts of seasonal influenza.

Keywords: climate factors; influenza; subtropical area; Shanghai; China

1. Introduction

While vaccination can effectively prevent seasonal influenza, it remains epidemics and lead to approximately 3 to 5 million cases and 290,000 to 650,000 deaths annually worldwide (World Health Organization, 2018). Generally, influenza peak once in the winter in temperate areas (Finkelman et al., 2007), however, it seems that the seasonal patterns in tropical and subtropical zones are more complicated. Several previous studies reported that the peaking of seasonal influenza occurred once a year (in winter or spring/summer) in some subtropical areas (Cheng et al., 2012), however, other studies found the peaks in subtropical regions were detected in both summer and winter (Iha et al., 2016; Liu et al., 2017). Furthermore, the transmission patterns of seasonal influenza were very diverse in China by region (Du et al., 2012; Shu et al., 2010; Yu et al., 2013). The seasonal patterns of seasonal influenza are driven by the complex interaction among influenza virus, climate factors and human activity patterns (Alonso et al., 2007; Surveillance and System, 2012; Tamerius et al., 2013).

Recently, there has an increasing interest in the association between climate variables and seasonal influenza activity. Low temperature has been reported to favour the transmission of influenza in temperate and tropical climate (Huang et al., 2017; Soebiyanto et al., 2014; Tsuchihashi et al., 2011; Xu et al., 2013), as well as to increase the mortality of influenza (Davis et al., 2012). A decrease of temperature during the preceding three days was correlated to an increased risk of influenza infections in cold climate (Jaakkola et al., 2014). Other climate variables, such as absolute humidity, relative humidity and rainfall have also been reported to be associated with seasonal influenza infections (Gomez-Barroso et al., 2017; Shaman and Kohn, 2009; Shaman et al., 2010b; Tamerius et al., 2013). Moreover, the geographical variation of seasonal patterns of influenza indicates that climate factors may promote influenza infections with complex interactive effects, such as the significant interactive effect between temperature and relative humidity (Wang et al., 2017). However, the majority of previous studies focused on tropical or temperate zones, little is known about the associations of multiple climate variables with different influenza types in subtropical regions.

Additionally, the transmission patterns of seasonal influenza can even be diverse in neighbouring regions sharing similar climate (Yu et al., 2013). It is necessary to specifically assess the response of influenza to climate variables by location. Understanding the relationship between climate factors and influenza can be seen as a foundation for developing early warning systems based on climate factors for seasonal influenza. This study aims to examine the associations of multiple climate factors (mean temperature (MeanT), diurnal temperature range (DTR), relative humidity (RH), and wind velocity (Wv)) with seasonal influenza A virus (Flu-A) and B virus (Flu-B) in subtropical Shanghai, China.

2. Methods

2.1 Study site and data collection

This study was conducted in Pudong New Area, where is the largest district of Shanghai City, the one of the largest metropolis worldwide (Fig. 1). To December 2017, there are more than 5.5 million population in the area (Government, 2017). Shanghai has a subtropical climate with four distinct seasons (Ye et al., 2019). The vaccination of seasonal influenza has yet to be included in the national immunization programme (Feng et al., 2010), the coverage rate of influenza vaccination of China and Pudong is below 2% and 1.4%, separately (Feng et al., 2010; Ye et al., 2019).

Weekly laboratory-confirmed positive influenza virus data were collected from two sentinel hospitals between June 1st, 2012 and December 31st, 2018 in Pudong New Area. The detailed process of sample collection and laboratory testing were reported in our previous work, please see (Ye et al., 2019). Weekly data on climate variables including MeanT (℃), RH (%), and Wv (m/s) were obtained from National Oceanic and Atmospheric Administration (NOAA) (Zhang et al., 2019). Moreover, we collected weekly maximum and minimum temperatures to calculated diurnal temperature range (DTR, DTR=maximum temperature-minimum temperature) (℃). We also calculated absolute humidity (AH) using relative humidity (RH) and temperature, based on Clausius-Clapeyron relation (Shaman and Kohn, 2009).

2.2 Data analysis

2.2.1 Generalized linear models (GLMs) with climate variables

Firstly, we used GLMs to initially fit the relationship between climate variables and Flu-A and Flu-B, separately (Limper et al., 2016). Multicollinearity among climate variables was checked and avoid through performing Spearman correlation analysis and variance inflation factors (VIF). Only one of the highly-correlated variables (*r* > 0.6 or VIF >5) was included in the model (Wu et al., 2015). AH was excluded in our final model, as this factor strongly associated with MeanT (Peci et al., 2019; Shaman et al., 2010b), with the Spearman correlation coefficient of 0.97 (p<0.05) (Table. S1). GLM with a negative binomial distribution was assumed to allow over-dispersion (Wang et al., 2018). We developed GLMs including all climate variables to adjust the relationships between climate factors and seasonal influenza. The model used in our study was given as follow:

$$\log\left[E(Y_t)\right] = \beta_0 + \beta_1(MeanT_t) + \beta_2(DTR_t) + \beta_3(RH_t) + \beta_4(Wv_t) + factor(WOY)$$

$$+factor(Holiday) \; + e_{\mathrm{t}}$$

where $E(Y_t)$ is the expected weekly count of positive Flu-A or Flu-B on week t; β_0 is the intercept; β_1 *(MeanT$_t$)*, β_2 *(DTR$_t$)*, β_3 *(RH$_t$)* and β_4 *(Wv$_t$)* denote the corresponding regression coefficients of MeanT, DTR, RH and Wv, respectively; Week of year (WOY) was included in the model adjusting for seasonality; Holiday refer to a binary variable for public holiday to control the impact of public holidays (Wang et al., 2018); e_t is the error term.

2.2.2 Distributed lag nonlinear models (DLNMs)

To better assess the potential non-linear impacts of climate factors on seasonal influenza transmission with delayed effects, DLNMs were developed for Flu-A and Flu-B, respectively (Gasparrini, 2011; Wood, 2006), with a negative binomial distribution to account for over-dispersion. The model were formulated as follow:

$$\log\left[E(Y_t)\right] \sim \alpha + \sum cb(climate\ variables, df_1, lag, df_2) + factor(WOY) + factor(Holiday)$$

where $E(Y_t)$ is the expected weekly count of positive Flu-A or Flu-B on week t; α is the intercept; *cb*(*climate variables*) represents the cross-basis matrix of climate factors to explore the potential cumulative and delayed effects with the corresponding df if applicable; WOY and Holiday represent indicator variables adjusting for seasonality and public holidays, separately.

The function in the cross-basis was chose as a natural cubic spline function to capture the potential non-linear associations (Dai et al., 2018). The maximum temporal lag was selected as 2 weeks, which based upon the potential lagged effects and the incubation period of influenza reported by previous studies (Dai et al., 2018). In order to better develop the models and assess the robustness of the models, the best df (from 3 to 6 *df*) for both climate variables and lag space in the cross-basis was chosen by the smallest Akaike information criterion (AIC). In our final model, 4 df was selected for both climate factors and lag space.

Then, we calculated the relative risk (RR) with corresponding 95% confidence interval (CI), relative to pre-determined reference value. The reference value in this paper was defined as the lowest point in the curve of the fitted association using GLMs (Wang et al., 2018).

2.2.3 Regression tree analysis

We developed regression tree models to identified the threshold values of the climate factors, which are most likely to be correlated to influenza infections (Zhang et al., 2018). We used weekly climate variables at 2-week lag as the independent variables and weekly Flu-A and Flu-B as the dependent variables. The selection of the best tree size based on cross-validation by checking estimated prediction errors. The model with an estimated error rate within one standard error of the minimum and the smallest tree size was selected as the best model (Breiman, 2017).

All data analyses were conducted by using R software (version 3.5.1; R Development Core Team, Boston, MA).

3. Results

3.1 Descriptive analysis

The total of 14,320 specimens were tested over the study period, with 2,405 positive specimens (Table S2). Most of the positive cases were detected as Flu-A (1,814, 75.4%). The mean weekly positive Flu-A and Flu-B were 5.2 and 1.7, separately. The statistical characteristics of weekly positive seasonal influenza viruses and climate variables were summarized in Table 1. Fig. 2 showed that Flu-A had annual winter/spring peak with summer peak in several years. However, Flu-B generally peaked during winter/spring weeks.

3.2 GLMs with climate variability

The results indicated that MeanT and RH were negatively associated with Flu-A, DTR and Wv were positively correlated to Flu-A when we included all climate factors in the model (Fig. 3). Moreover, MeanT, DTR and RH were negatively associated with Flu-B, Wv was positively correlated to Flu-B. Both the risk of Flu-A and Flu-B was peaking at 1.4℃ with RRs of 5.89 (95%CI: 2.04-18.33) (Fig. 3a) and 4.61 (95%CI: 1.49-13.57) (Fig. 3e), separately. However, there were inverse trends in the effects of DTR on Flu-A and Flu-B. The risks of Flu-A and Flu-B were significantly peaking at DTR of 15.8℃ (RR: 3.52, 95%CI: 1.88-7.13) (Fig. 3b) and 3.2℃ (RR: 7.46, 95%CI: 3.66-16.72) (Fig. 3f), respectively. Moreover, low RH increased the risk of seasonal influenza, the largest risks were found at 51.5% for Flu-A (RR: 1.032, 95%CI: 1.009-1.058) (Fig. 3c) and Flu-B (RR: 3.95, 95%CI: 2.00-6.98) (Fig. 3g). Additionally, high Wv posted risk to seasonal influenza, the largest RR were observed at 3.5m/s for Flu-A (RR: 1.68, 95%CI: 1.12-3.13) (Fig. 3d) and Flu-B (RR: 1.78, 95%CI: 1.04-3.02) (Fig. 3h).

3.3 Risk respond to climate variability by lag using DLNMs

Apparent non-linear cumulative associations between climate variables with Flu-A and Flu-B were observed when we applied DLNMs (Fig. 4). For MeanT, two peaks in the cumulative risk of Flu-A was found in the study, with the first peak at 1.4℃ (RR: 14.88, 95%CI: 8.67-23.31) and second peak at 25.8℃ (RR: 12.21, 95%CI: 6.64-19.83) (Fig. 4a). Moreover, the peaking risk of Flu-B was at 1.4℃ (RR: 26.44, 95%CI:

11.52-51.86) (Fig. 4e). In term of DTR, high DTR of 15.8℃ exerted the highest risk of Flu-A (RR: 23.05, 95%CI: 5.12-88.45) (Fig. 4b), however, that of Flu-B was observed at low DTR of 3.2℃ (RR: 38.25, 95%CI: 15.82-87.61) (Fig. 4f). Additionally, both more Flu-A and Flu-B was observed at low RH (51.5%), with the RRs of 9.98 (95%CI: 4.03-26.28) (Fig. 4c) and 4.63 (95%CI: 1.95-11.27) (Fig. 4g), separately. Furthermore, high Wv (3.5m/s) posted the highest risks to both Flu-A (RR: 7.48, 95%CI: 2.73-30.04) (Fig. 4d) and Flu-B (RR: 7.87, 95%CI: 5.53-11.91) (Fig. 4h).

Based on the findings above, we further analysed the lagged associations between climate variables at specific values and influenza by different time lag, relative to the reference values (Table 2). For low MeanT (1.4℃, the highest point in Fig. 4a and e) exerted the highest risk of Flu-A at 0-week lag (RR: 8.13, 95%CI: 2.44-18.83), but, Flu-B at 1-week lag (RR: 11.32, 95%CI: 8.84-14.58). Regarding DTR, the highest risk of Flu-A at DTR of 15.8℃ (the highest point in Fig. 4b) was observed at the lag of 1-week (RR: 5.11, 95%CI: 2.06-12.66), similarly, that of Flu-B at DTR of 3.2℃ (the highest point in Fig. 4f) was found at 1-week lag (RR: 11.29, 95%CI: 8.06-15.13). In term of RH, low RH of 51.5% (the highest point in Fig. 4c and g) had the highest risks of Flu-A and Flu-B both at 1-week lag, with RRs of 3.01 (95%CI: 1.61-5.63) and 2.35 (95%CI: 1.48-3.74), separately. Moreover, Wv of 3.5m/s (the highest point in Fig. 4d and h) at 0-week lag had the highest risk, with RRs of 6.10 for Flu-A (95%CI: 3.15-11.81) and 5.68 for Flu-B (95%CI: 2.69-12.02), separately. The details of RRs by time lag are shown in Table 2. The trends of lag-response curves of Flu-A and Flu-B are illustrated in Supplementary Fig. S1.

3.4 Regression tree analysis

Fig. 5 demonstrated that the climate variables played different roles in the occurrence of Flu-A and Flu-B in the study setting. DTR was the first classifying factor in the model of Flu-A, which indicated that DTR played the most important role in the occurrence of Flu-A. The mean weekly Flu-A increased by over 3.1-fold (44/14) when DTR was ≥ 12℃. However, the most significant climate factor in the occurrence of Flu-B was MeanT, which was identified as the first classifying factor in the model. An increase over 4.5-fold (19/4.2) in the mean weekly Flu-B was observed when MeanT was <22℃, as well as Wv was ≥1.6m/s and DTR was <8.7℃.

4 Discussion

To the best of our knowledge, this is the first attempt to assess the complex associations of multiple climate variables with different types of seasonal influenza viruses in subtropical China. Our study found that MeanT, DTR, RH and Wv were significantly associated with Flu-A and Flu-B by different time lags.

We found that MeanT was negatively associated with influenza, low temperature led to more influenza cases. This result is consistent with previous studies, cold temperature could lead to more influenza activity in China (Yu et al., 2013). A decline of 1°C in temperature increased influenza infections risk by 11% in Finland (Jaakkola et al., 2014). Moreover, 1°C decrease of temperature cased a rising of 8.55% in influenza cases in Hong Kong, and an increase of 32.14% in the UK (Wang et al., 2017). Low temperature may lengthen the survival of influenza virus, and lead to increasing contact rates through more people indoor crowding (Cheng et al., 2016; Liao et al., 2005). As a result, low temperature could contribute to the spread of influenza. It should be noted that another peak of RR in high temperature for Flu-A was observed in the study. This finding was supported by previous studies, which reported the semiannual epidemic in the summer in subtropical cities in China (Yang et al., 2018a; Yang et al., 2018b; Ye et al., 2019). The potential reasons for this semiannual epidemic required further research.

DTR was significantly associated with seasonal influenza in the study, with a positive relationship with Flu-A, and a negative relationship with Flu-B. In Beijing, an increased influenza cases in the elderly was associated with bigger DTR values (Lao et al., 2018). A study in Hong Kong found that DTR had positive impact on laboratory-confirmed influenza cases, the mean increase in weekly cases was 5.01% per 1°C increase in DTR, however, this study reported that the effect of DTR only exerted in dry period (when vapour pressure is less than 20 millibars (mb)), and the effect was not modified by influenza types (Li et al., 2018). The physiological mechanisms of DTR on the diseases were not elucidated, although there are several possible underlying mechanisms. Sudden temperature change may increase respiratory workload and induce the onset of a respiratory event (Imai et al., 1998), as well as influence humoral and cellular immunity (Bull, 1980).

Our study indicated that decline in RH promoted influenza activity, and the result is consistent with previous studies. Several previous studies indicated that low RH can favour the transmission of influenza (Hemmes et al., 1960; Lowen et al., 2007;

Schaffer et al., 1976; Sundell et al., 2016). Low RH can allow influenza virus particles to remain in the air for longer time because of the smaller size and lower velocity of settling (Yang and Marr, 2011). As a result, there is an increase of susceptibility to influenza infections (Eccles, 2002). Additionally, low RH can also preserve the viability of influenza virus. The infectivity can keep as 70.6-77.3% when RH was less than 23 % for 1 hour, however, the number decreased to 14.6-22.2% at RH ≥43% (Noti et al., 2013). Additionally, low AH could exert significant impact on influenza transmission. In China, the RR for influenza (H7N9) at low AH (5 mb) was 11.34 (95%CI: 8.72-14.74) when compared to high AH (20 mb) (Liu et al., 2018). Moreover, low AH may contribute to the onset and peak of influenza epidemics (Murray and Morse, 2011). In the temperate regions of the US, AH was used to predicted the seasonal patterns of influenza (Shaman et al., 2010a; Shaman and Kohn, 2009).

Additionally, high Wv was found to increase the risk of influenza infections in the study. High Wv could lead to increased infections of influenza, respiratory syncytial virus and severe acute respiratory syndrome (SARS) virus (du Prel et al., 2009; Firestone et al., 2012; Yuan et al., 2006). A field study indicated that an increased risk of influenza in horses was associated with Wv of > 30km/h (Firestone et al., 2012). In India, Wv was positively correlated to an increase risk for influenza (H1N1) (linear regression coefficient: 1.02, $p<0.05$) (Lopez et al., 2014). This may due to the effects of high wind speed on the longer travel of air-borne aerosols, which contributed to the transmission of influenza virus (Ssematimba et al., 2012).

There are different responses of influenza to climate factors in different climate zones. The area with temperate climate appeared to have greater risk in temperature and humidity, compared to subtropical regions (Wang et al., 2017). The author reported that this may due to a lower mean temperature and humidity in temperate areas than that in subtropical regions. Influenza virus can survive longer in low temperature, and cold weather also causes increased opportunity of infection by indoor crowding (Cheng et al., 2016; Liao et al., 2005). Furthermore, low outdoor temperature may lead to increased use of indoor heating facility, which would decline the indoor humidity and promote influenza infections (Chong et al., 2015).

Additionally, our results indicated that climate factors posted different effects on Flu-A and Flu-B activity. The previous results for the effects on two influenza types were not conclusive. A study from German observed a negative association of temperature with Flu-A hospitalization, but not with Flu-B (du Prel et al., 2009). The occurrence of Flu-B decreased when temperature increased in Hong Kong, however, no significant finding for Flu-A was reported in the study (Tang et al., 2010). Flu-A virus seems to change the antigen more frequently than Flu-B virus (Bouvier and Palese, 2008), which may influence the sensitivity to climate variability. Moreover, the different associations of Flu-A and Flu-B with DTR may partially resulted from the age distribution of influenza infections. Our previous study in Shanghai and other studies on a global scale showed that Flu-A virus is more transmissible among elderly than young children (FOX et al., 1982; FRANK et al., 1983; Longini Jr et al., 1982; Ye et al., 2019). It has been widely accepted that elderly people are more vulnerable to

DTR (Lim et al., 2012; Qiu et al., 2013), thus, Flu-A was positively correlate to DTR in the study. Additionally, the different seasonality of Flu-A and Flu-B may be another potential reason behind. Our previous work demonstrated that Flu-A peaked from December to January, while the peak of Flu-B can last to April (Ye et al., 2019). The effect of DTR on different influenza type is less well studied, further studies are required to explore such impact.

The regression tree models identified that DTR and MeanT were the key classifying factor in the models of Flu-A and Flu-B separately. This difference may reflect the nature of types of seasonal influenza viruses. In general, the results illustrated that the models could provide the threshold values of the climate variables in seasonal influenza activity linking with official surveillance data.

There are several strengths in the study. First, it is the first attempt to investigate the complex and delayed relationships between multiple climate factors and different types of seasonal influenza viruses in subtropical China. Second, this study based on the data of two sentinel hospitals, which have high surveillance coverage in the study area with well-trained clinicians (Ye et al., 2019). Third, our findings may also be relevant to the complex transmission patterns of influenza in other countries, especially for subtropical areas.

This study has several limitations. First, the accuracy of results might be impacted by age and sex, we hope can investigate such association by age and sex in our future work. Second, the data accuracy may influenced by the sample collection and processing approaches, as well as patient health seeking behaviour (Dowell, 2001; Lofgren et al., 2007). Third, air pollutions, host susceptibility and viral migration may also affect the transmission of influenza (Dowell, 2001; Feng et al., 2016; Lofgren et al., 2007).

5 Conclusion

The study found complex non-linear relationships between climate variability and seasonal influenza with different risky windows by type in subtropical China. The findings may provide important information for developing early warning systems based on climate factors for seasonal influenza. We suggest the careful use of meteorological variables in influenza prediction in subtropical regions, considering such complex non-linear associations in different types, which may facilitate government and health authorities to better minimize the impacts of seasonal influenza.

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W. H. and Z. L. designed this study. C. Y. and J. Y. collected the data. Y. Z., C. Y. and J. Y. analysed the data and drafted this manuscript with W. H. assistance. W. H., Z. L., Y. W., J. C., N. W., Z. X., W. Z. and L. H. interpreted the results and revised the manuscript. We thank the support of the two sentinel hospitals and NOAA to provide the influenza surveillance and climate data, respectively.

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Conflict of interest

The authors declare they have no actual or potential competing interests.

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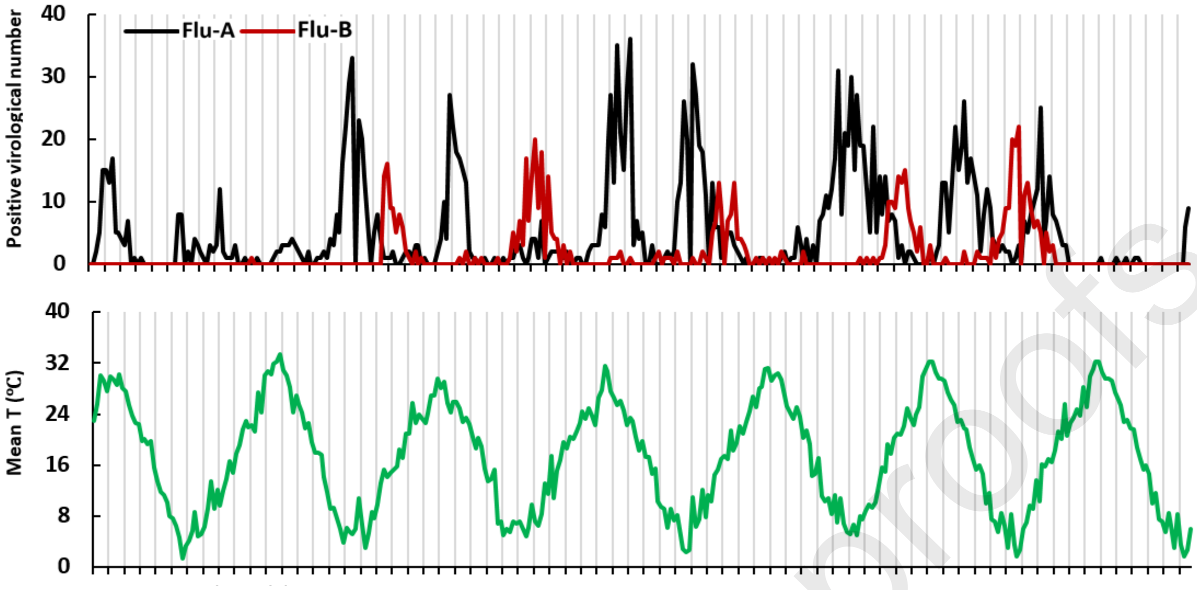

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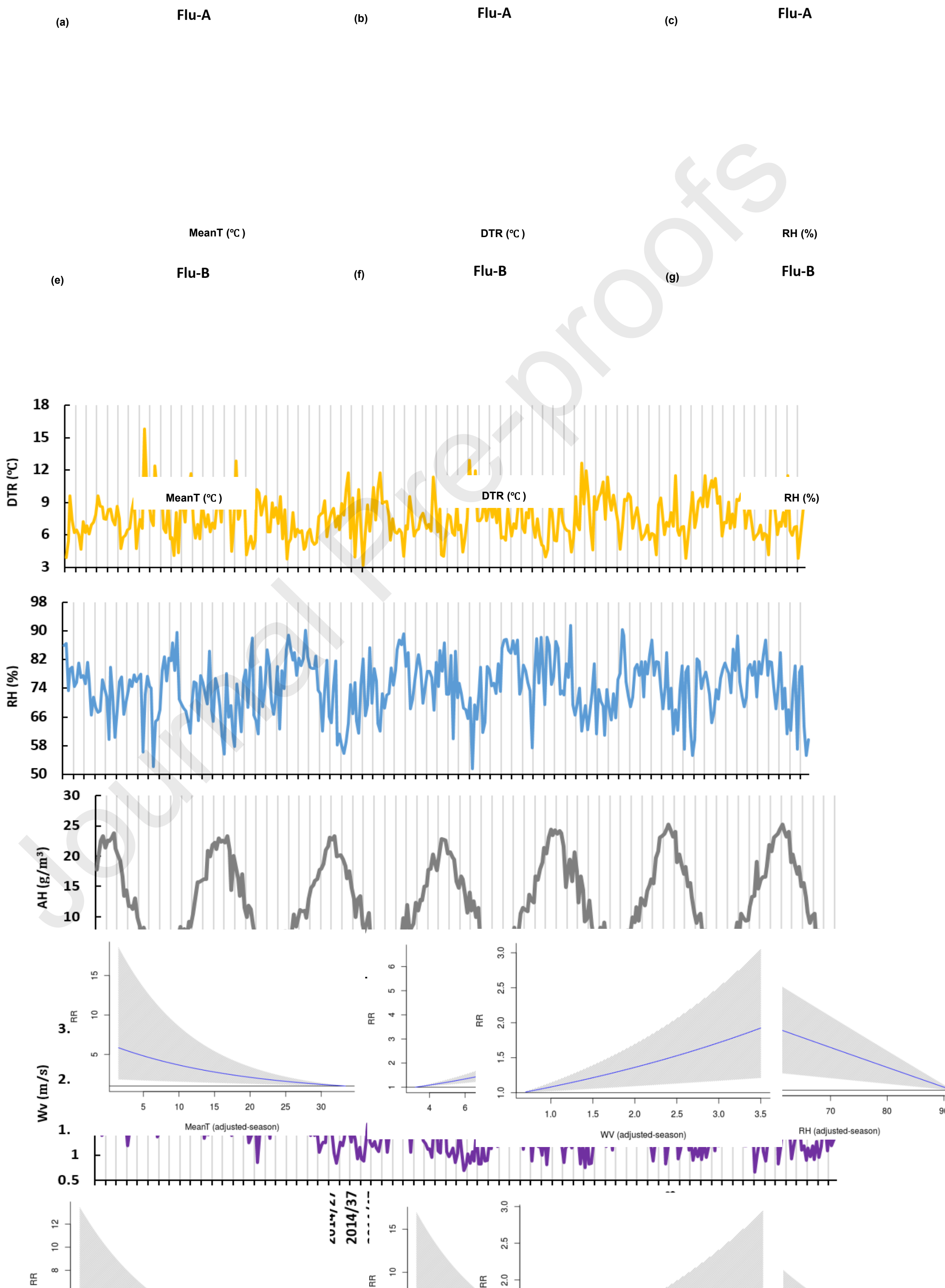
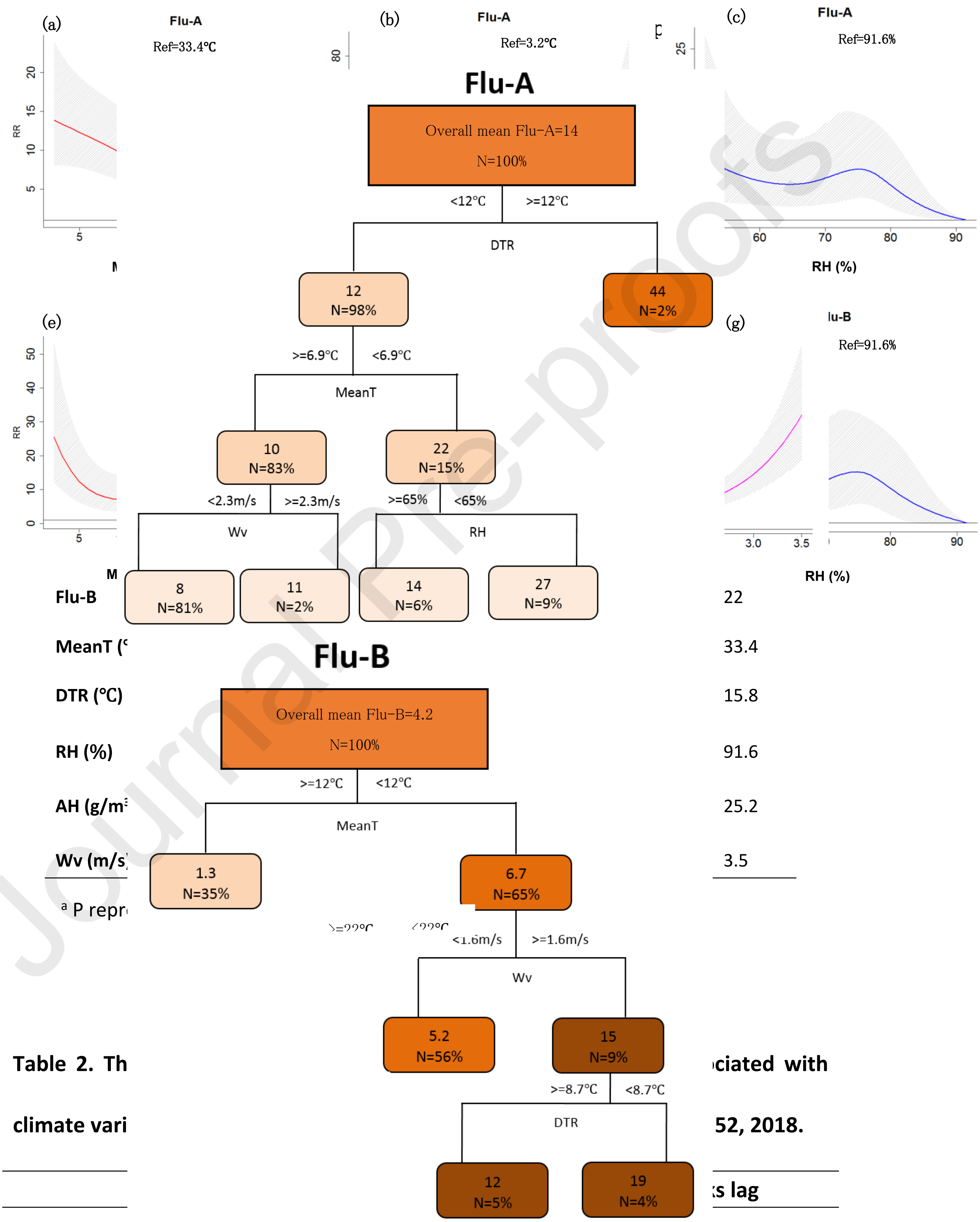
Fig. 1. The location of Pudong New Area in Shanghai, China.

Fig. 2. Weekly distribution of Flu-A, Flu-B and climate variables in Pudong New Area, from week 23, 2012 to week 52, 2018.


(a)
Flu-A
(b)
Flu-A
(c)
Flu-A
MeanT (℃)
DTR (℃)
RH (%)
(e)
Flu-B
(f)
Flu-B
(g)
Flu-B
DTR (℃)
RH (%)
AH (g/m³)
Wv (m/s)
MeanT (adjusted-season)
WV (adjusted-season)
RH (adjusted-season)
RR
2014/37

GLMs; Results were adjusted for seasonality and holidays).



Flu-B	22
MeanT (°	33.4
DTR (℃)	15.8
RH (%)	91.6
AH (g/m³	25.2
Wv (m/s)	3.5

[a] P repr

Table 2. Th ... ciated with climate vari ... 52, 2018.

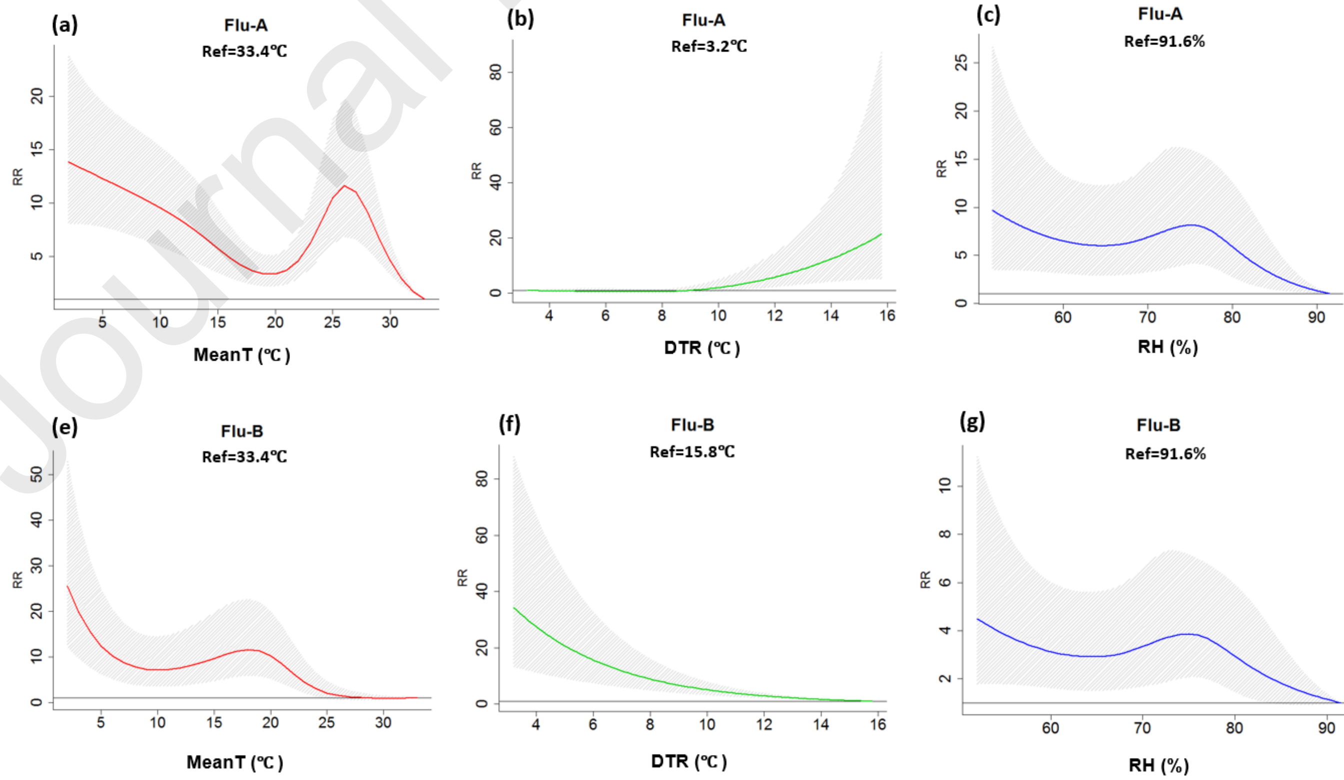
... s lag

MeanT			
Flu-A (1.4 vs. 33.4℃)	8.13 (2.44-18.83)*	1.51 (1.07-3.82)*	1.08 (0.92-1.19)
Flu-B (1.4 vs. 33.4℃)	9.62 (6.75-13.90)*	11.32 (8.84-14.58)*	7.74 (5.24-10.44)*
DTR			
Flu-A (15.8 vs. 3.2℃)	2.68 (1.07-6.71)*	5.11 (2.06-12.66)*	1.57 (0.69-3.60)
Flu-B (3.2 vs. 15.8℃)	6.35 (2.09-10.68)*	11.29 (8.06-15.13)*	5.94 (0.35-11.82)
RH			
Flu-A (51.5 vs. 91.6%)	1.68 (1.09-3.15)*	3.01 (1.61-5.63)*	1.91 (1.03-3.54)*
Flu-B (51.5 vs. 91.6%)	1.27 (1.03-1.49)*	2.35 (1.48-3.74)*	1.77 (1.52-2.07)*
Wv			
Flu-A (3.5 vs. 0.7m/s)	6.10 (3.15-11.81)*	1.72 (0.80-3.71)	0.86 (0.38-1.95)
Flu-B (3.5 vs. 0.7m/s)	5.68 (2.69-12.02)*	1.02 (0.41-2.51)	0.49 (0.19-1.26)

*: Significant results

Exposure-response associations

X-axis: The value of climate variable; Y-axis: 2-weeks lagged cumulative relative risk (RR), indicating the number of times more likely to have influenza compared to reference value (Ref); Solid line: RR value; Grey shadow: 95% confidence interval (95% CI).



Highlights

- High temperature only associated with influenza A occurrence.
- High diurnal temperature range (DTR) causes more influenza A cases.
- Low DTR causes more influenza B cases.
- High DTR and low temperature were the key drivers for influenza A and B separately.