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Different responses of influenza epidemic to weather factors among Shanghai, Hong Kong, and British Columbia

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Abstract Weather factors have long been considered as key sources for regional heterogeneity of influenza seasonal patterns. As influenza peaks coincide with both high and low temperature in subtropical cities, weather factors may nonlinearly or interactively affect influenza activity. This study aims to assess the nonlinear and interactive effects of weather factors with influenza activity and compare the responses of influenza epidemic to weather factors in two subtropical regions of southern China (Shanghai and Hong Kong) and one temperate province of Canada (British Columbia). Weekly data on influenza activity and weather factors (i.e., mean temperature and relative humidity (RH)) were obtained from pertinent government departments for the three regions. Absolute humidity (AH) was measured by vapor pressure (VP), which could be converted from temperature and RH. Generalized additive models were used to assess the exposure-response relationship between weather factors and influenza virus activity. Interactions of weather factors were further assessed by bivariate response models and stratification analyses. The exposure-response curves of temperature and VP, but not RH, were consistent among three regions/cities. Bivariate response model revealed a significant interactive effect between temperature (or VP) and RH ($P < 0.05$). Influenza peaked at low temperature or high temperature with high RH. Temperature and VP are important weather factors in developing a universal model to explain seasonal outbreaks of influenza. However, further research is needed to assess the association between weather factors and influenza activity in a wider context of social and environmental conditions.

Xi-Ling Wang and Lin Yang contributed equally to this work.

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Introduction

Influenza is an infectious disease causing substantial disease burden. The World Health Organization has estimated that 250,000–500,000 deaths and 3–5 million severe illnesses are associated with influenza every year globally (World Health Organization 2009). Influenza used to be considered as a "cold" disease as it usually returns every cold winter in temperate countries. However, accumulating studies have shown that influenza can be active throughout the year with unclear seasonal patterns in the warm tropics and subtropics where the disease burden of influenza was comparable to that in the temperate (Chow et al. 2006; Viboud et al. 2006; Wong et al. 2004; Wong et al. 2006; Yang et al. 2012). The understanding of various seasonal patterns of influenza outbreak is key to policy-makers in choosing an optimal time for influenza vaccination, so the investigation of underlying drivers for influenza seasonality has long been a research topic. The regional heterogeneity of influenza seasonal pattern is likely to be the outcome of complex interaction among the survival and transmission of influenza virus, the environment, and human behavior. Previous studies have proposed several seasonal factors, such as temperature, humidity, school schedule, travel and workflows, and vitamin D level. Weather factors (particularly temperature and humidity) have been most thoroughly explored by laboratory and epidemiological studies (Harper 1961; Lowen et al. 2007; Onozuka and Hagihara 2015). Absolute humidity (AH) measures the actual mass of water vapor in a particular volume of air and is highly correlated with temperature, whereas relative humidity (RH) is the ratio of the partial pressure of water vapor to the saturated pressure of water vapor at a given temperature reflecting human's feeling of humidity. Previous laboratory studies reported that low RH and cold temperature increased the survival of aerosolized influenza virus (Harper 1961; Hemmes et al. 1960) as well as virus transmission in animal models (Lowen et al. 2007; Schulman and Kilbourne 1962). Recent laboratory and simulation studies have proposed AH as an important seasonal factor that drives influenza seasonality (Shaman and Kohn 2009; Shaman et al. 2010; Shamanna and Bosch 2011). However, most of the findings so far could well explain the single winter peak of influenza in temperate climates, but could barely be applied to the subtropics and tropics where influenza can still be active under a hot and humid weather. Moreover, given the fact that the influenza peaks coincide with both high and low temperature in subtropical cities (Yang et al. 2008; Yu et al. 2013), it is unlikely that these weather factors independently affect the influenza seasonality in a linear manner. Nonlinear relationships between weather factors and influenza activity, as well as interactive effects between weather factors, shall be further assessed by more sophisticated statistical models.

Shanghai and Hong Kong are developed subtropical cities located in eastern and southern China, respectively. Although seasonal pattern of influenza are not well defined for both cities, Shanghai is likely to be dominated by a semi-annual influenza periodicity (Yu et al. 2013) while Hong Kong experiences one or two peaks of influenza irregularly in one epidemic year (Yang et al. 2008). Whether warmer and more humid climate in Hong Kong than that in Shanghai contributes to different influenza seasonality of these two subtropical cities remains unclear. We also included British Columbia, a province located on the west coast of Canada, as a comparison region. British Columbia has a typical temperate climate with a single influenza peak in winter. Therefore, this study aims to assess the associations of weather factors with influenza seasonality and compare the similarities and differences in the responses of influenza epidemic to weather factors in two subtropical cities of southern China (Shanghai and Hong Kong) and one temperate region of Canada (British Columbia).

Methods

Data

Weekly notified influenza cases from 2007 to 2011 in Shanghai were obtained from the national notifiable infectious diseases surveillance system, managed by the Chinese Center for Disease Control and Prevention. The notified influenza cases included clinical diagnosis and laboratory-confirmed cases. The criteria for clinical diagnosis included a dramatic increase in patients with upper respiratory infections in outpatients and emergency room settings during an influenza epidemic season, and the patient had symptoms of sore throat, cough, fever, etc. The laboratory-confirmed influenza cases were confirmed by immunofluorescence test or hemagglutinin inhibition test. Influenza surveillance data for Hong Kong were obtained from The Microbiology Laboratory of Queen Mary Hospital. Queen Mary Hospital was the largest public hospital located in the Hong Kong Island. Nasopharyngeal aspirates or swabs were collected from the patients with influenza-like symptoms and tested for influenza infection by immunofluorescence tests, and subtyped by culture or RT-PCR (Chan et al. 2002). Influenza virology data of this single laboratory have been demonstrated representative of the virus activity in the entirety of Hong Kong (Wong et al. 2006). Weekly laboratory-confirmed numbers of influenza for British Columbia were downloaded from the open-access website of British Columbia Center for Disease Control (http://www.bccdc. ca/dis-cond/DiseaseStatsReports/influSurveillanceReports. htm). British Columbia's influenza sentinel network was under Canadian influenza sentinel practitioner surveillance network.

Respiratory specimens were collected from sentinel sites and were tested for influenza infection by culture or RT-PCR. Different laboratory methods used in three regions may only have a minor impact on our study because this study primarily focused on patterns of influenza activity rather than number of cases.

Weather data of weekly mean temperature, RH, and total amount of rainfall for Shanghai and Hong Kong were derived from the Shanghai Meteorological Bureau and the Hong Kong Observatory, respectively. Weather data for Vancouver were downloaded from an open-access website of Environment Canada (http://ec.gc.ca/meteo-weather/default.asp?lang=En&n=FDF98F96-1). We used the Vancouver climate data to represent the climate in British Columbia as more than 50% of British Columbia population was in Greater Vancouver. Temperature, RH and rainfall were monitored by the local weather stations in the three regions. We calculated daily mean temperature and relatively humidity by averaging the measurements from all local weather stations, while calculated daily total rainfall by summing up the precipitation from all weather stations. Vapor pressure (VP) was calculated from temperature and RH and was regarded as a measurement for AH (Basu et al. 2008). During the study period, Hong Kong had the highest mean temperature (23.35 °C) among the three cities, followed by Shanghai (17.50 °C) and British Columbia (10.23 °C) (Table 1). The order of VP was in accordance with the order of temperature, which was not surprising considering VP and temperature were highly correlated in three regions. RH was generally comparable among the three regions ranging from 69.20 to 77.36% (Table 1).

The total resident populations by the mid of 2011 in Shanghai, Hong Kong, and British Columbia were 14.2, 7.1, and 4.5 million, respectively. The population age structures were in general comparable in the three cities. In Shanghai, the proportions of population aged 0–17, 18–64, and 65 or older were 10, 73, and 17%, respectively (Shanghai Statistical Bureau 2012). The proportions of population aged 0–14, 15–64, and 65 or older in Hong Kong were 12, 75, and 13% (Census and Statistics Department 2012) while the numbers for British Columbia were 15, 69, and 16% (Statistics Canada 2012).

Independent exposure-response model

For each city/region, the independent exposure-response relationships between environmental factors and virus activity were assessed by Poisson generalized additive models (GAM) with a logarithm link. This model used the nonparametric smoothing functions to explore the linear and nonlinear association between explanatory and outcome variables. Because VP and temperature were highly correlated (Spearman correlation ranges from 0.95 to 0.98 in the three regions), separate models were built by including either VP or RH to avoid the

collinearity problem. A typical form of model with temperature as covariate is as follows:

$$E(flu_t) = \alpha + s(t) + s(temp_t) + s(RH_t) + s(rain_t)$$
$$+ offset(\log(population_t)) + pandemic_t \quad (1)$$

where $E(flu_t)$ denotes the expected notified number of influenza at week t; here, $t = 1, 2, \ldots, 260$. Although weekly notified number of influenza cannot fully capture influenza cases due to under-ascertainment and underreporting, it can generally represent the influenza activities. $s(t)$, $s(temp_t)$, $s(RH_t)$, and $s(rain_t)$ denote the thin plate smoothing functions of time trend, temperature, RH, rainfall, and VP, respectively. Here, the smoothing function of time trend was used as to adjust for confounding of unmeasured long term and seasonal factors. An offset of total resident population by year ($offset(\log(population_t))$) was added to adjust for temporal variation of population. $pandemic_t$ was a dummy variable to adjust for the 2009 H1N1 pandemic period from April 26, 2009, to May 1, 2010, for Shanghai, and from April 26, 2009, to January 2, 2010, for Hong Kong and British Columbia. The combination of degrees of freedom (df) for these smoothing functions was chosen to minimize the generalized cross validation (GCV) scores of the model (Hastie and Tibshirani 1990). A model was also developed for VP by replacing $s(temp_t)$ with $s(VP_t)$ in model I, in order to assess the effect of VP.

Bivariate surface model

Given the previous findings that temperature, VP, and RH were consistently found associated with influenza seasonality, we only assessed the interaction between temperature and RH, or between VP and RH in the subsequent analyses. We adopted a bivariate surface model under the same assumption of Model I (Hastie and Tibshirani 1990). By adding a bivariate smoothing function, this model avoids artificial definition of exposure categories and allows the assessment of joint effects of these two factors on virus activity without a strong assumption of linearity (Daniels et al. 2000; Greenland 1993). This modeling approach allows more flexibility in assessing the interaction of environmental factors. A typical form of bivariate surface model is as follows:

$$E(flu_t) = \alpha + s(t) + s(temp_t, RH_t) + s(rain_t)$$
$$+ offset(\log(population_t)) + pandemic_t \quad (2)$$

where $s(temp_t, RH_t)$ represents a bivariate spline smoothing function of weekly mean temperature and RH. The df of smoothing functions were fixed to 5 for temperature, RH, and VP. The df for time trend and rainfall were the same as model I. We then drew the bivariate exposure-response surface plots derived from the above model to examine the interaction between

Table 1 Descriptive statistics of weekly mean temperature, relative humidity, vapor pressure, total rainfall, and weekly influenza virus activity from 2007 to 2011 in Shanghai, Hong Kong, and British Columbia

Variables	Mean	SD	Percentile				
			Min	25	50	75	Max
Shanghai							
Temperature (°C)	17.50	8.80	0.60	9.50	18.20	25.40	32.30
Relative humidity (%)	69.20	8.20	40.90	64.10	69.60	75.50	87.90
Vapor pressure (hPA)	15.90	8.80	3.30	8.50	14.00	23.90	32.50
Rainfall (mm)	31.90	43.80	0.00	2.10	14.40	46.00	280.90
Weekly influenza isolate numbers during inter-pandemic period[a]	14.80	20.67	0.00	3.00	9.00	17.00	173.00
Weekly influenza isolate numbers during 2009 pandemic period[a]	51.36	54.59	0.00	5.00	24.00	94.00	191.00
Hong Kong							
Temperature (°C)	23.35	4.97	11.39	19.59	24.34	27.95	30.29
Relative humidity (%)	77.36	8.34	51.00	73.14	78.50	83.32	93.57
Vapor pressure (hPA)	23.24	7.42	8.21	16.97	23.71	30.91	33.81
Rainfall (mm)	41.60	72.02	0.00	0.25	9.00	53.73	560.90
Weekly influenza isolate numbers during inter-pandemic period[b]	16.67	18.83	0.00	4.00	9.00	24.25	110.00
Weekly influenza isolate numbers during 2009 pandemic period[b]	86.36	87.85	3.00	22.25	38.00	157.50	310.00
British Columbia							
Temperature (°C)	10.23	5.53	-4.81	5.82	9.61	15.31	24.17
Relative humidity (%)	76.47	8.24	51.42	70.72	76.52	82.63	95.26
Vapor pressure (hPA)	9.90	3.05	2.46	7.56	9.27	12.39	18.47
Rainfall (mm)	20.83	20.82	0.00	3.95	16.70	30.05	130.00
Weekly influenza isolate numbers during inter-pandemic period[c]	14.66	25.06	0.00	0.00	1.00	21.00	117.00
Weekly influenza isolate numbers during 2009 pandemic period[c]	205.50	342.40	3.00	32.25	63.00	149.50	1243.00

[a] The pandemic period for Shanghai is from April 26, 2009, to May 1, 2010, while the remaining period is considered as inter-pandemic period

[b] The pandemic period for Hong Kong is from April 26, 2009, to January 2, 2010, while the remaining period is considered as inter-pandemic period

[c] The pandemic period for British Columbia is from April 26, 2009, to January 2, 2010, while the remaining period is considered as inter-pandemic period

temperature and RH. A model was also developed for VP by replacing $s(temp_t, RH_t)$ with $s(vp_t, RH_t)$ in model II, in order to assess the interactive effect of VP and RH.

Stratification model

Because the bivariate surface model (model II) was unable to provide the effect estimates and their statistical significance, we adopted an alternative method to assess the interaction between temperature and RH, as well as between VP and RH. Stratification models were developed by adding the interaction terms of weekly average temperature (or VP) and three dummy variables for the periods with high, medium, and low RH. The first and third quartiles of city/region-specific RH were defined as cutoff points for these periods. A typical model for interaction of temperature and RH is as follows:

$$E(flu_t) = \alpha + s(t) + \beta_1 temp_t + \beta_2 temp_t * RH.m_t + \beta_3 temp_t * RH.h_t$$
$$+ \beta_4 RH.m_t + \beta_5 RH.h_t + \beta_6 RH_t + \beta_7 rain_t + offset(\log(population_t))$$
$$+ pandemic_t \quad\quad (3)$$

where $RH.m_t$ and $RH.h_t$ denote the dummy variables for the periods with medium and high RH levels. The statistical significance of the interaction terms between temperature and RH was assessed by the likelihood ratio test of full model (model III) and a partial model without the interaction term (model I). We did not add the linear interaction term $temp_t * RH_t$ (or $vp_t * RH_t$) into the model as the results from model II suggested a nonlinear interaction between temperature and RH (or VP and RH) on influenza seasonality. The above analysis was repeated by replacing temperature with VP, to investigate the interaction effect of VP with RH.

Sensitivity analysis

The lag effects of weather factors were also assessed through adding into the models the weather variables up to 3 weeks before the present week. Sensitivity analysis by excluding the pandemic period was conducted to examine the robustness of our main results. The statistical significance in this study was defined as $P < 0.05$.

The ethical approval of this study was obtained from the Queensland University of Technology Medical Research Ethics Committee (approval number 1400000721), and permission to use the data was obtained from the relevant data custodians. All statistical analyses were performed using the mgcv package of R software (version 3.2.0.) (R Development Core Team 2015). The core R-code for statistical models was included in the supplementary materials.

Results

Influenza was active year-round in subtropical cities of Shanghai and Hong Kong (Fig. 1). Influenza usually occurred in winter and summer/autumn in Shanghai (Fig. 1). The seasonality of influenza in Hong Kong showed a semi-annual pattern during the study period, with two peaks observed in winter and summer within 1 year (Fig. 1). Weekly numbers of influenza in British Columbia had a clear winter peak annually, which was very different from those in Shanghai and Hong Kong (Fig. 1). The first wave of pandemic influenza was found in all three cities/regions during May–December 2009, but only Shanghai was attacked by the second wave in the winter of year 2010.

Independent exposure-response model

The exposure-response curves for the independent effects of temperature, RH, and VP are shown in Fig. 2. In general, the patterns of temperature and VP on influenza seasonality were consistent among the three areas when different ranges of the weather factors were considered. Influenza activity increased as the temperature increased from the lowest to around 5 °C, then decreased as the temperature continued increasing up to around 22 °C, and finally increased again as the temperature increased to the highest (Fig. 2). The exposure-response curves of VP had a U-shape, with trough at around 20 hPA for both Shanghai and Hong Kong (Fig. 2). The maximum weekly mean VP was 18.47 hPA in British Columbia, and influenza activity decreased steadily as the VP increased (Fig. 2). The exposure-response curves for RH showed heterogeneous patterns among the three cities. For Shanghai, influenza activity tended to increase when RH increased from the lowest to around 60%, then remained unchanged when RH ranged from 60 to 80%, and finally increased again when RH exceeded 80% (Fig. 2). For Hong Kong, influenza activity showed an upward trend as RH increased. For British Columbia, the pattern of RH on influenza seasonality was opposite to that of Shanghai with a downward trend, unchanged and again a downward trend when RH increased.

Bivariate surface model

Figure 3 shows the exposure-response surface plots for the joint effects of temperature and RH, and VP and RH on influenza virus activity in Shanghai, Hong Kong, and British Columbia. In Shanghai, there were apparent changes in curves of temperature across the levels of RH and the patterns were distinct from their independent exposure-response curves (Fig. 3a). The temperature effect decreased steadily at low RH, but it first decreased and later turned upward at high RH in Shanghai (Fig. 3a). The peaks of influenza infection risk were observed at low temperature or at high temperature with high RH (Fig. 3a). The exposure-response surface plot for Hong Kong showed an upward trend for influenza risk when temperature increased across different levels of RH (Fig. 3c). The exposure-response surface plot for British Columbia showed an exact opposite trend compared with Hong Kong (Fig. 3e). However, it is of note that these two plots may not be directly comparable due to the different ranges of temperature and RH in Hong Kong and British Columbia. In general, the exposure-response surface plots demonstrated a U-shaped relation between VP and influenza infection risk across RH levels, although the VP was too low in British Columbia to observe the upward turning point (Fig. 3b–f).

Stratification model

The stratification analysis revealed that temperature and VP were significantly associated with influenza virus activity, with negative estimates consistently found across the RH levels for Shanghai and British Columbia, but positive estimates for Hong Kong (Table 2). The percentage change of notified influenza numbers associated with per unit increase in temperature or VP was highest at low relative humidity for Shanghai and at middle relative humidity for Hong Kong and British Columbia (Table 2). All the percentage changes were much higher in temperate region of British Columbia than subtropical cities of Shanghai and Hong Kong (Table 2).

Sensitivity analysis

Similar results were found in the models with the effects of weather factors lagged up to 3 weeks (lag 1–3 weeks) (Supplementary materials). The sensitivity analysis by excluding the pandemic period also showed similar results, which demonstrated the robustness of results in the main study (Supplementary materials).

Discussion

Our study comprehensively explored the linear, nonlinear, and joint effects of weather factors on influenza epidemics in both

Fig. 1 Time series plots of weekly numbers of influenza from 2007 to 2011 in Shanghai (**a**), Queen Mary Hospital in Hong Kong (**b**), and British Columbia (**c**)
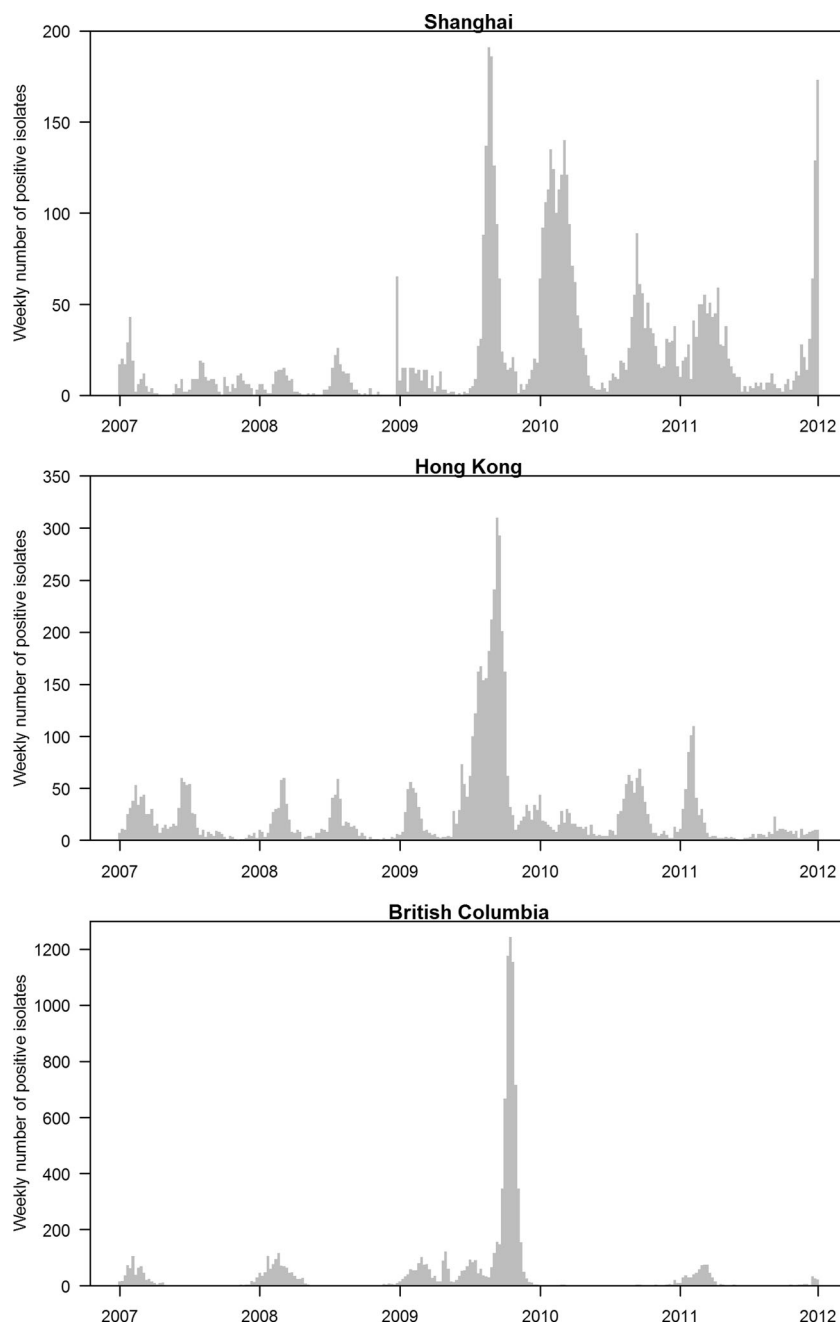
temperate and subtropical regions. We chose Shanghai, Hong Kong, and British Columbia as our study sites, because all the three cities/regions had influenza laboratory surveillance data in high quality, which facilitated the modeling of influenza seasonality. Although the geographical area of British Columbia is much larger than Shanghai and Hong Kong, more than 50% of the population is concentrated in the city of Great Vancouver, which is a metropolitan area and economically comparable to Shanghai and Hong Kong. The three cities/regions distribute in different climate regions, which make the investigation of associations of influenza seasonality with weather factors feasible. However, the three sites can only represent a small part of cities

all over the world, and we will include more cities under different climates and social status in the future if data are available.

The independent exposure-response curves of temperature and VP, but not RH, showed a regional homogeneity among Shanghai, Hong Kong, and British Columbia as long as we scaled the ranges of weather factors. Maximal influenza activity was reached under the scenarios of low temperature or high temperature and high RH. Most previous hypotheses, if not all, for the seasonality of influenza incidence were developed in the temperate regions, and none of them could fully explain the influenza peaks during warm seasons in subtropical/tropical regions (Lipsitch and Viboud 2009). Our results
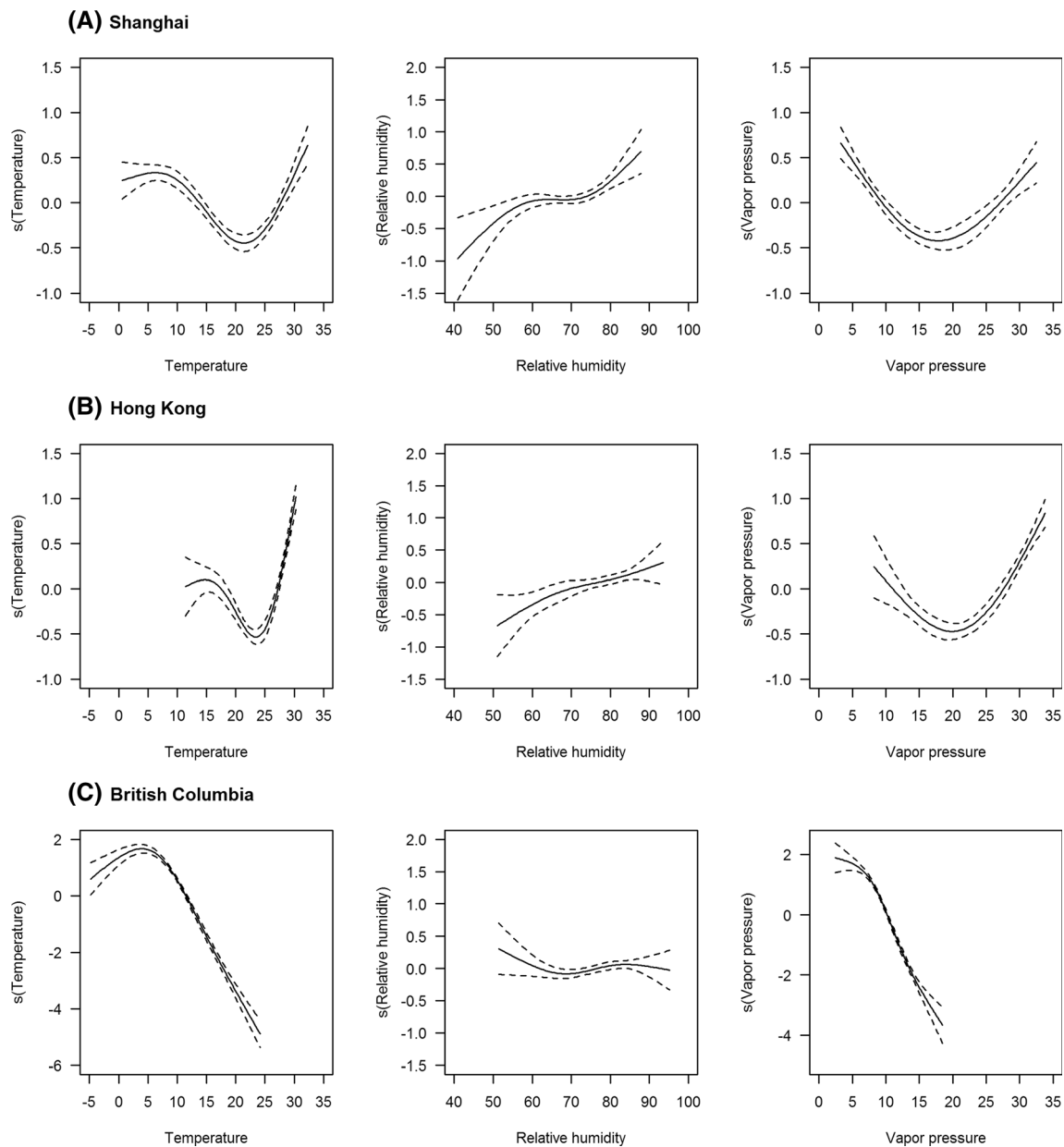
Fig. 2 Exposure-response curves for the independent effects of temperature, relative humidity, and vapor pressure on influenza seasonality in Shanghai (**a**), Hong Kong (**b**), and British Columbia (**c**)

suggested a possibility to find a universal model applicable to different climates. The future hypotheses for seasonal variations of influenza should take into account of interaction between different seasonal factors, and further population and experimental studies under different weather conditions are warranted to reveal the mystery of influenza seasonality.
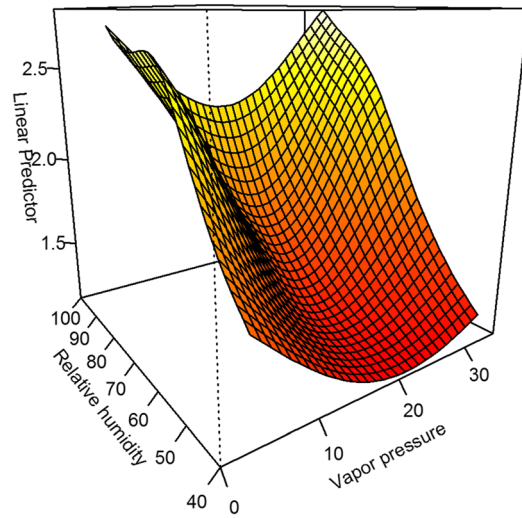
Our exposure-response curves of temperature and VP were partly consistent with some previous laboratory findings on virus transmission. Lowen and colleagues showed that transmission rates of influenza virus A/H3N2 between the hosts decreased when room temperature increased from 5 to 30 °C (Lowen et al. 2007). Tamerius et al. estimated a U-shaped relationship between the likelihood of an influenza peak and monthly specific humidity (Tamerius et al. 2013). Shaman and Kohn demonstrated a negative linear relationship between transmission rates of viruses and VP within the range of 5 to 20 hPA, based on the same laboratory data (Shaman and Kohn 2009). Some studies also explored the survival and transmission rate of aerosolized viruses at different RH levels, but the results were inconsistent between different studies (Tellier 2009). The experiments in guinea pigs showed that transmission was most efficient at RH 20 and 35% at a fixed temperature of 20 °C. However, these extremely dry conditions were seldom reached in all of three regions in our study. The same group also found that transmission was more efficient at an RH of 65% than those at 50 and 80% when ambient
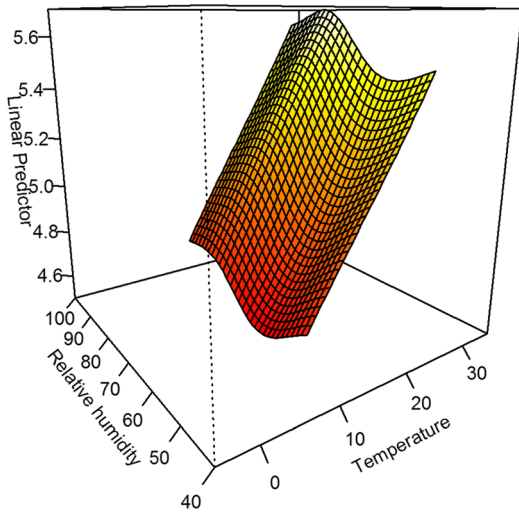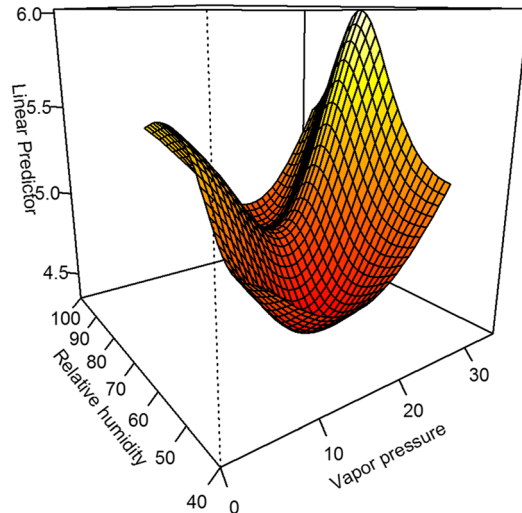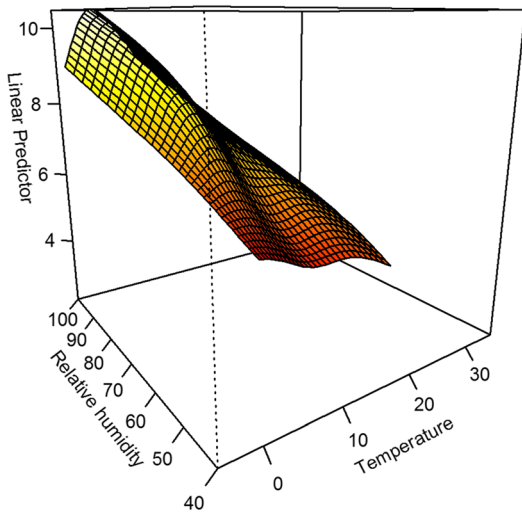
(A) Shanghai
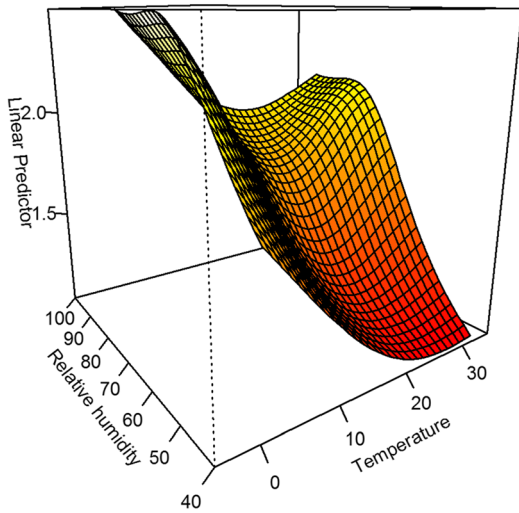
(B) Shanghai

(C) Hong Kong

(D) Hong Kong

(E) British Columbia
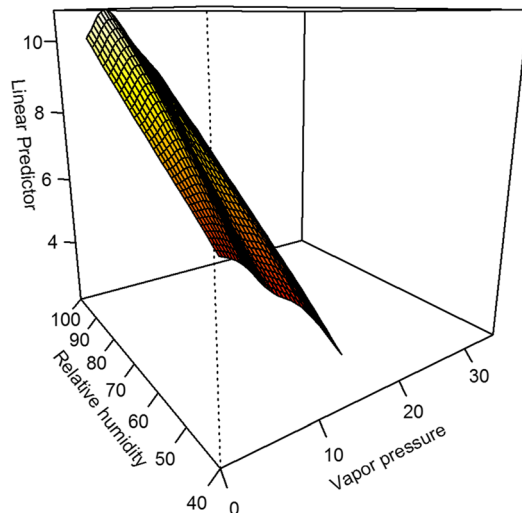
(F) British Columbia

◀ **Fig. 3** Exposure-response surface plots of the joint effects of weather factors on influenza virus activity. **a** Temperature and relative humidity in Shanghai. **b** Vapor pressure and relative humidity in Shanghai. **c** Temperature and relative humidity in Hong Kong. **d** Vapor pressure and relative humidity in Hong Kong. **e** Temperature and relative humidity in British Columbia. **f** Vapor pressure and relative humidity in British Columbia

temperature was 20 °C. Although these results seem contrast to our exposure curves, the role of weather factors in regulating virus transmission could be complicated due to the uncertain transmission routes (Brankston et al. 2007). Influenza viruses are believed to spread by droplets, aerosols, and direct contact, but it is unclear how the viruses switch between these routes. The experiments using guinea pigs showed that airborne transmission was completely blocked at 30 °C and proposed that contact transmission was the major route under a high temperature (Lowen and Palese 2009; Lowen et al. 2008). However, it is of note that ups and downs of virus activity in the community are affected not only by its transmission and survival efficiency in the environment but also by host susceptibility, though the latter is less likely directly linked to weather factors. In general, the patterns of VP from the surface plots are in line with their independent exposure-response curves, with U-shape for Shanghai and Hong Kong and steady downward trend for British Columbia. But significant VP-RH and

Table 2 Percentage change of influenza numbers associated with per unit increase of weather factors

Factor	Percentage change	95% CI	
Shanghai			
Temperature (low RH)	−3.32	−3.93	−2.71
Temperature (mid RH)	−1.10	−2.46	0.29
Temperature (high RH)	−0.80	−2.24	0.67
VP (low RH)	−4.50	−5.37	−3.62
VP (mid RH)	−0.72	−2.63	1.22
VP (high RH)	0.11	−1.84	2.09
Hong Kong			
Temperature (low RH)	2.99	1.95	4.05
Temperature (mid RH)	8.55	5.89	11.28
Temperature (high RH)	6.49	3.71	9.33
VP (low RH)	4.44	3.56	5.32
VP (mid RH)	6.28	4.25	8.36
VP (high RH)	4.82	2.63	7.06
British Columbia			
Temperature (low RH)	−25.23	−26.00	−24.44
Temperature (mid RH)	−32.14	−33.57	−30.69
Temperature (high RH)	−12.24	−14.59	−9.83
VP (low RH)	−39.97	−41.06	−38.85
VP (mid RH)	−48.63	−50.55	−46.64
VP (high RH)	−20.82	−24.55	−16.91

CI confidence interval

temperature-RH interactions found in our study suggested that VP alone is unlikely the sole weather factor that contributes to seasonal variation of influenza virus activity.

Stratification analysis revealed that the percentage changes of influenza numbers associated with per unit increase of weather factors were much higher in temperate region of British Columbia than subtropical cities of Shanghai and Hong Kong. British Columbia had a temperate climate with lower average temperature and absolute humidity than the other two subtropical regions. We speculated that influenza activity may be more sensitive to small changes at cold temperature/low absolute humidity. Future epidemiological studies including more temperate countries and laboratory studies are required to test the hypothesis. The lagged effect of weather factors should be taken into consideration when investigating the association between environmental factors and influenza activity. Our findings by lagging the weather factors 1–3 weeks are in accord with our main analysis, suggesting that the weather factors are likely to have short-term effect on influenza survival and transmission.

The difference between influenza type A and B viruses has been widely reported. Influenza A viruses tended to have more frequent antigenic change and transmit more efficiently than influenza B viruses (Bouvier and Palese 2008), causing a heavier disease burden on mortality and morbidity (Reichert et al. 2004; Simonsen et al. 2000). However, the previous findings on association of weather factors and these two types of viruses were neither consistent nor conclusive. A German study found an inverse association of temperature with pediatric hospitalization of influenza A, but not with influenza B hospitalization (du Prel et al. 2009). Another Hong Kong study found the isolation proportion of influenza B decreased as temperature increased, whereas influenza A was only associated with RH in a linear manner (Tang et al. 2010). But unfortunately, in this study, influenza type/subtype data were unavailable, thus unable to elucidate the association between weather factors and influenza type/subtypes.

There are several limitations in this study. First, we compared two cities with a large province with diverse climate due to data availability. Weather data of Great Vancouver used in this study may not fully represent the weather exposure of the population in British Columbia although more than 50% of its population is concentrated in Great Vancouver. Nevertheless, the inclusion of a temperate region widens the range of temperature, RH, and VP in the association of weather with influenza epidemics. Second, the quality of influenza surveillance data might be heterogeneous among the three regions because there is potential heterogeneity in influenza surveillance procedures and patient health seeking behavior. Third, this is an ecological study so that ecological fallacy may exist. Fourth, there are some other seasonal factors that could also play a role in regulation of influenza seasonality remained unadjusted for in our study. Several hypotheses have been proposed that

except weather factors, influenza seasonality is driven by other factors including antigenicity change of virus strains, host susceptibility, and behavior changes (Dowell et al. 2001; Lofgren et al. 2007; Murry et al. 2004). However, there are no data available to quantify the seasonal variation of antigenic change and behavior change of human hosts. The wide use of air conditioners in summer may decrease the indoor temperature that people are truly experiencing and in winter increase the temperature. On the other hand, indoor heating may also decrease RH levels in winter. Unfortunately, there is no data to show the prevalence of air conditioner usage in the regions under study; therefore, it is unlikely for us to adjust for this factor in our model. Nevertheless, we used a smoothing function of time and seasonal trend as an adjustment for unmeasured confounders although it may not be adequate. In the future, a model with more comprehensive data shall be considered to disentangle the mystery of influenza seasonality.

Conclusions

Although seasonal influenza transmission showed a great regional heterogeneity, our results demonstrated that the effects of temperature and VP were in general similar between the temperate and subtropical regions. These findings suggest the possibility to find a universal model to explain the seasonal outbreaks of influenza epidemics and develop an early warning system based on weather factors for influenza, in which the interaction of different weather factors might also be considered. More data from other regions with a variety of climate conditions are needed to confirm the results of this study.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflicts of interest.

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