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Seasonal Influenza Activity in Hong Kong and its Association With Meteorological Variations

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Influenza seasons appear consistently in the temperate regions, but are more variable in tropical/subtropical regions. The determinant for such variation remains poorly understood. This study documented the activity of influenza over a 10-year period in Hong Kong; examining its association with changes in temperature and relative humidity. The two types of influenza exhibited different correlations with meteorological variations. Influenza A showed two seasonal peaks occurring respectively in winter/spring and summer months in most years. Influenza B showed a clear winter/spring peak, but its activity during summer months was more variable. Cold and humid conditions were associated with a higher activity of both influenza A and B. In contrast, hot and humid conditions were associated with a higher activity of influenza A, but were associated with only a moderate, less consistent increase in the activity of influenza B. A trend of increase in the magnitude of summer peaks of influenza A, but not influenza B, was observed. A hypothetical 2°C rise in temperature would decrease the proportion of favorable days for influenza A in December–April from 78% to 57%, but an increase from 58% to 71% in May–November; with a similar effect (from 83% to 62%) for influenza B during December–April, but a modest change (from 17% to 18%) during May–November. The presence of two seasonal peaks of influenza annually emphasizes the need to evaluate the duration of protective immunity offered by vaccination. Further study on the effects of climate change and global warming on the activity of influenza is warranted. ***J. Med. Virol. 81:1797–1806, 2009.***

KEY WORDS: influenza; season; meteorology; subtropical; Hong Kong

INTRODUCTION

Influenza epidemics occur throughout the world and cause significant health and economic burden which can be explosive and disastrous [Cox and Subbarao, 1999]. The activity of influenza has a clear and consistent seasonal distribution in the temperate regions with annual winter peaks lasting for 5–10 weeks in November–March in the northern hemisphere, and in May–September in the southern hemisphere [Cox and Subbarao, 2000]. These consistent peaks allow vaccination programs to be launched at the same time every year. In contrast, the temporal pattern of influenza is more variable in the tropical and subtropical regions, where multiple peaks can occur at different periods within a year [Chew et al., 1998; Tsai et al., 2001; Chiu et al., 2002; Shek and Lee, 2003; Wong et al., 2004; Yap et al., 2004]. Such deviation from the classical winter peak can mask the disease burden [Chiu et al., 2002], and create difficulties in maintaining an efficient vaccination program.

The seasonal nature of influenza is intriguing and remains poorly understood. Viral mutations, host susceptibility to infection and seasonal host behavior have been suggested to play a contributory role [Dowell, 2001; Dowell and Ho, 2004]. While the determinants for the seasonal nature of influenza are multiple, meteorological variations are likely to play a key role.

Southeast Asia is regarded as an epicenter for the emergence of new strains of human and avian influenza viruses [Shortridge, 1997; Cox and Subbarao, 2000]. Whether this is related to a greater spread of viral

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activity throughout the year in this region remains to be elucidated. Currently, little is known on the relationship between meteorological variation and the activity of influenza, especially in Southeast Asia. Hong Kong represents one of the few cities within this region where the activity of influenza is well documented, and therefore provides an opportunity to study such a relationship. This study examined the association between the activity of influenza and variation of the two key meteorological elements, temperature and relative humidity, recorded during the period 1997–2006.

MATERIALS AND METHODS

Data Source and Location

Hong Kong has a high population density. The territory covers 1,104 km^2 of which 25% is developed, where 6.8 million people reside. Located on the coast of Southern China (22.3°N, 114.2°E), Hong Kong has a subtropical climate, tending towards temperate for half of the year. January and February are the coldest months during which temperatures below 10°C are not uncommon. March and April are the spring months with the occasional spells of high humidity. May–September is hot and humid with afternoon temperatures often exceeding 31°C. October–December is generally fine and dry with comfortable temperatures [Lee et al., 2006; Hong Kong Observatory, 2008].

In this retrospective study, the number of laboratory-confirmed influenza A and B cases admitted to the Prince of Wales Hospital were used as indicators of the activity of influenza. The Prince of Wales Hospital is a 1,400-bed regional general hospital located in the Northeast part of Hong Kong, serving a population of about 1.2 million. Vigorous virological investigation of respiratory tract infections is routine at the Prince of Wales Hospital. All respiratory specimens submitted to the laboratory are tested for influenza without prior selection. The daily temperature and relative humidity recorded by the Hong Kong Observatory's automatic weather station in the Shatin district where the Prince of Wales Hospital is situated, were retrieved for analysis.

Data on laboratory-confirmed influenza admission and meteorological variation for the period 1997–2006 were collected. The activity of influenza A was exceptionally high because of the arrival of new strains A/Sydney/05/97 and A/Wisconsin/67/05, respectively in 1998 and 2005. The sudden antigenic drift occurred during these 2 years may have dominated the effect of meteorological variation. Therefore, influenza A cases detected in 1998 and 2005 were excluded from the climatic correlation analyses. The transmission of respiratory viruses in Hong Kong was greatly reduced by the massive use of face masks and school closure as measures to prevent the severe acute respiratory syndrome (SARS) in 2003 [Lo et al., 2005]. To avoid biases due to unusual human intervention, influenza A and B cases detected in 2003 were also excluded from the climatic correlation analyses.

Association Between Influenza Activity and Variation in Temperature and Relative Humidity

Based on previous studies [Hemmes et al., 1960; Schaffer et al., 1976; Lowen et al., 2007], it was hypothesized that changes in temperature and relative humidity would affect the survival and transmission of influenza viruses, and therefore might influence the activity of influenza in a given population. There will always be a time lag for changes in climatic effects to be reflected in hospital admissions. This time lag comprises of an incubation period which ranges from 1 to 4 days for influenza [Cox and Subbarao, 1999], and the delay from the onset of symptoms to hospital admission. To account for this time lag, each calendar day was taken as a reference point. The temperature and relative humidity conditions of the previous 7 days (Days 6–0) were correlated with the number of influenza cases admitted in the next 7 days (Days 1–7). The average occurrence of influenza (N_T) in different temperature domains (T to $T + \Delta T$) was calculated by the formula:

$$N_T = \frac{\sum_{i}^{n} C_i f(t_i)}{\sum_{i}^{n} f(t_i)}$$

where i is an index from 0 to n, t_i the mean temperature for the ith 7-day period, C_i the total number of influenza cases for the $i + 1$th 7-day period, and $f(t_1)$ a function which

$$\begin{cases} = 1 & \text{when } T < t_i \leq T + \Delta T \\ = 0 & \text{otherwise} \end{cases}$$

The numerator on the right-hand side of the equation represents the sum of all C_i comprising the previous 7-day mean temperature (t_i) falling within the temperature domain from T to $T + \Delta T$ during the data period. The denominator is the total number of occasions with $T < t_i \leq T + \Delta T$ during the same data period.

Similarly, the average occurrence of influenza (N_H) in different relative humidity domains (H to $H + \Delta H$) was determined by the formula:

$$N_H = \frac{\sum_{i}^{n} C_i f(h_i)}{\sum_{i}^{n} f(h_i)}$$

where i is an index from 0 to n, h_i the mean relative humidity for the ith 7-day period, C_i the total number of influenza cases from $i + 1$th 7-day period, and $f(h_i)$ a function which

$$\begin{cases} = 1 & \text{when } H < h_i \leq H + \Delta H \\ = 0 & \text{otherwise} \end{cases}$$

The same approach was used to assess the combined effect of temperature and relative humidity on the occurrence of influenza (N_{TH}).

Climatic Zones Associated With High and Low Influenza Activity

The pattern recognition approach was used to identify climatic zones (combinations of temperature and relative humidity) which were associated with periods of high and low activity of influenza. To achieve this, three non-overlapping 7-day periods capturing the largest number of influenza cases were identified from the winter season of each year. A three non-overlapping 7-day period was used as it covered the whole influenza season for most of the years. These periods were regarded as "favorable" periods for influenza. The data also showed a summer peak for influenza in most of the years, therefore similar "favorable" periods were also identified from the summer months of years with observable summer peaks. The three non-overlapping 7-day periods with the lowest number of cases during the low seasons of each year were regarded as "unfavorable" for influenza. "Favorable" and "unfavorable" periods for influenza A and B were identified separately as the data indicated that the activity of influenza A and B were not always synchronized. When there were more than three 7-day periods showing the same rank (the highest or lowest three) of influenza activity, all these periods were included for analysis.

The daily mean temperature and relative humidity of the preceding 7 days of these "favorable" and "unfavorable" periods were used to construct phase diagrams to define climatic zones that were "favorable" or "unfavorable" for influenza. Each calendar month was placed on the phase diagram based on the average temperature and relative humidity recorded in 1997–2006.

RESULTS

Influenza Seasons

During the 10-year study period, 6,076 laboratory-confirmed influenza A and 1,462 influenza B cases were admitted to the Prince of Wales Hospital. The number of admissions varied from 244 to 1,183 per year for influenza A, and 51–268 for influenza B. In general, there were two peaks of influenza activity occurring respectively at the junction between winter and spring, and during the summer months of each year (Fig. 1).

The winter/spring peak for influenza A occurred most commonly in February and March, whereas the summer peak was observed mostly in June and July, and a shift in the magnitude of the peaks was also observed. In the early years (1998–2000), the winter/spring peaks for influenza A were higher than the summer peaks. In 2001–2002, the magnitude of the winter/spring and summer peaks were similar. Year 2003 was interrupted by community measures for controlling SARS [Lo et al., 2005]. From 2004 to 2006, the magnitude of the summer peaks became larger than the winter/spring peaks.

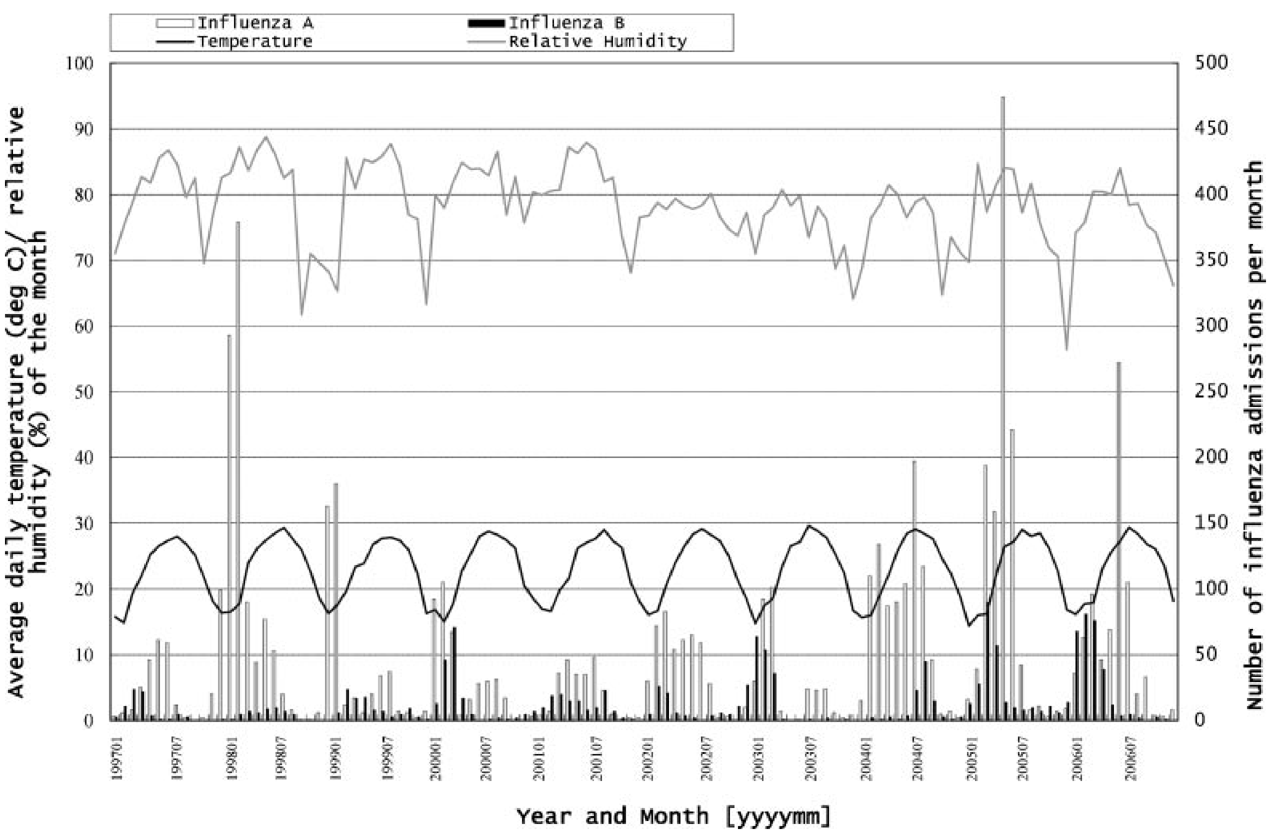

Fig. 1. Number of influenza admissions and variation in temperature and relative humidity from 1997 to 2006 in Hong Kong.

The winter/spring peaks for influenza B also occurred most commonly in February and March. However, the summer peaks were more variable and less prominent. An obvious peak was observed between June and October in four of the 10 years. In 2000 and 2002, there was only a slight increase in cases during the summer months; whereas influenza activity was similar throughout the second half of 2005. Overall, the magnitude of the winter peaks was higher than the summer peaks, and no trend of change was observed.

Temperature, Relative Humidity, and Influenza Activity

Figure 2A,B shows the variation in the average occurrence of influenza with respect to different temperature

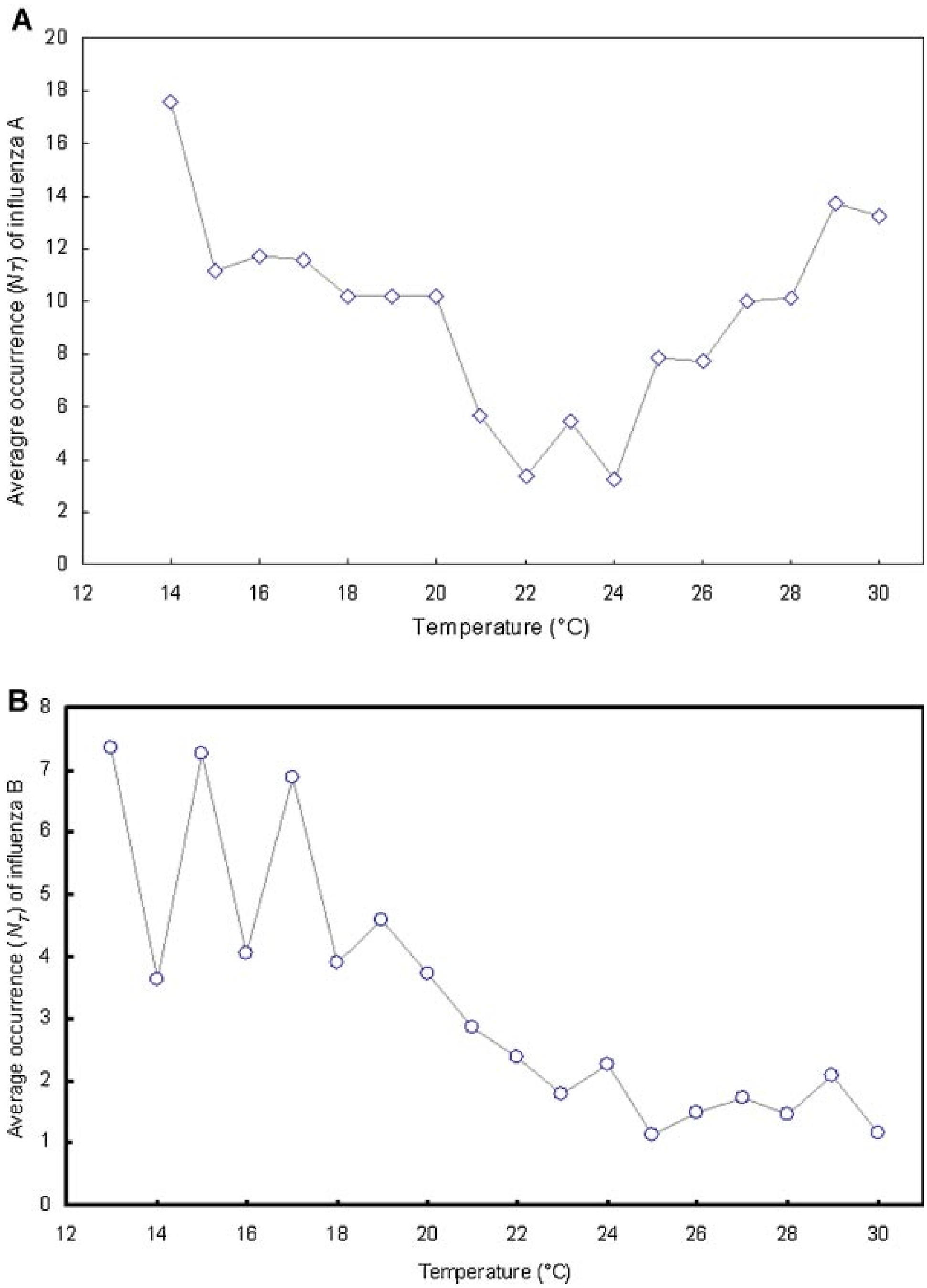

Fig. 2. Influenza occurrence and variation in temperature. Average occurrence of influenza (N_T) was defined as the average number of influenza cases observed during a 7-day period for a given temperature domain. In these plots, temperature ranges that occurred less than twice during the study period are not included.

domains (N_T). The occurrence of influenza A and B exhibited a different association with temperature variation. Influenza A showed a bimodal pattern with a greater occurrence at cooler (14–20°C) and warmer (25–30°C) temperatures, and the lowest occurrence was observed at 21–24°C. The occurrence of influenza B was highest at cooler temperatures (13–19°C), then declined rapidly between 20 and 23°C, and then fluctuated at low levels in higher temperatures.

The variation in the average prevalence of influenza with respect to different relative humidity domains (N_H) is shown in Figure 3A,B. Although the prevalence of influenza A and B seemed to increase with humidity, the degree of correlation was weak.

Figure 4A,B shows the average prevalence of influenza with respect to different temperature and relative humidity domains (N_{TH}). A higher activity of influenza A was observed in cold and humid conditions, as well as in hot and humid conditions; whereas influenza B showed a greater activity in cold and humid conditions only. The activity of both influenza A and B were lower in dry and milder climates.

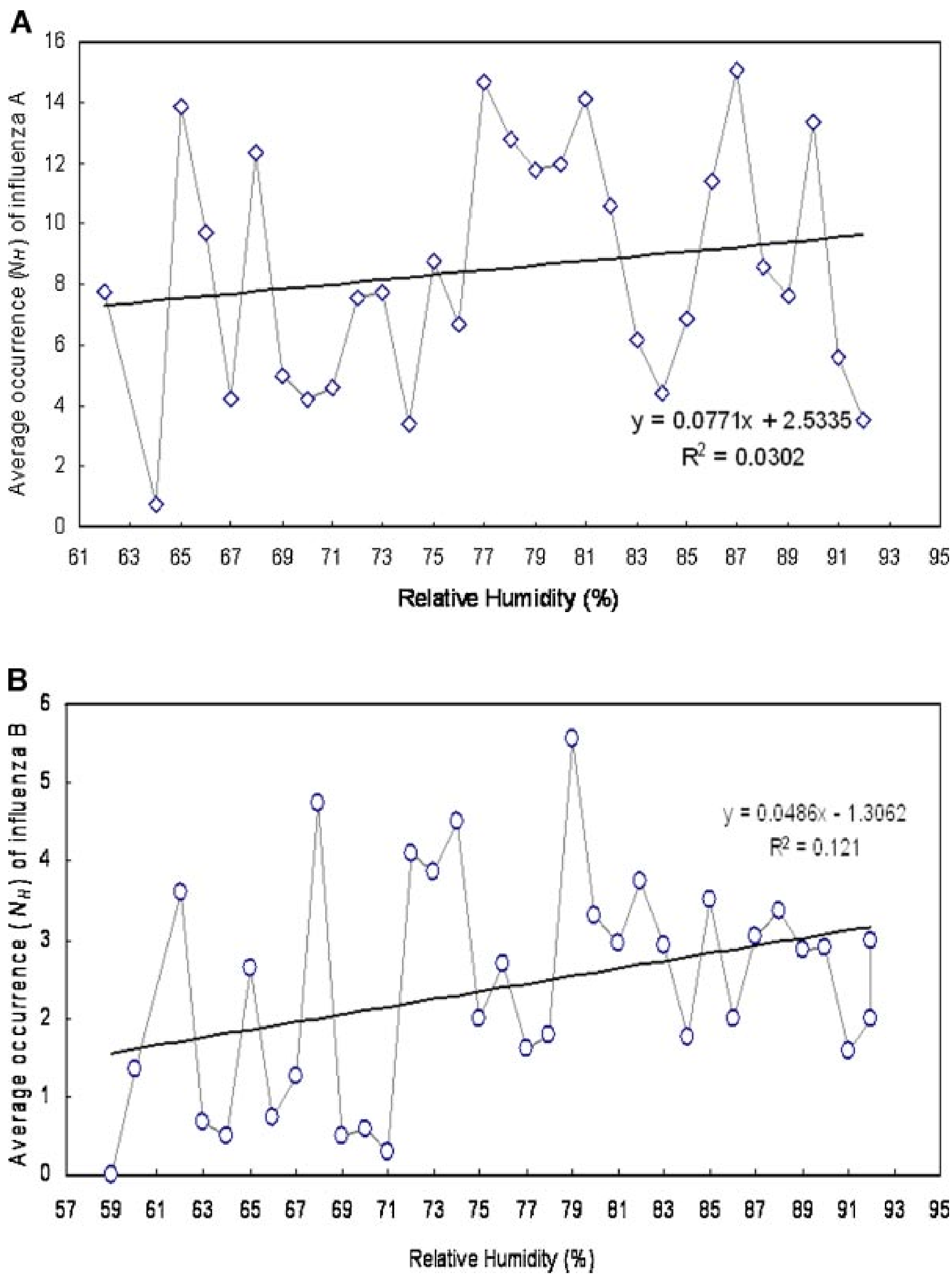

Fig. 3. Prevalence of influenza and variation in relative humidity. **A**: Influenza A. **B**: Influenza B. Average occurrence of influenza (N_H) was defined as the average number of influenza cases observed during a 7-day period for a given relative humidity domain. In these plots, relative humidity ranges that occurred less than twice during the study period are not included.

A

7-day mean relative humidity (%)	7-day mean temperature (°C)															
	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
95 – 100												1.57				
90 – 95						0.14	1.71		0.71	0.86	1.43	0.86	0.68	1.00		
85 – 90		0.00	2.71	3.00	1.75		1.36	0.90	1.33	0.38	1.89	3.64	1.79	1.02	1.43	
80 – 85	0.14	2.00	2.29	1.19	1.29	1.41	1.38	0.18	2.29	0.43	2.20	0.63	1.03	1.58	1.36	0.36
75 – 80	2.97	0.57	1.10	1.45	2.24	1.39	0.00	1.62	0.43	1.05	0.77	0.73	2.04	2.29	2.47	2.37
70 – 75	0.29	4.57	0.97	0.86	0.79	3.05	0.25	0.00	0.07	0.07	0.05	0.43	2.71	1.43		2.21
65 – 70	0.14	1.14	2.14	1.83	0.14	0.14	0.00	0.14		0.14		0.67	2.57	0.14	0.00	
60 – 65		1.14	2.29		0.14	2.86		0.00		0.00	0.21		0.14			
55 – 60		4.21	0.14						0.00		0.00					
50 – 55								0.00								
45 – 50																

B

7-day mean relative humidity (%)	7-day mean temperature (°C)																	
	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
95 – 100														0.29				
90 – 95					0.14			1.00	0.43		0.14	0.43	0.10	0.43	0.29	0.14		
85 – 90			3.00	0.39	3.29	0.07	0.62	0.00	0.43	0.71	0.38	0.48	0.23	0.33	0.32	0.19	0.33	
80 – 85		0.29	0.36	1.93	1.19	1.14	0.50	0.46	0.55	0.30	0.64	0.86	0.31	0.21	0.21	0.19	0.32	0.29
75 – 80		2.43	1.66	0.11	0.43	0.52	1.14	0.95	0.14	0.43	0.09	0.14	0.11	0.16	0.14	0.38	0.28	0.14
70 – 75			0.10	1.71	1.66	0.49	0.26	0.10	0.46	0.21	0.10	0.00	0.05	0.24	0.14	0.06	0.43	0.00
65 – 70	1.36	0.00	0.14	0.14	0.00	0.11	0.00	0.24	0.00	0.14	0.00	0.07		0.10	0.14	0.43	0.14	
60 – 65	2.29	0.00		0.14	0.50	0.14	0.00	0.29		0.00		0.14	0.14		0.00			
55 – 60		0.07		0.07	0.21		0.43				0.00		0.00					
50 – 55				0.57						0.00				0.00				
45 – 50	0.00																	
40 – 45		1.00																

Fig. 4. Prevalence of influenza and variation in temperature and relative humidity. **A**: Influenza A. **B**: Influenza B. Average occurrence of influenza (N_{TH}) was defined as the average number of influenza cases observed during a 7-day period for a given temperature and relative humidity domain. Numbers in the matrix refers to the N_{TH} of the corresponding combination of temperature and relative humidity. Temperature and relative humidity combinations occurring less than twice during the study period are not included. $N_{TH} > 1$ to 2 in light pink, >2 to 3 in pink, >3 to 4 in red, and >4 in deep red.

Climatic Zone and Influenza Activity

Figure 5A,B is the phase diagrams showing the temperature and relative humidity conditions of the peak and trough periods of influenza activity as determined by the pattern recognition approach. Three distinct climatic zones were observed for influenza A, including two "favorable" zones which corresponded to the winter/spring and summer peaks, and a "unfavorable" zone for the trough seasons.

For influenza B, one "favorable" climatic zone was observed which corresponded to the winter/spring

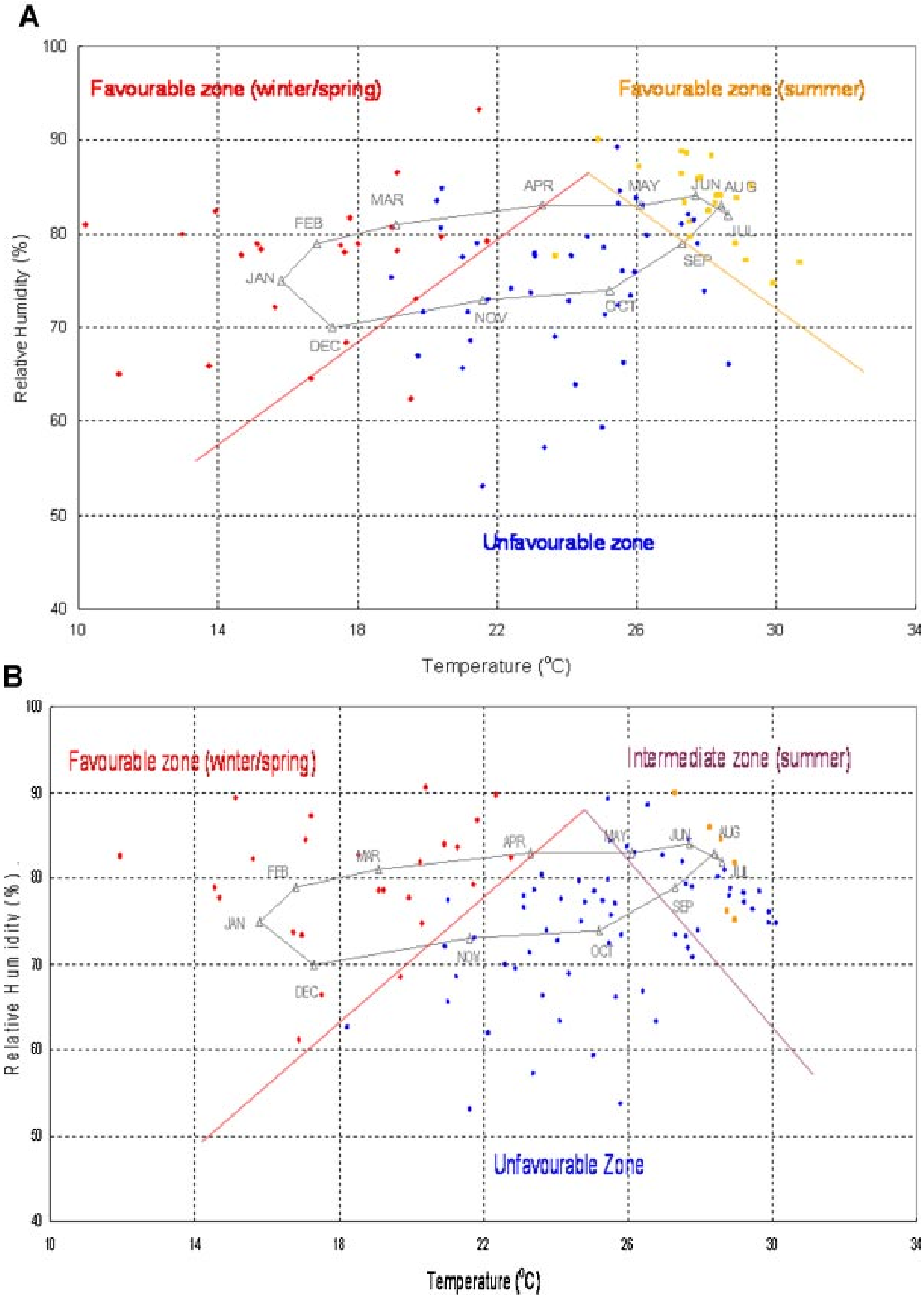

Fig. 5. Location of calendar months with respect to influenza climatic zones. Temperature and relative humidity conditions of the peak and trough influenza periods as identified by the "pattern recognition" method are plotted. Red diamonds represent winter/spring peak periods. Orange squares represent summer peak periods. Blue circles represent trough periods. **A**: Areas above the red and orange lines are regarded as "favorable" climatic zones for influenza A. The area below these lines is regarded as "unfavorable" climatic zone for influenza A. **B**: The area above the red line is regarded as "favorable" climatic zone for influenza B. The area above the purple line is regarded as "intermediate" climatic zone which comprises of a mixture of blue circles and yellow squares. The area below the red and purple lines is regarded as the "unfavorable" climatic zone. The placement of calendar months with respect to influenza climatic zones is based on the average temperature and relative humidity recorded in 1997–2006, and indicated by gray triangles.

peaks. An "intermediate" climatic zone comprising a mixture of summer peaks and trough seasons, and a "unfavorable" zone which corresponded to the trough seasons was also observed (Fig. 5B).

When the average temperature and relative humidity of each calendar month in 1997–2006 was correlated with the climatic zones, December–April and May–September fell in the "favorable" zone for influenza A activity (Fig. 5A). Similarly for influenza B, December–April fell in the "favorable" zone, whereas May–September fell in the "intermediate zone."

To examine the possible effect of temperature rise on the proportion of favorable periods for influenza in each calendar month, the proportion of days in each calendar month between 1997 and 2006 with temperature and relative humidity conditions that could be regarded as "favorable" for influenza activity was counted, and the counting was repeated after raising the temperature by 2°C. Since an intermediate zone was observed for influenza B (Fig. 5B), days with climatic conditions falling in this zone were multiplied by a factor of 0.22 which reflects the proportion of peak periods (orange squares in Fig. 5B) within the "intermediate" zone. It was found that an increase of 2°C would have reduced the proportion of favorable days for influenza A from 78% to 57% during December–April, whereas an increase from 58% to 71% was observed during May–November (Fig. 6A). The effect on influenza B during December–April was similar (83–62%), but the effect on May–November was small (increase from 17% to 18%) (Fig. 6B).

DISCUSSION

Determinants for the seasonal pattern of influenza are complex and involve biological, environmental and

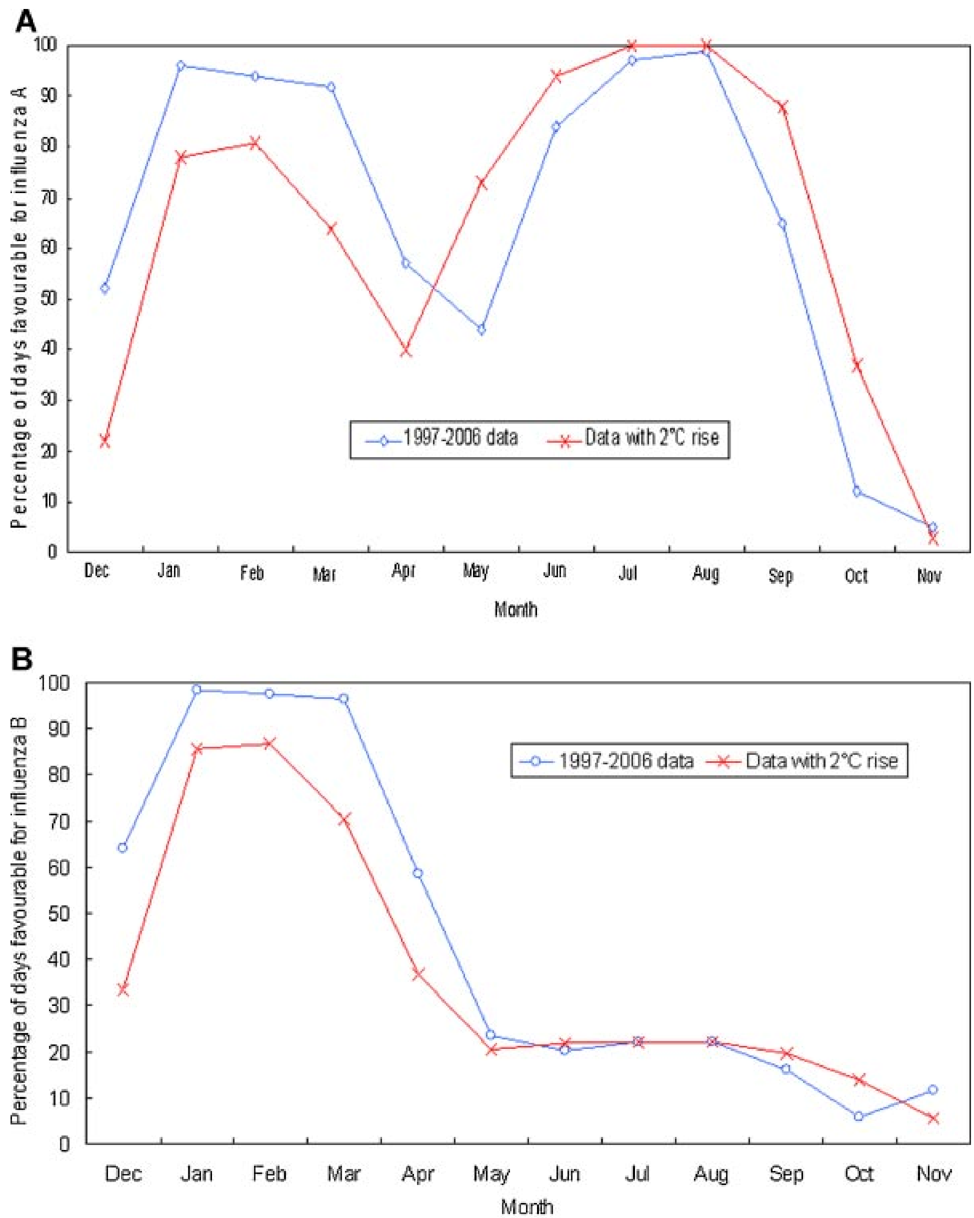

Fig. 6. Change in the proportion of days in each calendar month favorable for influenza due to a 2°C rise in temperature The number of days favorable for influenza in each month from 1997 to 2006 is counted based on the climatic zones as depicted in Figure 5A,B, and is represented by a blue line for influenza A in (**A**), and influenza B in (**B**). Red lines represent the predicted situation when the temperature of the whole period is increased by 2°C.

social elements [Tellier, 2006; Lofgren et al., 2007]. Climatic factors can exert direct effects on the survival and transmission of influenza viruses [Hemmes et al., 1960; Lowen et al., 2007], and alter indirectly the host behavior or health that affect susceptibility to an influenza infection [Dowell, 2001]. This study examined the association between meteorological variations and activity of influenza at a population level which can be interpreted as a final outcome of all direct and indirect effects. The approach of using hospital admission data to indicate the activity of influenza has advantages of being based on a more consistent population and testing threshold, and more importantly reflecting clinically significant infections. Nevertheless, it should be noted that the current study was based on data collected from a single center which may have potential biases because of the age structure and vaccination coverage of the catchment population.

While influenza A and B are very similar viruses, the current results indicate that they exhibit notable different associations with climatic variations. While a winter/spring peak was observed for both influenza A and B, the summer peak was less obvious for influenza B. Furthermore, the trend of a shift in the activity of influenza A from winter/spring to summer in recent years was not observed for influenza B. Cooler (14–19°C) and humid (>70%) climate was associated with a higher activity of both influenza A and B, hotter (25–30°C) and humid (>70%) climate was associated with a higher activity of influenza A, but less consistently for influenza B.

The association between cold weather and influenza epidemic is often regarded as an accepted assumption, despite the lack of biological justification [Dowell, 2001; Dowell and Ho, 2004; Tellier, 2006]. The use of indoor heating in winter lowers the relative humidity, and relative humidity below 40% has been shown to favor the survival of influenza viruses [Hemmes et al., 1960]. This explanation seems logical for the temperate region where winter is severe. However, winter in the subtropical region is often not sufficiently cold to require indoor heating. The current study data showed that a humid climate (relative humidity >70%) was associated with a higher activity of both influenza A and B. Relative humidity can exert effects at different levels. Low relative humidity leads to rapid evaporation of water from exhaled aerosols and form droplet nuclei making them small enough to remain airborne for a longer period of time [Parry et al., 2007]. Aerosolized influenza virions have been found stable maximally at a lower relative humidity (20–40%), and minimally at a mid-range relative humidity (50%), and moderately at a high relative humidity (60–80%) [Schaffer et al., 1976]. Theoretically, breathing dry air causes desiccation of the nasal mucosa, epithelial damage and reduced mucociliary clearance resulting in increased susceptibility to respiratory tract infections. Using the guinea pig model, it was found that cold and dry conditions favored the transmission of influenza [Lowen et al., 2007]. Data from the current study indicate that a considerable fluctuation in the activity of influenza could occur within the range of relative humidity (between 59% and 93%) seen commonly in Hong Kong. Given the humid climate of subtropical coastal areas such as Hong Kong where the average humidity is about 78% [Lee et al., 2006], natural variation in relative humidity does not seem to pose a substantial impact on the activity of influenza in this region.

The observation of a consistent summer peak for influenza A is intriguing. Summer in Hong Kong, like other tropical and subtropical coastal areas, is hot and humid where the use of air-conditioning is common. The effect of air-conditioning on influenza transmission is not known. Air-conditioning lowers the absolute humidity, but the condensation process can trap potentially virus-bearing aerosols within the unit itself; and the difference in air exchange rate could further complicate its overall effect. Whether the current observation of a summer peak for influenza, especially for influenza A, is a direct or indirect result of the increased use of indoor air-conditioning deserves further studies.

Overall, influenza A causes a much greater health impact in Hong Kong as it accounted for 80% of influenza-associated admissions recorded over the last 10 years. The presence of two annual seasonal peaks for influenza A is also of concern. The duration of immunity after influenza vaccination has not been evaluated systematically, but the rapid decline in antibody levels suggests a short duration of protection. The observation that the activity of influenza A was shifting from winter/spring to summer emphasis an urgent need to evaluate whether the current vaccination program being conducted before each winter can offer sufficient protection lasting until the summer months.

As stated in the Fourth Assessment Report (AR4) of the Intergovernmental Panel on Climate Change (IPCC), warming of the climate system is unequivocal and widespread over the world. Such anthropogenic warming could lead to abrupt and irreversible effects [Solomon et al., 2007; Russell et al., 2008]. Understanding the association between climate changes and influenza activity is a crucial step in predicting the effects of global warming on influenza activity, if there is any. Although the current study is not able to differentiate between casual and causal associations, the results have raised a possibility that climate changes may affect the seasonal distribution of influenza. A recent analysis on the global circulation of influenza A H3N2 suggests that East and Southeast Asia forms a pouch for virus evolution and formation of seed viruses for Oceania, North America, Europe, and South America [McMichael, 2004]. If the temporary overlapping epidemics are a key to maintain this evolutionary pouch, it would be important to monitor whether global warming may extend this pouch by extending the activity of influenza throughout the year in areas that used to have a single annual winter epidemic. This possibility of a change in the activity of influenza as a consequence of global warning should not be discarded, as environmental influence on the emergence of infectious diseases has been well demonstrated historically [Leung et al., 2007].

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