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# Meteorological factors and El Nino Southern Oscillation are associated with paediatric varicella infections in Hong Kong, 2004–2010

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## SUMMARY

Varicella accounts for substantial morbidities and remains a public health issue worldwide, especially in children. Little is known about the effect of meteorological variables on varicella infection risk for children. This study described the epidemiology of paediatric varicella notifications in Hong Kong from 2004 to 2010, and explored the association between paediatric varicella notifications in children aged <18 years and various meteorological factors using a time-stratified case-crossover model, with adjustment of potential confounding factors. The analysis found that daily mean temperature, atmospheric pressure and Southern Oscillation Index (SOI) were positively associated with paediatric varicella notifications. We found that an interquartile range (IQR) increase in temperature (8·38 °C) at lag 1 day, a 9·50 hPa increase in atmospheric pressure for the current day, and a 21·91 unit increase in SOI for the current day may lead to an increase in daily cases of 5·19% [95% confidence interval (CI) 1·90–8·58], 5·77% (95% CI 3·01–8·61), and 4·32% (95% CI 2·98–5·68), respectively. An IQR increase in daily relative humidity (by 11·96%) was associated with a decrease in daily paediatric varicella (−2·79%, 95% CI −3·84 to −1·73). These findings suggest that meteorological factors might be important predictors of paediatric varicella infection in Hong Kong.

**Key words**: Case-crossover study, chickenpox, Hong Kong, meteorological factors, varicella.

## INTRODUCTION

Varicella (chickenpox), caused by the ubiquitous varicella-zoster virus (VZV), is one of the most common vaccine-preventable infectious diseases. It is most common in children, but people can get chickenpox at other ages if they have not received chickenpox vaccine [1]. The main clinical presentation includes an itchy rash and red spots or blisters all over the body, serious complications may occur, such as secondary bacterial skin and soft tissue infections, cerebellitis, encephalitis, pneumonia and coagulopathy [1, 2]. Varicella-associated hospitalizations are common, especially in children, posing a significant disease burden for the healthcare system [3].

Seasonal patterns for the incidence of varicella have been reported in a number of areas. For example,

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a winter peak was observed in India, Thailand, Sri Lanka and other countries [4–6]. A bimodal seasonal pattern has been reported in Hong Kong with peaks in summer and winter [3]. The seasonality of varicella incidence indicated that meteorological factors might play an important role in the epidemiology of this disease. However, the possible association between varicella and various meteorological factors, such as temperature, rainfall and humidity have not yet been systematically investigated, particularly in children. Temperature has been associated with chickenpox incidence in Taiwan [7]. In a Japanese study, Kokaze *et al.* [8] showed that the annual temperature variation affected the seasonal variations of chickenpox incidence. A recent study in Hong Kong showed that lower relative humidity was associated with higher paediatric varicella-associated hospital admissions [3]. El Niño Southern Oscillation (ENSO) is a systematic pattern of global climate variability. Southern Oscillation Index (SOI), an indicator of ENSO activity, is defined as the normalized atmospheric pressure difference between Darwin in Australia and Tahiti in the South Pacific. SOI can affect the epidemiological patterns of many infectious diseases [9–12]. So far, few studies have been conducted to examine the effect of SOI on the transmission of chickenpox.

The objective of this study was to investigate the association between various meteorological factors and paediatric varicella notifications in Hong Kong using a time-stratified case-crossover approach. The distribution of paediatric varicella notifications in terms of age, sex, and time is also described.

## MATERIALS AND METHODS

Hong Kong is located in eastern Asia, bordering the South China Sea to the south, west, and east, and the mainland China to the north. It has a typical monsoon-influenced climate with wet and hot summers and dry and cool to mild winters. Hong Kong has an area of 1092 $km^2$, and a population of 7·2 million. Figure 1 shows the geographical location of the study area.

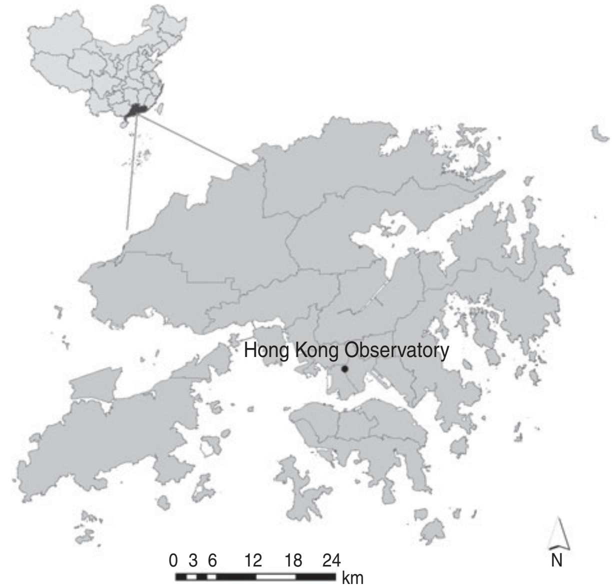


**Fig. 1.** Map of Hong Kong, showing the position of the weather monitoring station.

We obtained the varicella notification data of all children and adolescents aged <18 years from the Centre of Health Protection (CHP), Department of Health, Hong Kong Special Administrative Region Government, for the period 1 January 2004 to 31 December 2010. Varicella is one of the statutory notifiable infectious diseases in Hong Kong, it is compulsory for medical practitioners in both public and private sectors to report all cases of varicella to the CHP via a centralized notification system [13]. A chickenpox case was defined as an acute maculopapular vesicular rash without other explanations. Chickenpox is considered an easily diagnosed childhood disease due to the presence of often pathognomonic rash and therefore rarely subject to misdiagnosis and miscoding [2, 14]. Hong Kong residents are provided with a comprehensive range of medical and health services by the public and private sectors. Insurance is not necessary to use the public facilities operated by the Hospital Authority.

Meteorological data including daily mean air temperature (°C), mean relative humidity (%), rainfall (mm), mean atmospheric pressure (hPa) and mean wind speed (m/s) were obtained, during the study period, from daily meteorological reports from the Hong Kong Observatory website (http://www.hko.gov.hk/). Daily SOI data were obtained from the website of the Australian Bureau of Meteorology (http://www.longpaddock.qld.gov.au/). Spearman's correlation coefficients were used to evaluate the interrelationships between the various weather factors.

A time stratified case-crossover model was conducted to examine the association between meteorological factors and reported paediatric varicella infection in Hong Kong. The case-crossover study was initially proposed to examine the individual-level disease triggers such as traffic accidents, sexual activity, and acute myocardial infarction [15]. Later development in a bidirectional case-crossover study [16] and time-stratified case-crossover design [17] found wider applications in population-level time-series data and allowed the control periods to be either before or after the event, making it possible to adjust for the effect of long-term trend and seasonality on exposure and outcome.

Epidemiological studies have proposed several different methods to select the control periods. The advantages and limitations of these selection methods on risk estimation have recently been described in detail [18]. Based on previous experience [19], we chose our referent periods by using a time-stratified design. Specifically, the case periods and control periods were selected from the same day of the week in order to control for any day of week patterns in varicella notifications [18]. Each case day had three matching control days within a 28-day stratum. So the first stratum for this study was 1 January to 28 January 2004, the second stratum was 29 January to 25 February. For example, if a varicella notification was on 27 January 2004, then the control days should be 6, 13 and 20 January 2004. The case-crossover method controls for any long-term trends and seasonal patterns in varicella notification and meteorological variables [18, 19]. When using the case-crossover design, confounders related to individual characteristics, such as age and sex, are inherently controlled for. Studies have demonstrated that the case-crossover gives unbiased estimates in the presence of strong seasonal confounding [20–23].

The 'season' package of R version 2.14.1 (R Foundation, Vienna) was used to fit the time-stratified case-crossover [24]. In the present study, the weather variables were correlated with each other, and the weather variables were potential risk factors of varicella infections. Therefore, when examining the effect of weather variable A, the other weather variables can act as a confounding factor. A univariable model was first fitted for each meteorological factor, and then multivariable models were used to control the influence of all other meteorological factors, meaning that for one specific meteorological variable, all the other meteorological variables were treated as potential confounding factors in the multivariable models; however, when there was high correlation between two variables, they were not included in the same model due to concerns of collinearity. The incubation period of chickenpox is about 7–10 days, so we estimated the linear effect of the meteorological variables according to different lag structures including the current day (lag 0) up to 10 days before (lag 10). The effect of lag 1 means the effect of yesterday's weather condition on the current day's varicella infection. We report the excess risk (ER), defined as the percentage increase in daily paediatric varicella notifications for each interquartile range (IQR) increase in each meteorological factor, with 95% confidence intervals (95% CI). The logistic regression model provides odds ratio (OR) estimates [25]. The OR is an approximate measure of the relative risk (RR), which is often used to calculate excess risk (ER) by: $RR-1)/RR \times 100\%$. The ER used in this study provided exactly the same information with the OR. Because the OR value is relatively small, say, 1·001, it is a common practice to present this as an ER of 0·1% [12, 26]. To test the linearity assumption of the relationship between the logarithm of daily paediatric varicella notifications and the meteorological variables, we visually inspected the dose–response curve derived using a smoothing function in a generalized additive model [27]. This was done through the 'mgcv' package in R. We plotted the residuals (the difference between fitted and observed values) of the model against the time to examine the residual normality and constant variance assumptions. All statistical analyses were two-sided and values of $P<0{\cdot}05$ were considered statistically significant.

## RESULTS

During the 7-year period, a total of 74 077 notifications for varicella infection from all sources were observed in the paediatric population in Hong Kong. The annual paediatric chickenpox notification cases from 2004 to 2010 ranged from 5738 to 16 187/year, with a mean of 10 582/year, the corresponding annual incidence ranged from 508·5/100 000 to 1370·7/100 000 children, with a mean of 891·6/100 000 children (Table 1). The monthly distribution of paediatric chickenpox notifications is shown in Figure 2. A bimodal distribution of cases was observed, with notifications peaking in December and January, as well as in June and July. There were a total of 39 911 (53·9%) male and 34 166 (46·1%) female cases reported for varicella, with a slightly higher annual incidence in males (1253/100 000) than females (1147/100 000). The mean age was 6 years. A total of 1360 (1·8%) patients were infants aged <1 year, 33 928 (45·8%) were preschool children

Table 1. *Notification figures, mid-year population, and estimated annual incidence rates for reported paediatric varicella in Hong Kong, 2004–2010*

| Year | No. of varicella notifications | Mid-year population | Annual varicella incidence (1/100 000 children) |
|---|---|---|---|
| 2004 | 10 600 | 1 264 300 | 838·4 |
| 2005 | 10 687 | 1 232 000 | 867·5 |
| 2006 | 13 111 | 1 204 100 | 1088·9 |
| 2007 | 16 187 | 1 180 900 | 1370·7 |
| 2008 | 7753 | 1 160 400 | 668·1 |
| 2009 | 5738 | 1 128 400 | 508·5 |
| 2010 | 10 001 | 1 112 300 | 899·1 |

aged 1–5 years, 34 077 (46·0%) were pre-teens aged 6–12 years, and 4712 (6·4%) were teenagers aged 13–17 years. The corresponding annual incidences for these age agroups were 343·9, 2859·5, 1179·1 and 278·4/1 00 000 respectively. The preschool children (1–5 years) had the highest incidence.

The descriptive statistics for ambient weather conditions and paediatric varicella notifications are shown in Table 2. There was an average of 29 daily paediatric varicella notifications in Hong Kong during the study period. The mean levels of ambient temperature, relative humidity, atmospheric pressure, and rainfall were 23·4 °C, 78·2%, 1012·8 hPa, and 8·0 mm, respectively. The time-series of ambient temperature, relative humidity, atmospheric pressure and paediatric varicella notification are given in Figure 3. There were obvious seasonal patterns in the weather variables and paediatric varicella notifications. Table 3 shows the correlations between various weather variables. The weather variables were significantly correlated with each other, e.g. between daily mean temperature and pressure ($r=-0{\cdot}84$). Due to the relatively high correlation between temperature and pressure, they were not included in the same model in the multivariable analyses.

In the univariable analysis, it was found that daily mean temperature (at lags 5–6 days), rainfall (at lags 2–3 days), atmospheric pressure (current day) and SOI (at lags 0–4 and 6 days) were positively associated with paediatric varicella notification, while relative humidity (at lag 3–4 days) was negatively associated with paediatric varicella notification in Hong Kong (Fig. 4, Supplementary Table S1). Two multivariable models were fitted as daily mean temperature and pressure were highly correlated with each other,

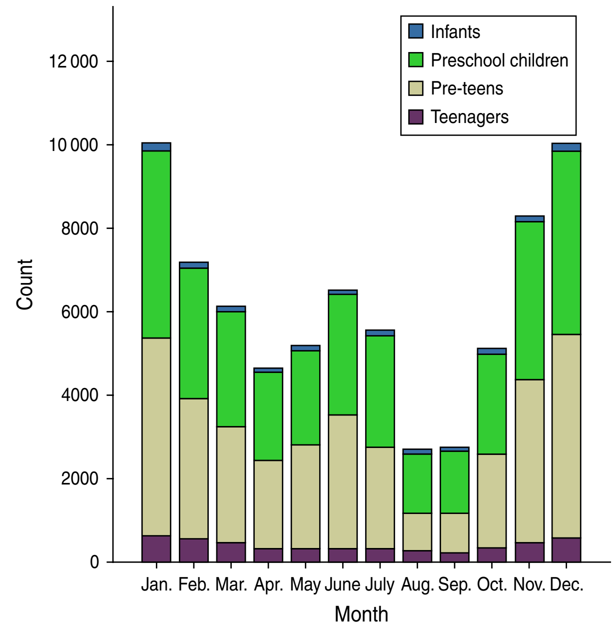


**Fig. 2** [*colour online*]. Monthly distribution of paediatric varicella notifications in Hong Kong, 2004–2010 (infant, <1 year; preschool children, 1–5 years; pre-teens, 6–12 years; teenagers, 13–17 years).

which generally yielded consistent results. The ambient temperature (at lag 1–4 days), pressure (at lag 0, 3–5 and 8–10 days) and SOI (at lag 0–9 days) were significantly associated with increased paediatric varicella notification, and relative humidity (at lag 2–7 days) was associated with decreased paediatric varicella notification. The corresponding ERs were 5·19% (95% CI 1·90–8·58) per IQR increase (8·38 °C) in mean temperature at lag 1 day; −2·79% (95% CI −3·84 to −1·73) per 11·96% increase in relative humidity at lag 3 days; 5·77% (95% CI 3·01–8·61) per 9·50 hPa increase in atmospheric pressure for the current day; and 4·32% (95% CI 2·98–5·68) per 21·91 unit increase in SOI for the current day.

Supplementary Figure S1 (available online) shows the diagnostic graphs of the multivariable models, illustrating the residuals against time. There were no discernible patterns and no autocorrelation in the residuals, indicating acceptable goodness of fit of the models.

The dose–response curves for various meteorological variables and daily paediatric varicella notifications are shown in Figure 5. An approximately linear relationship was observed for the associations between meteorological variables and varicella notifications.

Table 2. *Descriptive statistics for ambient weather parameters and reported paediatric varicella notifications in Hong Kong, 2004–2010*

| | Minimum | Median | Maximum | Mean | S.D. |
|---|---|---|---|---|---|
| Temperature (°C) | 8·8 | 24·6 | 31·8 | 23·4 | 5·1 |
| Relative humidity (%) | 31·3 | 79·4 | 98·1 | 78·2 | 10·6 |
| Atmospheric pressure (hPa) | 992·5 | 1012·6 | 1030·7 | 1012·8 | 6·3 |
| Rainfall (mm) | 0·0 | 0·0 | 82·5 | 8·0 | 12·5 |
| Southern Oscillation Index | –76·1 | 2·1 | 54·2 | 1·5 | 17·1 |
| Daily varicella notifications | 0·0 | 23·0 | 195·0 | 29·0 | 23·6 |

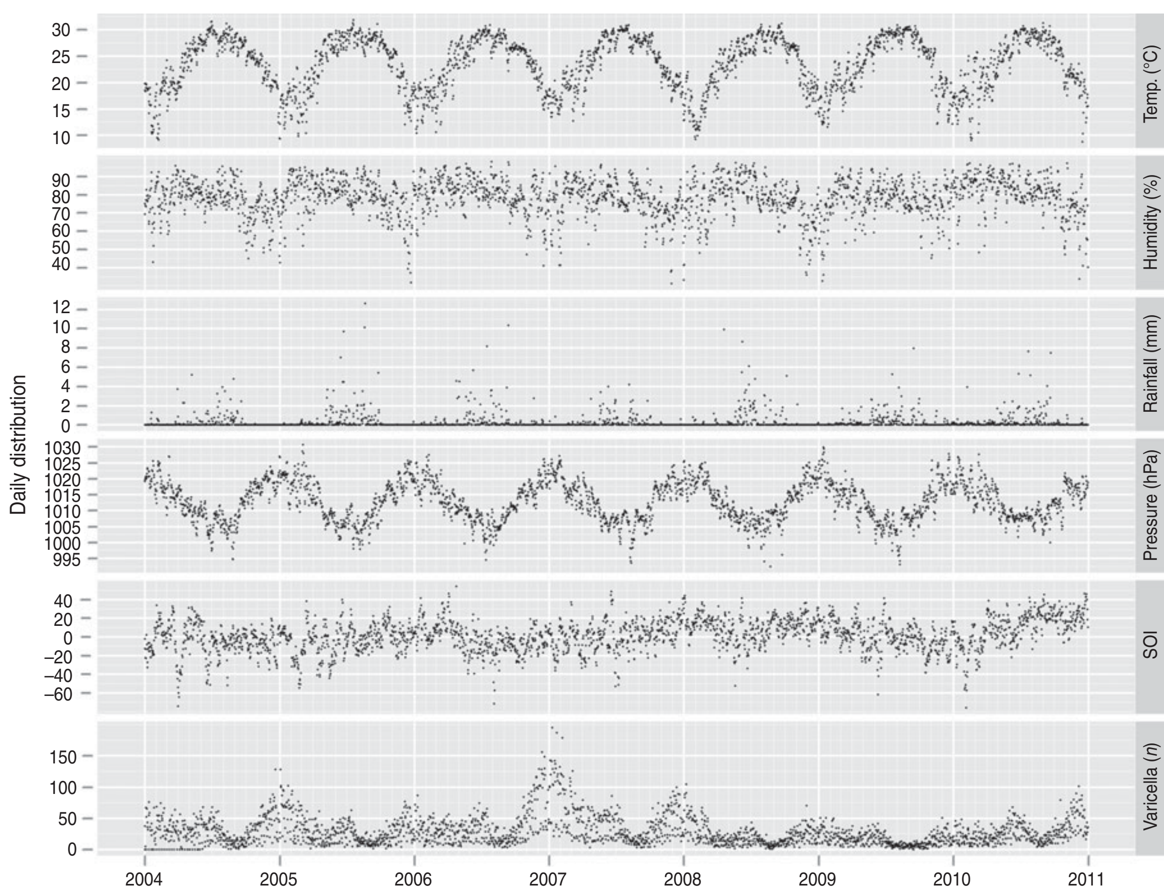


**Fig. 3.** Time-series of ambient temperature, relative humidity, rainfall, atmospheric pressure, Southern Oscillation Index (SOI) and reported paediatric varicella notifications in Hong Kong, 2004–2010.

## DISCUSSION

This is the first case-crossover study quantifying the short-term effects of meteorological factors on paediatric varicella notifications in Hong Kong. In the current study, the time-stratified case-crossover analysis found that both local meteorological variations (in particular temperature, rainfall and atmospheric pressure) and regional climatic variability measured by the SOI were significantly associated with daily paediatric varicella notifications in Hong Kong. Ambient temperature, rainfall, pressure, and SOI were positively associated with daily paediatric varicella notifications, while relative humidity was negatively associated with daily paediatric varicella notifications.

Our result that temperature was associated with elevated varicella notifications is consistent with previous findings. Wu *et al.* [7] showed that season and temperature were significantly related to increased varicella incidence in Taiwan, while Kokaze *et al.* [8]

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Table 3. *Spearman's correlations between daily weather variables in Hong Kong, 2004–2010*

| | Temperature | Humidity | Rainfall | Pressure | SOI |
|---|---|---|---|---|---|
| Temperature | 1·00 | | | | |
| Humidity | 0·10 | 1·00 | | | |
| Rainfall | 0·16 | 0·67 | 1·00 | | |
| Pressure | −0·84 | −0·37 | −0·38 | 1·00 | |
| SOI | −0·05 | −0·07 | −0·05 | 0·04 | 1·00 |

SOI, Southern Oscillation Index.
$P < 0.05$ for all values.

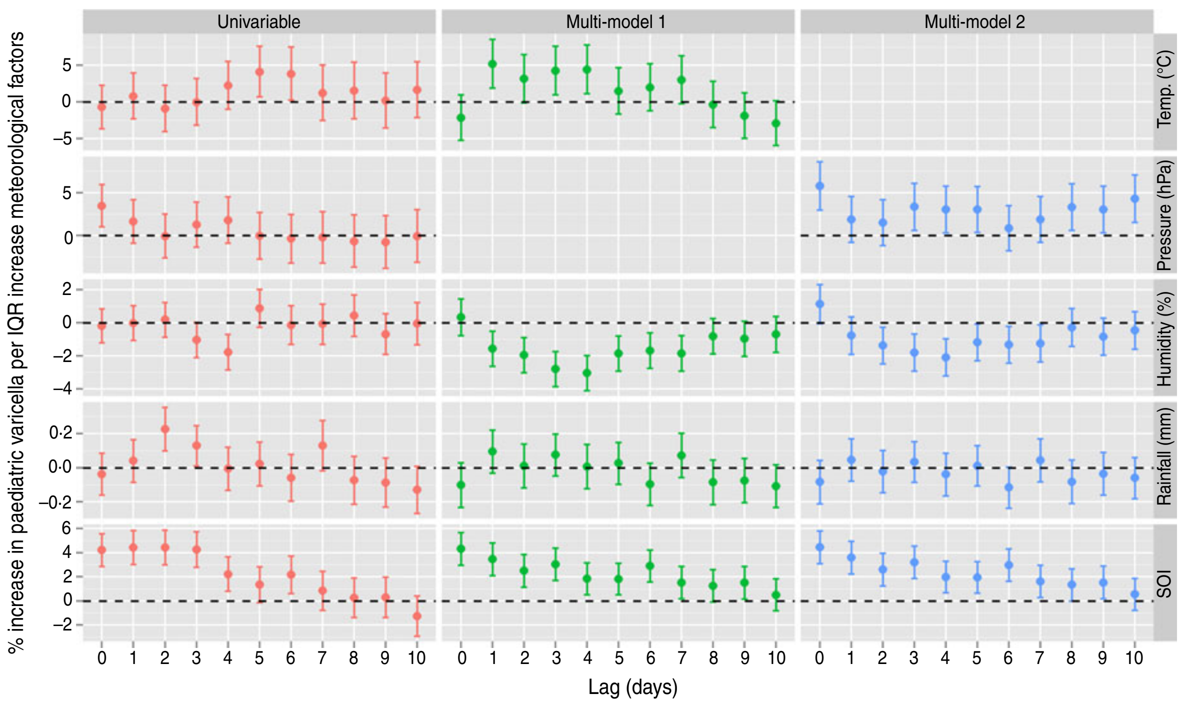


**Fig. 4** [*colour online*]. The univariable and multivariable analyses for the association between meteorological variables and reported daily paediatric varicella notifications in Hong Kong, 2004–2010 (the effect estimates were excess risk per IQR increase in the weather variables; two multivariable models were fitted: model 1 including temperature, rainfall, relative humidity, and SOI; model 2 including pressure, rainfall, relative humidity, and SOI.

demonstrated that the annual temperature variation affected the seasonal variations of varicella incidence in Japan. Previous studies have shown that *in vitro* VZV yield and point of maximum titre were dependent on temperature of incubation [28, 29]. It can be expected that the temperature also affects both VZV titre and *in vivo* activity. Varicella incidence has been reported to peak during cooler months in studies from India, Thailand, Sri Lanka and other countries [4–6]. It is possible that geographical variations, differences in weather conditions, as well as population characteristics could account for the discrepancy. On the other hand, our finding of negative association between relative humidity and varicella notifications was consistent with other studies [4, 30]. For example, varicella-associated hospital admissions have been reported to be twice as common in the cool, dry season compared to the hot monsoon period in Sri Lanka [31]. One of our previous studies in Hong Kong also demonstrated that lower relative humidity in cool seasons was associated with a higher number of paediatric varicella hospital admissions [3].

The findings of this study are interesting given the expected increasing influence of global climate change on the local weather conditions and transmission pattern of infectious diseases [32, 33]. In Hong Kong, negative SOI values are usually associated with El Niño conditions (dry and warm) and positive values

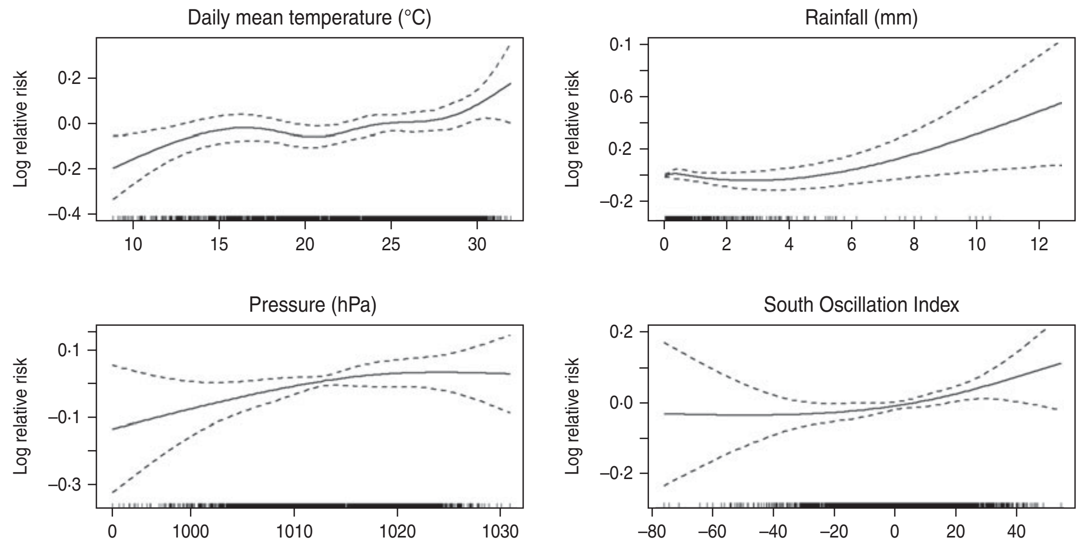


**Fig. 5.** Smoothing plots of daily weather variables against reported paediatric varicella notifications in Hong Kong.

with La Niña conditions (wet and cool) [34]. It is known that the SOI is a useful predictor for rainfall, with higher SOI values associated with higher rainfall. The current study found that rainfall, as well as the SOI, was positively associated with varicella notifications in Hong Kong.

VZV can be excreted from the respiratory tract or vesicles of varicella patients and disseminated into the environment via an aerosol route or airborne spread [35, 36]. However, the exact mechanism for the association between temperature, rainfall, atmospheric pressure, relative humidity and SOI with varicella notifications observed in this study remains unclear. With a lower relative humidity, air particles would be smaller and VZV could be suspended longer in the air and travel over a longer distance, thereby increasing transmission opportunity. In an arid environment, the chickenpox patients with drier skin could suffer from excessive itchiness where scratching could facilitate viral spread to the environment. In addition, it is possible that during hot seasons with high temperature, children tend to stay indoors with air-conditioning which in turn increases domestic transmission. Given the limited indoor space in Hong Kong, children may have a greater opportunity of close contacts between each other, hence facilitating varicella transmission. However, all these hypotheses warrant further research on the exact mechanisms involved.

There are a number of strengths in the present study. First, individual-level risk factors for varicella, such as vaccination status, living environment and behaviours, were inherently controlled for in the case-crossover analysis. Second, confounding effects due to time trends of exposure and effects were also adjusted with the time-stratified case-crossover study design. Third, instead of weekly or monthly data used in previous studies, we used daily varicella notifications and meteorological data, enabling temporal analysis at a finer resolution. Fourth, as one of the statutory notifiable infectious diseases in Hong Kong, it is compulsory for medical practitioners in both public and private sectors to report all varicella cases to the CHP via a centralized notification system. Our dataset was therefore reliable with a good representation of paediatric varicella cases in the whole Hong Kong population.

On the other hand, a few limitations should be noted when interperating findings from this study. First, it was based on the notification data from the CHP and thus underreporting was possible because children with mild disease symptoms might not seek medical attention. However, our notification dataset included varicella cases reported from various sources, ranging from healthcare systems, governmental departments, to schools and institutions, which could pick up the records of the patients with milder symptoms [3]. Second, the notification of varicella cases depended solely on the clinical features, without confirming the diagnosis by any microbiological or serological tests, hence resulting in potential misdiagnosis. However, varicella is considered to be an easily recognizable disease, even by laymen [2, 37]. For hospitalized patients, the diagnosis of varicella mainly relies on clinical presentation, not requiring further tests for confirmation. Third, it was assumed that the weather variables measured by the Hong Kong Observatory were uniform across the whole of Hong Kong. The measurement error for personal exposure may lead to bias in the estimated association; however, Hong Kong is a very small territory with linear dimension of only about 40 km in width and 30 km in length, and the weather data was believed to be representative of the whole of Hong Kong [38]. Fourth, the use of a case-crossover design ensured that non-temporally varying predictive variables for varicella notifications were automatically controlled for. However, residual confounding was still possible due to the temporally varying variables not adjusted in the current study, e.g. the temporal pattern of household ventilation. Fifth, without access to geographical data (e.g. residential or place of exposure), the potential association between geographical variation in weather and varicella notifications was not explored. The incorporation of geographical data could be an important enhancement to our current findings. It is important to note that varicella transmission is multifactorial [39, 40]; besides meteorological factors, other environmental and host factors may also play a role in the transmission of the disease. Our current study focused only on the meteorological factors and further studies to incorporate other information such as demographic factors, geographical data, population density, as well as behavioural data are warranted.

In conclusion, chickenpox remains an important public health issue in Hong Kong. Ambient temperature, air pressure, relative humidity and SOI might be important predictors of paediatric varicella incidence. Weather variables should be considered by health practitioners and public health policy makers in the prevention and control of this disease, especially in the context of global climate change.

## SUPPLEMENTARY MATERIAL

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0950268813002306.

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## DECLARATION OF INTEREST

None.

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