Forecasting influenza epidemics in Hong Kong using multiple streams of syndromic and laboratory surveillance data: abridged secondary publication

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KEY MESSAGES

1. This study provided an integrated framework to identify potential drivers of influenza transmission in terms of associations and the ability to forecast the intensity (attack rate and peak magnitude) and the peak timing of influenza epidemics in Hong Kong.
2. Ability to predict influenza epidemic outcomes in a timely manner is instrumental in assisting public health planning strategies and assessing the effects of interventions.

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Introduction

Forecasting influenza outbreaks is a challenging task because even two consecutive annual outbreaks of the same virus can have very different impacts. Furthermore, the seasonal characteristics of influenza differ between temperate and tropical locations. In Hong Kong, a sub-tropical city, influenza epidemics can occur at any time of year, with a peak in winter almost every year and a second peak in spring, summer, or autumn in many years.[1] The lack of real-time dynamics and characteristics of epidemics adversely affects public health planning. For example, hospitals may suddenly experience a surge in influenza cases without warning or adequate preparation.

We previously found that absolute humidity and ambient ozone were associated with influenza transmissibility in Hong Kong.[2] The comparative results of two diverse modelling frameworks could represent advances in the real-time forecasting (short-term and long-term) of influenza incidence (or attack rate), peak timing, and peak intensity in Hong Kong (Fig 1).[1] We aimed to forecast seasonal influenza transmission and the effects of extrinsic driving factors in Hong Kong. We hypothesised that (1) real-time forecasting could be improved by integrating multiple surveillance data streams concerning influenza transmissibility in Hong Kong and that (2) the inclusion of driver data from multiple streams plus their predicted associations with influenza transmission could improve forecast accuracy and reduce uncertainty. We also assessed the effects of public health and social measures for COVID-19 on influenza dynamics in Hong Kong.

Methods

We retrieved weekly records of the influenza-like illness (ILI) consultation rate and proportion of specimens testing positive for influenza virus from the Centre for Health Protection of Hong Kong for the period 1998 to 2020. We then estimated the ILI+ proxy, a measure of influenza virus activity in the community.[2] We also retrieved daily mean meteorological variables and pollutants from the Hong Kong Observatory and the Hong Kong Environmental Protection Department, as well as the timing of school holidays along with school closures in response to epidemics/pandemics in Hong Kong.

We first identified potential drivers of influenza transmissibility and their associations. Transmissibility was measured by the instantaneous reproduction number (R_t), defined as the mean number of secondary infections caused by a typical single infectious person at time t. We estimated R_t from daily ILI+ proxy using a simple branching process model. We used R_t to derive an alternative measure of transmissibility, the transmission rate (β_t), which was strongly influenced by susceptibility depletion. We performed regression analysis with R_t and β_t to investigate the association between influenza transmissibility and each driver (meteorological, pollutant-related, and social) in Hong Kong.[2,3]

Using a generalised linear model with a log-link function, we assumed that the ILI+ proxy followed a negative binomial distribution with expected ILI+ proxy $\lambda(t + k)$ for the following k weeks, with $k \in (0,1,2,3)$ at week t. We constructed possible predictive model variants by incorporating various

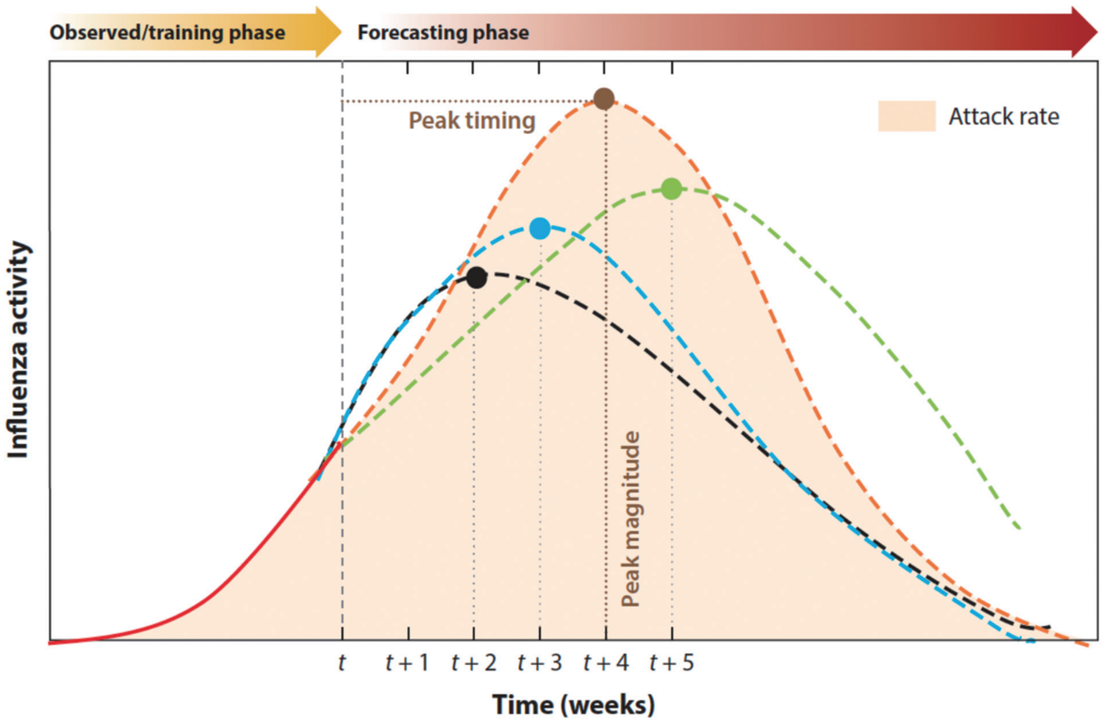

FIG 1. Forecasts of four different models in terms of peak timing, peak magnitude, and attack rate

combinations of drivers in the model, along with a periodic cubic spline basis in the base model. We conducted 10-fold cross-validation to assess model prediction performance for the period 2010 to 2019 (avoiding the 2009 swine flu pandemic) to select the best predictive model for short-term forecasting (1-4 weeks ahead) in 2020. Model variants were validated and ranked using weighted interval score, root mean square error, root mean square log error, mean absolute error, and mean rank. The model with the lowest weighted interval score was selected for further influenza forecasting beginning in the 3rd week of January 2020. We then constructed a predictive model for long-term forecasting (up to 52 weeks ahead) of influenza activity in 2020.

We constructed a general susceptible-vaccinated-exposed-infectious-recovered-susceptible compartmental model, which included seasonal vaccination, waning immunity, population demography, sociodemographic factors, and seasonal factors. We hypothesised that the transmission rate $\beta(t)$ is modulated by drivers such as seasonality (using a spline or standard periodic function), climatic factors, pollutants, sociodemographic factors, and noise driven by other extrinsic factors. Model variants with various combinations of drivers were constructed, as were their effective forms of association with $\beta(t)$ identified in the exploratory data analysis. We developed a problem-based inferential framework using the Markov chain Monte Carlo method to obtain the joint posterior distribution of model parameters with the adaptive Metropolis-Hastings algorithm, which was implemented with four chains; each chain included 100 000 iterations with a burn-in period of 30 000 iterations. Forecasting performances of the different models were determined by temporal cross-validation using the inferential approach with different training periods: 8, 6, and 4 years. The model with the lowest mean rank was selected for further forecasting with uncertainty (95% prediction interval [PI]) beginning in the 3rd week of January 2020.

The impact of public health and social measures for COVID-19 pandemic on seasonal influenza transmission was significant.[4] In Hong Kong, such measures were well-established by the 3rd week of January 2020. We compared the long-term forecasts of influenza cases and observed cases in 2020 to quantify the impact of the COVID-19 pandemic. We evaluated attack rates and peak magnitude for the winter-spring period (December 2019 to March 2020), the summer period (May 2020 to September 2020), and the whole 2019/20 season (October 2019 to September 2020); these periods corresponded to winter, summer, and seasonal epidemics,

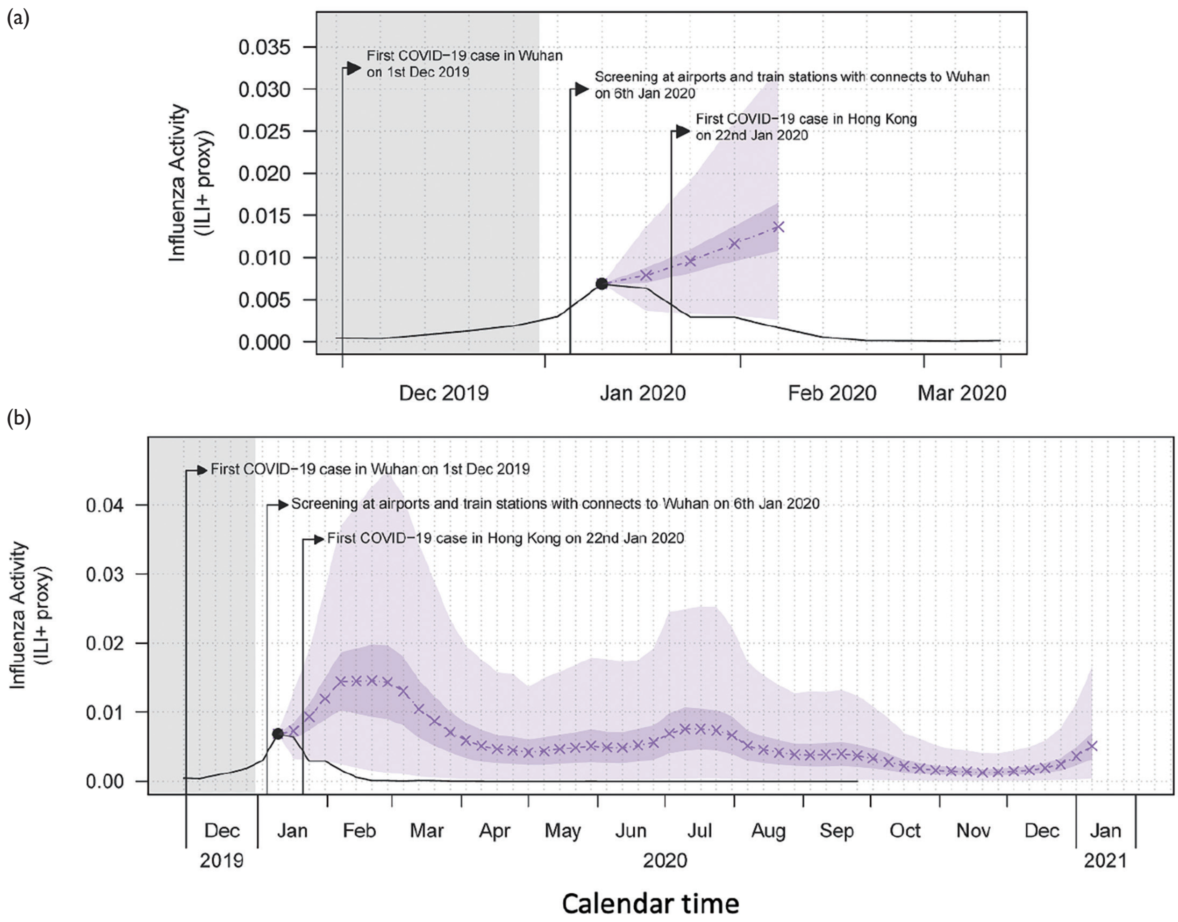

FIG 2. Statistical framework–based (a) short-term (1-4 weeks ahead) and (b) long-term (1-52 weeks ahead) forecasts beginning in the 3rd week of January 2020 in Hong Kong
Abbreviation: ILI+, influenza-like illness positive

respectively.[3] This mechanistic framework enabled fitting the observed influenza data from 2020 and quantifying the impact on transmissibility by evaluating reductions in transmission rate and number of cases related to the public health and social measures for COVID-19.

Results

Influenza viruses circulated annually, with peaks during January to March and July to September in most years. Over the entire study period of 1300 weeks, 1056 (81%) weeks were identified to be influenza epidemic, with 58 distinct influenza epidemics (types/subtypes). We observed changes in the seasonal patterns of annual influenza activity before, during, and after pandemics and epidemics (including swine flu pandemic in 2009, SARS epidemic in 2003, and COVID-19 pandemic). We found nonlinear associations of influenza transmissibility (R_t and β_t) with mean absolute humidity (U-shaped) and ambient ozone (negative power form) in Hong Kong. The U-shaped association with absolute humidity partially mimicked the winter and summer epidemics in sub-tropical areas. These extrinsic drivers were significant and could explain up to 18% of variation in the transmissibility.

The mechanistic framework–based forecast was comparable with the statistical framework–based forecast (Figs 2 and 3). Beginning in the 3rd week of January 2020, the short-term forecast (1-4 weeks ahead) of incidence reached 1.4% (95% PI=0.3%-3.4%) in the 1st week of February. Under the counterfactual scenario without the effects of public health and social measures for COVID-19, the long-term forecast suggested that a winter-spring influenza epidemic with a peak on the 16th to 22nd of February 2020 could have appeared, followed by a summer epidemic with a smaller peak on the 19th to 25th of July 2020. The winter-spring epidemic (December 2019 to March 2020) would have peaked with a weekly incidence of 1.5% (95% PI=0.2%-4.4%) and an attack rate of 14.4% (95% PI=9.4%-20.9%). In contrast, the summer epidemic (May 2020 to September 2020) would have had a lower incidence

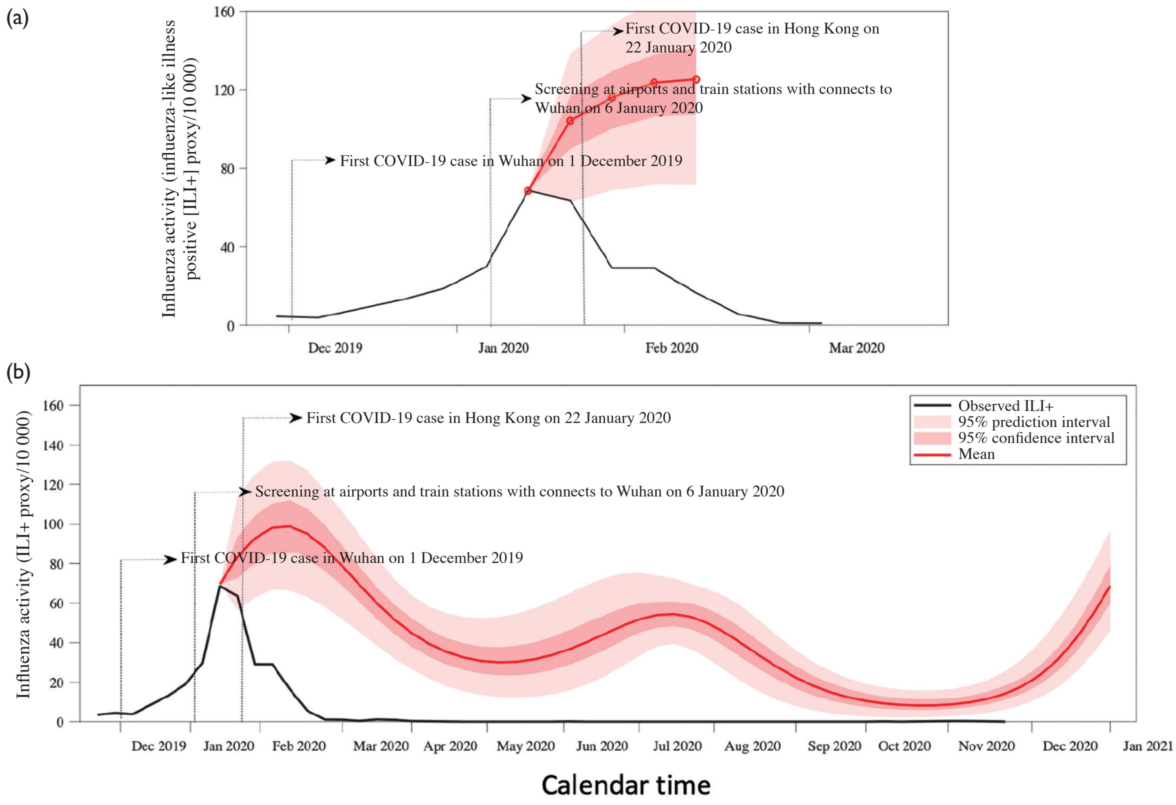

FIG 3. Mechanistic framework–based (a) short-term (1-4 weeks ahead) and (b) long-term (1-52 weeks ahead) forecasts beginning in the 3rd week of January 2020 in Hong Kong

and attack rate. The overall attack rate in the 2019/20 season was estimated to be 27.7% (95% PI=21.0%-35.7%), whereas the median attack rate was 23.7% (range, 11.5%-36.8%) between 2011/12 and 2018/19. The mechanistic framework–based forecast was more robust, with smaller uncertainty bounds (Figs 2 and 3).

Using the statistical framework, COVID-19 public health and social measures potentially led to a reduction of 87.9% (95% PI=84.1%-90.6%) in attack rate during the 2019/20 season. Similarly, the mechanistic framework estimated a reduction of 50.0% (95% credible interval=41.8%-59.9%) in transmissibility.

Discussion

Unlike temperate regions where influenza epidemics show strong seasonality during the winter period, tropical and sub-tropical regions show year-round influenza activity.[1] Thus, it is challenging to forecast influenza activity in tropical and sub-tropical regions. We found that both the statistical and mechanistic frameworks were comparable in terms of forecasting attack rate, peak magnitude, and peak timing in a timely manner. This finding is instrumental in assisting public health planning strategies.

Ambient ozone concentrations and school holidays/closures were significant drivers of short-term forecasts, whereas absolute humidity (with a U-shaped association) was the most important driver of long-term forecasts.[3] This indicated that low absolute humidity was associated with influenza transmission in temperate regions,[1] whereas low and high absolute humidity were associated with influenza transmission in tropical regions.[3] The negative associations between ozone concentration and influenza activity/transmissibility could explain the enhanced immunity against influenza virus infection observed under high ozone concentrations.[2]

The 3rd week of January 2020 was chosen as the first week of forecasting because there was no sustained influenza activity during that week in Hong Kong. We forecasted an attack rate of 27.7% in the 2019/20 season, which is close to the median attack rate of 23.7% in preceding seasons (2011/12 to 2018/19). Importantly, our frameworks could forecast outcomes in real time, as demonstrated in the annual national-level influenza forecasting competition "Predict the Influenza Season Challenge" at the United States Centers for Disease Control and Prevention.[5]

There were limitations in the present study.

First, the ILI+ proxy parameter was influenced by health-seeking behaviour and laboratory surveillance capacity, which could have been suppressed during the COVID-19 pandemic. Second, we could not stratify the analysis according to influenza virus subtype because no such information was available. Third, evolution (antigenic drift and shift) of influenza virus over time was not considered.

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Disclosure

The results of this research have been previously published in:
1. Ali ST, Cowling BJ, Wong JY, et al. Influenza seasonality and its environmental driving factors in mainland China and Hong Kong. Sci Total Environ 2022;818:151724.
2. Ali ST, Cowling BJ. Influenza virus: tracking, predicting and forecasting. Annu Rev Public Health 2021;42:43-57.

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