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Modelling the Measles Outbreak at Hong Kong International Airport in 2019: A Data-Driven Analysis on the Effects of Timely Reporting and Public Awareness

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Background: Measles, a highly contagious disease, still poses a huge burden worldwide. Lately, a trend of resurgence threatened the developed countries. A measles outbreak occurred in the Hong Kong International Airport (HKIA) between March and April 2019, which infected 29 airport staff. During the outbreak, multiple measures were taken including daily situation updates, setting up a public enquiry platform on March 23, and an emergent vaccination program targeting unprotected staff. The outbreak was put out promptly. The effectiveness of these measures was unclear.

Methods: We quantified the transmissibility of outbreak in HKIA by the effective reproduction number, $R_{\mathrm{eff}}(t)$, and basic reproduction number, $R_0(t)$. The reproduction number was modelled as a function of its determinants that were statistically examined, including lags in hospitalization, situation update, and level of public awareness. Then, we considered a hypothetical no-measure scenario when improvements in reporting and public enquiry were absent and calculated the number of infected airport staff.

Results: Our estimated average R_0 is 10.09 (95% CI: 1.73−36.50). We found that $R_0(t)$ was positively associated with lags in hospitalization and situation update, while negatively associated with the level of public awareness. The average predicted basic reproduction number, r_0, was 14.67 (95% CI: 9.01−45.32) under the no-measure scenario, which increased the average R_0 by 77.57% (95% CI: 1.71−111.15). The total number of infected staff would be 179 (IQR: 90−339, 95% CI: 23−821), namely the measure induced 8.42-fold (95% CI: 0.21−42.21) reduction in the total number of infected staff.

Conclusion: Timely reporting on outbreak situation and public awareness measured by the number of public enquiries helped to control the outbreak.

Keywords: measles, outbreak, reproduction number, statistical modelling, public awareness, airport

Introduction

Measles is a highly contagious viral disease, and it transmits through air droplets. It once brought numerous deaths, averagely 2.6 million deaths per year,[5] in particular among children in the pre-vaccine era and in developing countries nowadays.[6,7] Although the introduction of vaccines in mid-1960s substantially reduced the number of incidences, measles remains a burden worldwide due to <100% effectiveness of the vaccine and low vaccination coverage and high transmissibility.[6] Globally 110,000 measles deaths

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occurred in 2017, and most of them were under the age five.[5] In the last decade, measles infections in Hong Kong were at low level under local mandatory immunization programme, only sporadic imported cases were reported. The vaccination coverage among children (aged from 2 to 5 years) has remained at 95% since 2005, which was higher than the global average 83% (since 2000).[8] The annual number of cases remained less than 50 for the last 10 years before 2019, see Figure 1.[3] However, a measles outbreak occurred in Hong Kong International Airport (HKIA) from March to April 2019.[9,10]

There were total of 58 cases confirmed between March 1 and April 30.[1,11] Among them, 29 were staff of the HKIA who works at the airport, 28 were other individuals, including 5 cases under age 16, and 1 imported case. Zero death case was recorded.[12] For all cases, epidemiological investigation and relevant contact tracing after the hospital-visit (or admission) were conducted. Over roughly a half (50.9%) were the airport staff, 72.4% of all cases sought doctor or medical consultation within 3 days after symptom onset. Among these cases, 51.7% (30 out of 58) sought for doctor consultation at least one day before hospital-visit (or admission). There were 65.5% of the cases were reported (by news press release) within 3 days after hospital admission, whereas 10.3% were reported 7 days or more after admission. The outbreak situation updates were released by the Centre for Health Protection (CHP) in Hong Kong on a daily basis after the diagnosis of the first case. A public enquiry hotline platform was set up for measles-related enquiries on March 23. The emergency vaccination program was launched for airport staff who aged 52 years or younger, did not have two-dose vaccination and showed seronegative, on the same day. Unexpectedly, the outbreak stopped before vaccine-induced immunity (with a 14-day lag post-vaccination)[13] should have taken effect. We suspected that the public awareness and series of emergency response activities could have contributed to the immediate cease of the outbreak.

Objective

In this study, we reconstructed the time-varying basic reproduction number, $R_0(t)$, of measles in this outbreak based on the surveillance data. We tested the association between $R_0(t)$ and three potential determinants including the lags in hospital admission, situation updates, and the cumulative number of public enquiries (as a measure of the level of public awareness). We modelled $R_0(t)$ as a function of these factors. We predicted and simulated the transmission dynamics of this outbreak under a hypothetical scenario that such measures were absent. We evaluated the number of infected staff reduction due to these measures.

Materials and Methods

We modelled the transmission dynamics of the measles outbreak in HKIA retrospectively.

Measles Surveillance Data

The aggregated monthly number of measles cases from 2009 to 2019 were collected from the Centre for Health Protection (CHP) in Hong Kong.[3] The cases time series was shown in Figure 1.

We downloaded the information of all measles infected staff from the online press release of the CHP.[1] The information and data included the number of infected staff that were laboratory confirmed with respiratory specimens, the timeline from onset of rash or fever, the number of airport staff vaccinated and the daily number of enquiries received by CHP.[1] The infected staff time series are shown in Figure 2A. The preliminary outbreak investigation was carried out in,[9] and the time series plot with both infected local residents and airport staff can also be found in.[2]

Susceptibility of Airport Staff

We denoted the proportion of susceptible airport staff among all airport staff at time t as $S(t)$, ranging from 0 to 1. According to the pilot report conducted by CHP in March 2019,[1] 86% of all staff were seropositive against measles prior to the airport immunization program (see https://www.info.gov.hk/gia/general/201903/31/P2019033100734.htm for the details), which means $S(0)$ = (1 − 86% =) 14%, ie, the initial susceptibility was 14%. More detailed information can be found in Supplementary Information S1. Referring to the official report of the HKIA,[4] there were totally 73,000 HKIA staff. We calculated the cumulative proportion of staff vaccinated (since March 23, 2019) over time. For simplicity, we assume a 100% vaccine effectiveness and a 14-day delay allowing the immunity to take effect. Thus, $S(t)$ was approximated as [(1–86%) – (cum. # of vaccinated)/73,000] × 100%, with a 14-day lag. The calculated $S(t)$ was shown in Figure 2B.

Estimating the Reproduction Numbers

We considered and reconstructed two types of time-varying reproduction numbers in this work, and they are

- effective reproduction number, $R_{eff}(t)$, and
- basic reproduction number, $R_0(t)$.

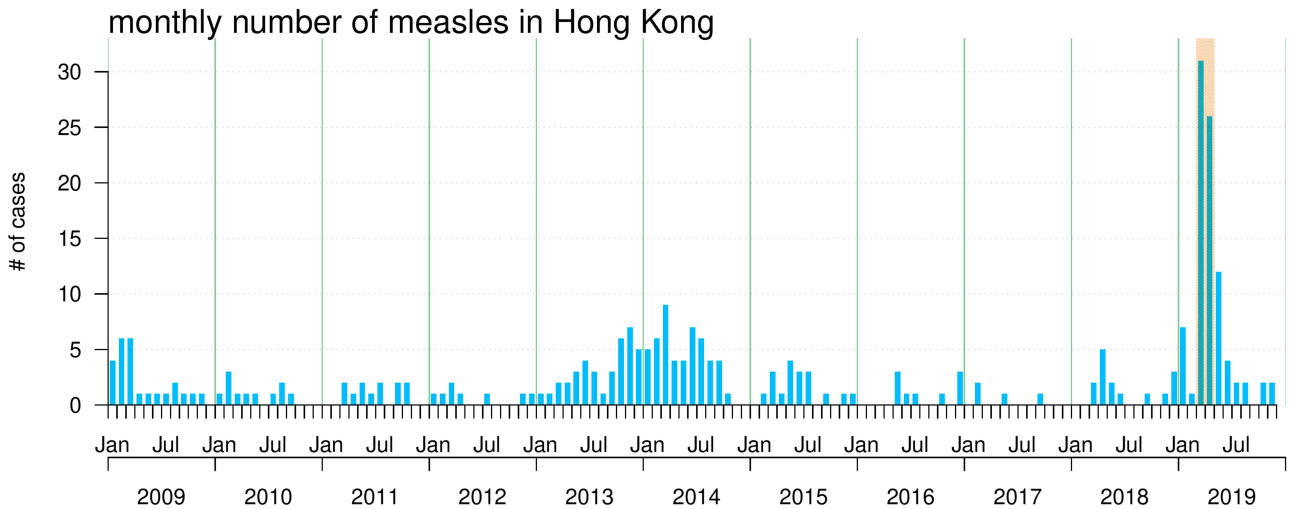

Figure 1 The monthly number of measles cases in Hong Kong from January 2009 to December 2019. The orange area highlighted the period from March to April 2019 when the outbreak in the airport occurred.

Effective Reproduction Number

In this study, we focused on the outbreak within the HKIA. This is implemented by considering the other (non-airport staff) cases had limited or negligible contribution to the measles transmission among airport staff. Airport is relatively isolated from the general population, and it is less likely that an infected person with symptom would travel or pass virus to a staff than an infected staff passes virus to his/her co-workers. Hence, different from the previous study,[14] the reproduction numbers studied in this work are defined among airport staff, namely staff-specified reproduction number. More detailed justification can be found in Supplementary Information S2, and the limitation of this setting can be found in the discussion.

The instantaneous transmissibility of the airport measles outbreak can be quantified by the time-varying effective reproduction number, denoted by $R_{\mathrm{eff}}(t)$, which is also known as the instantaneous reproduction number and sometimes denoted by R_t. We estimated $R_{\mathrm{eff}}(t)$ by the approach proposed by Wallinga and Teunis[15] that used the serial interval (SI) to calculate the transmission ability over a (short) period of time. The SI was defined by the time between the timing of symptom onsets of two successive cases in a chain of transmission.[16] Following,[17–19] the $R_{\mathrm{eff}}(t)$ can be expressed as a ratio of $C(t)$ over $\int_0^\infty w(k)C(t-k)\mathrm{d}k$. Here, the $C(t)$ was the numbers of infected airport staff, and time t represents the rash onset date. The function $w(\cdot)$ is the distribution of the SI of measles. According to the Centers for Disease Control and Prevention (CDC),[13] "measles may be transmitted from 4 days before to 4 days after rash onset"; and "from exposure to rash onset averages 14 days (7–21 days)". Thus, measles cases are unlikely infectious in the first (7 – 4 =) 3 days. The infectiousness of a patient is a function of time since infection and proportional to the distribution function of the serial interval, $w(\cdot)$, if we set the timing of infection of the primary case as the time zero of $w(\cdot)$ and assume the generation interval equals the serial interval. Following previous works,[13,20] we define $w(\cdot)$ as a Gamma distribution with a mean of 8.7 days, a SD of 2 days and a time delay, ie, time shift, of +3 days to account for the latent period, thus the mean of SI is (8.7 + 3 =) 11.7 days. The 95% credible intervals (CI) of $R_{\mathrm{eff}}(t)$ were estimated based on the Gamma priors of each $R_{\mathrm{eff}}(t)$.[18,21,22] The **R** package '*Epiestim*' was adopted for estimating $R_{\mathrm{eff}}(t)$.[15,22] The estimated $R_{\mathrm{eff}}(t)$ series are shown in Figure 2C.

Basic Reproduction Number

The $R_0(t)$ is an intrinsic feature of the diseases which is not dependent on the level of susceptibility, but related to other pathogenic factors, external (meteorological) factors, hosts' behavioral factors and social distance, etc. We calculated $R_0(t)$, and also modelling its associations with other factors.

Following the theoretical epidemiology of the infections disease,[23–25] we quantified the transmissibility of measles with the time-varying basic reproduction number, $R_0(t)$, as a ratio of $R_{\mathrm{eff}}(t)$ over $S(t)$, ie, $R_0(t) = R_{\mathrm{eff}}(t)/S(t)$. Here, $S(t)$ was approximated by using the number of vaccine staff. The estimated $R_0(t)$ series are shown in Figure 2D.

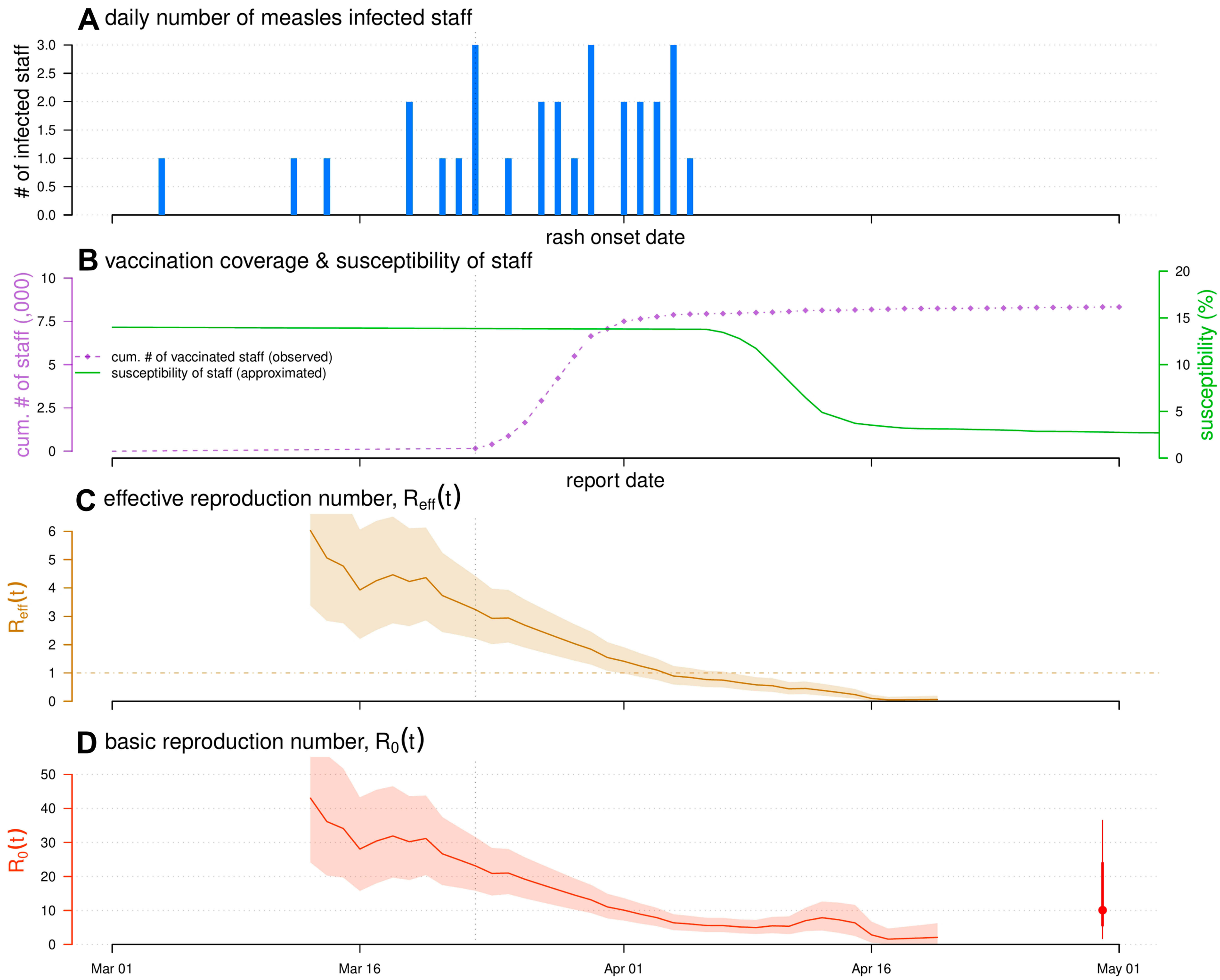

Figure 2 The epidemiological features of the measles outbreak in HKIA from March to April 2019. Panel (**A**) shows the daily number of infected staff sorted by the rash onset date. Panel (**B**) shows the cumulative number of staff vaccinated (purple dotted line) since March 01, 2019, and the approximated susceptibility ($S(t)$, green line) of all staff. The measles vaccination program for airport staff was launched on March 23, 2019, and it was indicated by the vertical dashed line. Panel (**C**) shows the estimated effective reproduction number, $R_{\text{eff}}(t)$. The horizontal dashed line marks the level of $R_{\text{eff}} = 1$. Panel (**D**) shows the basic reproduction number, $R_0(t) = R_{\text{eff}}(t)/S(t)$. In panel (**D**), the dot and bar at the right-hand side summarized the mean and 95% percentile of $R_0(t)$ respectively. In panels (**C**) and (**D**), the solid line represents the estimated mean, and the shaded area represents the 95% confidence interval (CI).

Potential Determinants of Measles Transmission in the Airport Outbreak

We explored the potential determinants of the measles transmission that could affect the outbreak, which will be further considered in the modelling analysis. For each individual measles infected staff, we consider the timeline following path.

$$\text{Infected} \rightarrow \text{Prodrome onset} \rightarrow \text{Hospital visit and admitted} \rightarrow \text{Lab. confirmed} \rightarrow \text{Press released} \rightarrow \text{Recovered.} \tag{1}$$

Here, in path (1), the "press release" represented the official outbreak situation update regarding the newly confirmed measles cases that was publicly released by CHP, and all situation reports can be found in.[1]

Hospital Admission Lag

A timely hospital admission was likely to prevent continuous spread of measles from a primary infected staff in the airport. The lag of hospital admission was measured by the time interval between the prodrome onset and the date of hospital admission of each infected staff. It is the time interval between "prodrome onset" and "hospital visit & admitted" in the above path.[1] For example, one case started to show prodrome(s) on March 23, and he/she was admitted to hospital (for treatment) on March 26. Thus, the delay of hospital admission was (26 – 23 =) 3 days.

Reporting lag

For each infected staff, the lag of reporting was measured by the time interval between the hospital admission and the date of the outbreak situation update that reported the same infected staff. It is the time interval between "hospital visit and admitted" and "Press released" in path (1). For example, one measles case was admitted by hospital (for treatment) on March 24, and he/she was reported by situation report released on March 28. Thus, the reporting lag was (28 – 24 =) 4 days. According to the CHP documentation,[1] all confirmed measles cases in Hong Kong between March and April 2020 have been hospitalized.

Level of Public Awareness

We proposed to use the cumulative number of public enquiries (via a hotline) since March 23, 2019, as a proxy to measure the level of public awareness of the measles outbreak in the airport. It is commonly accepted that high level of public knowledge on the risk of infection would help stop the spread of infectious disease.

Time series plots of the aforementioned potential determinants can be found in Supplementary Information S3.

Associating Basic Reproduction Number with Key Determinants

In order to model the possible impacts of the three potential determinants on $R_0(t)$, we first tested the hypothesized "causality" between $R_0(t)$ and potential determinants, ie, hospital admission lag, reporting lag and public awareness, and selected the key determinants that were likely to affect the measles transmission in the airport. Then, we modelled the $R_0(t)$ as a mathematical function of the selected key determinants, ie, the predictor variables in the model, by using multivariate regression model. We use the trained regression model to predict $R_0(t)$ by varying the value of determinants for further simulation analysis.

Selecting the Determinants by Granger Causality Test

To rule out possibility of a spurious association, we employed both pairwise and multivariate Granger causality tests (GCT) to evaluate the hypothesized "causality" between $R_0(t)$ and potential determinants.[26,27] The GCT was used to test the likelihood of causal relationship. We conducted the GCTs with the order determined by the partial autocorrelation functions (PACF) of $R_0(t)$. In the GCT sense, a factor Y against X is significant means that factor X is likely to be relevant in predicting Y significantly. Then, the hypothesized causality between X and Y cannot be rejected.[28] In other words, a factor Y against X is significant in GCT indicates that factor X is likely to contain additional information other than Y itself, so that X has significant contribution in predicting Y.

With a significant, p-value < 0.05, GCT outcome between $R_0(t)$ and a potential determinant, we selected this determinant as the key determinant, and included in the further modelling analysis. Otherwise, one potential determinant would be excluded from our consideration with insignificant GCT outcome.

Multivariate Regression Model

The $R_0(t)$ was modelled as a mathematical function of the selected key determinants by using multivariate regression model.[14,29–32] Since only the determinants with significant GCT outcome can be included in the regression model, the regression coefficients (of each predictor), denoted by β, were also controlled by the significance levels of GCTs. We denoted p_1, p_2 and p_3 as the p-values of the GCTs between $R_0(t)$ and the three determinants, ie, hospital admission lag (X_1), reporting lag (X_2) and public awareness (X_3), respectively. Then, the multivariate regression model was given in Eqn (2).

$$\mathbf{E}[\log R_0(t)] = \beta_1(p_1)X_1(t) + \beta_2(p_2)X_2(t) + \beta_3(p_3)X_3(t) + \beta_0 \tag{2}$$

Here, the E(·) represented the expectation. The β_i is the regression coefficient for the i-th variable, X_i, for the index i = 1, 2 or 3. The $\beta_i(p_i)$ was forced to be 0 if p_i is larger than or equal to 0.05. If $p_i < 0.05$, $\beta_i(p_i) = \beta_i$ that was a constant regression coefficient to be estimated. The β_0 denotes the interception term.

We used the data in Figure 2D for $R_0(t)$ and in Figure S1 for the X_1, X_2 and X_3 to fit the regression model and estimate the β_is by using the standard ordinary least squares (OLS) approach. For the convenience in the further simulation in the next section, we denoted the estimated value of β_i by b_i for the index i = 0, 1, 2 or 3.

The **R** function "*lm*()" was adopted for fitting the regression model and estimating the β_is.

A hypothetical scenario without timely reporting or public enquiry

We intended to repeat transmission dynamics of the measles airport outbreak under a scenario that there was lack of improvement in reporting and public enquiry. In our regression framework in Eqn (2), the hypothetical scenario could be achieved by fixing the reporting lag (X_2) and level of public awareness (X_3) at the values at the early stage of the airport outbreak. Therefore, we fixed $X_2(t)$ to be 6 days, ie, the reporting lag on March 23, and $X_3(t)$ to be 0 for time t from March 23 to April 30. For the sake of convenience, we denoted the new series of "X_2(t)" by $x_2(t)$, and the new series of "X_3(t)" by $x_3(t)$. We kept the values of $x_2(t)$ and $x_3(t)$ before March 23 unchanged, ie, $x_2(t) = X_2(t)$ and $x_3(t) = X_3(t)$ for t prior to March 23. Please also note that due to the cumulative public enquiry was 0 prior to March 23, $x_3(t) = X_3(t) = 0$ for t prior to March 23. For t from March 23 to April 30, we have $x_2(t) = 6$ days and $x_3(t) = 0$. While the reporting lag and public awareness were changed to mimic the "what-if" scenario, the series of $X_1(t)$ were unchanged.

We predicted (or reconstructed) the basic reproduction number under this scenario by using the fitted regression model.[2] We denoted the predicted basic reproduction number by $r_0(t)$, and thus it could be modelled as in Eqn (3).

$$\mathbf{E}[\log r_0(t)] = b_1X_1(t) + b_2x_2(t) + b_3x_3(t) + b_0 \quad (3)$$

Here, b_is were the estimated regression parameters, β_is, by fitting Eqn (2) for the index i = 0, 1, 2 or 3. By the nature of OLS, the log(r_0) followed a normal distribution, and thus $r_0(t)$ followed a log-normal process that determined by the observations of $X_1(t)$, assigned values of $x_2(t)$ and $x_3(t)$ as well as the estimated distribution of b_is.

With $r_0(t)$ predicted by using Eqn (3), we could further calculate the effective reproduction number under this scenario, denoted by $r_{\text{eff}}(t) = r_0(t)\cdot S(t)$. Given $S(t)$ was a series, it was obvious that $r_{\text{eff}}(t)$ followed a similar log-normal process that was derived from the same process of $r_0(t)$.

Simulating the number of infected staff under the hypothetical scenario

With predicted values of $r_{\text{eff}}(t)$, the epidemic curve could also be predicted (reconstructed) by using the equation of $R_{\text{eff}}(t)$ backwardly. We simulate this renewable transmission process started at March 24 and ended at April 30. In other words, we calculate $R_{\text{eff}}(t)$ with $C(t)$ and $w(t)$ given, and thus we may simulate the number of cases, $c(t)$, given $r_{\text{eff}}(t)$ and $w(t)$. Here, we denoted the simulated daily number of infected staff by $c(t)$ for the day t. Then, $c(t) = C(t)$ for t on or before March 23, but $c(t)$ was to be simulated for t after March 24, where $C(t)$ represented the observed daily number of infected staff. The "cutoff" date was fixed to be March 23, and the reason is that the public enquiry platform was set up on the same day. Hence, $c(t)$ for t after March 24 was given in Eqn (4).

$$c(t) \doteq r_{eff}(t)\int_0^{\infty} w(k)c(t-k)dk \quad (4)$$

Here, $w(\cdot)$ is the distribution of the measles SI defined earlier. We generated 10,000 random samples of $r_{\text{eff}}(t)$ from the associated log-normal process to account for the estimation uncertainty. Thus, we simulated the renewable transmission process in Eqn (4) for 10,000 times with each $r_{\text{eff}}(t)$ samples. In accounting for the observational (or measuring) noises, we further allowed a Poisson-distributed perturbation at every time step of Eqn (4). Henceforth, we calculated the simulation mean of the 10,000 $c(t)$ series and treated 95% percentiles as the 95% confidence interval (CI).

We summarized the notations used in this study in Table 1.

Results and Discussion

Figure 1 shows the time series of monthly number of measles cases for the past 10 years before 2019. We

Table 1 Summary Table of the Notations

Notation	Description	Remarks	Sources
$C(t)$	daily number of infected staff	observed	Surveillance
$c(t)$	daily number of infected staff	observed and predicted	surveillance and Eqn (4)
$w(k)$	distribution of SI	from previous studies	referenced
$R_{\text{eff}}(t)$	effective reproduction number	estimated	$C(t)\Big/\int_0^{\infty} w(k)C(t-k)\mathrm{d}k$
$r_{\text{eff}}(t)$	effective reproduction number	predicted or reconstructed	$r_0(t)\cdot S(t)$
$S(t)$	susceptibility of staff	approximated	cum. staff vaccinated
$R_0(t)$	basic reproduction number	estimated	$R_{\text{eff}}(t)/S(t)$
$r_0(t)$	basic reproduction number	predicted or reconstructed	Eqn (3)

observed the incidence number in March and April 2019, during the airport outbreak, was remarkably higher than other months. Figure 2A shows the time series of daily number of measles infected airport staff, $C(t)$ in Eqn (1) from March to April 2019. The number of infected staff increased in March, peaked around April 1, and decreased to zero by April 5. Figure 2B shows the cumulative number of vaccine staff since March 23, and the approximated susceptibility, $S(t)$. It appeared that $S(t)$ remained at the initial level, ie, 14% before vaccine programme, until April 6, which was after the end of airport outbreak on April 5. Surely the vaccination program was effective in reducing $S(t)$, see Figure 2B, it was not soon enough to bring immediate stop of the outbreak in HKIA. Hence, it indicated that the control of this outbreak was unlikely owe to the vaccine programme, though the vaccination will develop sufficiently high herd immunity and protect the staff from the risk of infections in the (near) future, ie, next few years. Therefore, we considered the public awareness and series of emergency response activities might contribute to the immediate stop of the outbreak in HKIA.

Figure 2C shows the estimated $R_{\text{eff}}(t)$ series of the outbreak in airport, which decreased below 1 around April 1. The R_{eff} at the early stage of the outbreak was estimated of 6.03 (95% CI: 3.38−9.30). Figure 2D shows the calculated $R_0(t)$ series, which was estimated of 43.09 (95% CI: 24.16−66.44) at the early stage of the outbreak and consistent with previous study.[7] The average R_0 was estimated of 10.09 (95% CI: 1.73−36.50) during the entire period of the outbreak. In the first week of April, when $S(t)$ remained at 14%, the $R_0(t)$ decreased from 10 to 6, which brought $R_{\text{eff}}(t)$ decreased below 1, and thus had the outbreak under control. Both $R_{\text{eff}}(t)$ and $R_0(t)$ presented downward trends, and the outbreak in HKIA would stop eventually.

The hospital admission lag and situation update (ie, reporting) lag showed decreasing trends, see Fig S1(a) and S1(b). The decreasing in these two lags implied the improvement in the timely healthcare service and reporting efforts during the outbreak in HKIA. The cumulative public enquiries were shown in Fig S1(c), which measured the level of public awareness of the risk of the outbreak in the airport. We tested the hypothesized "causality" between $R_0(t)$ and these three potential determinants, ie, hospital admission lag (X_1), reporting lag (X_2) and level of public awareness (X_3, measured by cumulative public enquiries). The GCT results were all significant, ie, p-values < 0.05, for all three determinants, and thus they were all included in the regression model. The significant GCT results implied the likelihood of the causality between the measles transmission, in terms of R_0, in HKIA and the three key determinants.[26,32] Caution should be taken when interpreting these causalities, given the nature of this data-driven study and relatively short time interval of the outbreak.

We developed the regression model in Eqn (4) and showed the fitting results of $R_0(t)$ in Figure 3A. The fitted regression model had coefficient of determination, R-squared, of 0.85 with p-value <0.0001 from the Wald test. We found a positive association between $R_0(t)$ and hospital admission lag and reporting lag, but negative association between $R_0(t)$ and level of public awareness. Then, we reconstructed the transmission dynamics of the outbreak in HKIA under the scenario that there was lack of improvement in reporting lag and public enquiry by using Eqns (3) and (4). We predicted the $r_0(t)$ by using Eqn (3), which is shown in Figure 3A. The average predicted r_0 was 14.67 (95% CI: 9.01−45.32), which increased 77.57% (95% CI: 1.71−111.15) from the average R_0. The $r_{\text{eff}}(t)$ series could be calculated, and we presented $r_{\text{eff}}(t)$ in Figure 3B. The average predicted r_{eff} was 2.05 (95% CI: 0.28−6.34). We found the criterial threshold that $r_{\text{eff}}(t) < 1$ was likely to occur later than that of $R_{\text{eff}}(t)$, which suggested the measles transmission in HKIA could be under control later without timely situation updated and public awareness.

Given $r_{\text{eff}}(t)$ in Figure 3B, we simulated the transmission process of the outbreak in HKIA by using Eqn (4) and showed the simulation results of number of infected staff, $c(t)$, in Figure 3C. We found the predicted number of infected staff, $c(t)$, would be likely to increase without improvement in reporting or public enquiry. The total number of infected staff between March 24 and April 30 was estimated of 179 (IQR: 90−339, 95% CI: 23−821). Comparing to the observed 19 infected staff during the same period, it was likely that the improvement in reporting and public awareness during the outbreak in HKIA had saved 8.42-fold (95% CI: 0.21−42.21) of the infected staff since March 24, 2019. Therefore, we call for attention to the contributions of the timely healthcare services, reporting and boost public awareness in control of this outbreak in HKIA.

Naturally, as expected, rapid (or timely) outbreak situation updates, promptness of infection prevention and control actions,[11,33–35] timely hospitalization and quarantine,[36]

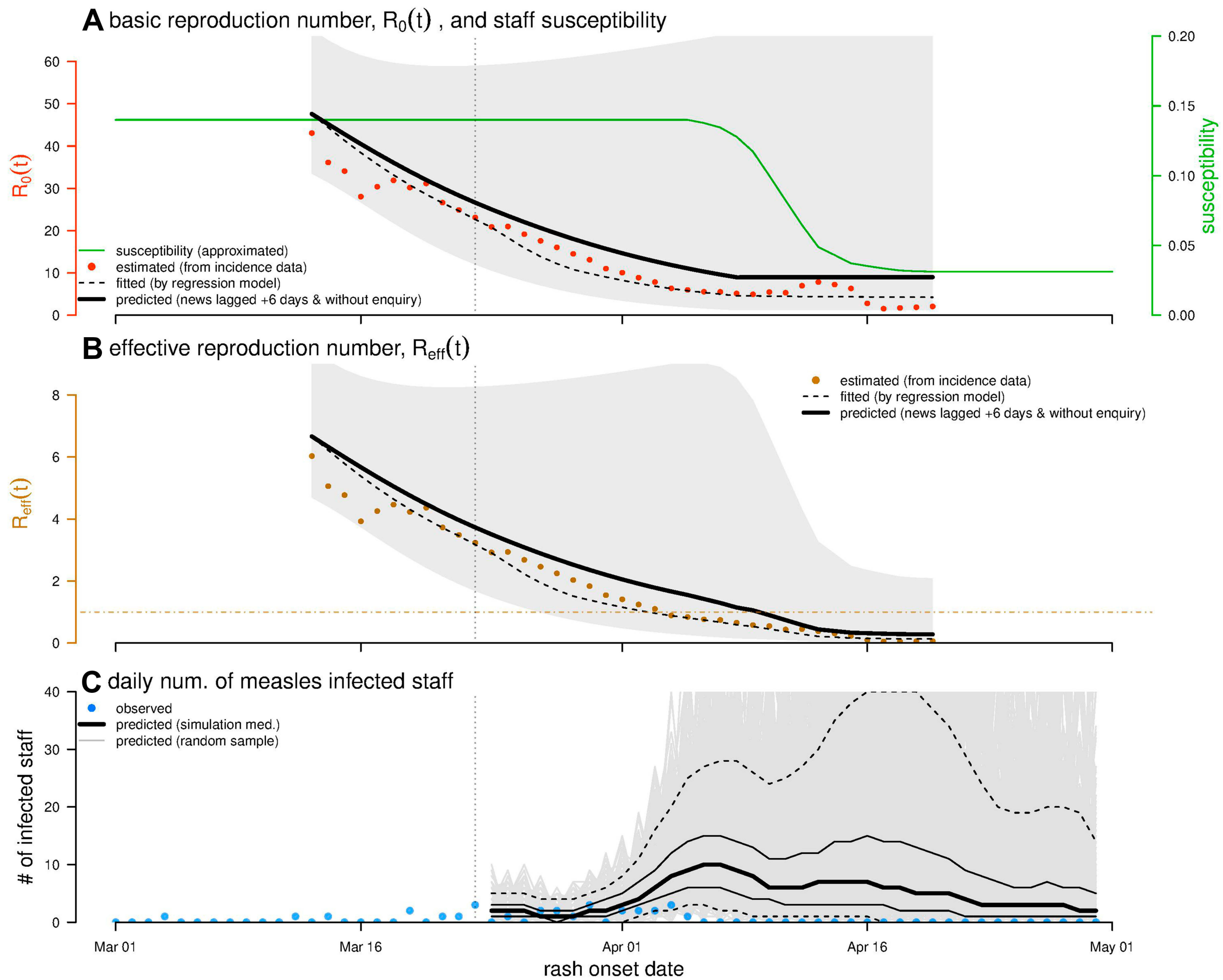

Figure 3 The prediction and simulation results of the reproduction numbers and number of infected staff. Panel (**A**) shows the estimated (brown dots, consisting with Figure 2D and fitted (dashed curve) $R_0(t)$, and predicted (bold curve) $r_0(t)$. The green curve is the approximated $S(t)$, as the same as in Figure 2B. Panel (**B**) shows the estimated (brown dots, consisting with Figure 2C and fitted (dashed curve) $R_{\text{eff}}(t)$, and predicted (bold curve) $r_{\text{eff}}(t)$. The shading area represents the 95% CI of the prediction. Panel (**C**) shows the observed (blue dots, consisting with Fig 2(a)) $C(t)$, and predicted (black and grey curves) number of infected staff, $c(t)$. The black bold curve is the simulation median, the black thin curves are the lower and upper bounds of the interquartile range (IQR), and the black dashed curves are the lower and upper bounds of the 95% CI. The grey curves show 10,000 simulation samples.

sufficient healthcare resources and boost public awareness,[37–39] which reflected by the high number of enquires,[32,40-43] were protective factors to reduce the risk of infectious disease transmission. These factors, eg, the three determinants in this study, could possibly efficiently lower $R_0(t)$ as well as $R_{\text{eff}}(t)$ in this outbreak in HKIA,[44,45] as which the similar phenomenon was also identified in the severe acute respiratory syndrome (SARS) outbreak in Hong Kong previously.[46,47] These findings reconfirmed existing epidemiology theory.[24,37,38,40,48,49]

This study has limitations. First, the assumption of 100% vaccine effectiveness is for simplification, and it may be unrealistic for long-run setting, ie, it would be slightly lower than 100%. Considering the effect of vaccination has been removed in deriving $R_0(t)$ from $R_{\text{eff}}(t)$, a slight decrease in vaccine effectiveness will not affect our main results. Second, although the relationships between hospital admission lag (X_1), reporting lag (X_2) and public awareness (X_3) and $R_0(t)$ were tested by GCTs, the independent pairwise effects between each determinant and $R_0(t)$ were difficult being disentangled due to potential associations among X_i s. However, this shortcoming had little impact on our modelling framework since the regression model yield reasonable signs, ie, positivity or negativity, of the estimated coefficients, b_is. Thus, our main results still hold. Third, due to the observed data were only available from March to April, we were unable to conduct the model simulation excess April with our full parametric modelling framework. Nevertheless, the predicted number of infected staff, $c(t)$, were decreasing since mid-April, and it is likely to die out quickly by the early May owe to the low level of $R_{\text{eff}}(t)$. Fourth, the initial susceptibility of all airport staff was fixed at 86% according to the pilot serological survey on March 29, 2019, see Supplementary Information S1. We note that this survey, though randomly conducted, merely included 100 airport staff out of 73,000 in total. By using a Normal approximation on the binomial distribution, the 95% CI was approximated from 82% to 90%. This narrow 95% CI was unlikely to affect our main conclusions. Fifth, the Wallinga and Teunis[15] approach for the $R_{\text{eff}}(t)$ calculation are supposed to be implemented on the number of measles infections time series. However, due to lack of data, we used the number of reported cases as a proxy of the real number of infections, which can be achieved by assuming a constant reporting ratio and thus will not bias the $R_{\text{eff}}(t)$ estimates. Last but not the least, the analysis was conducted under the within airport setting and limited to only considering the "staff-to-staff" transmission path as justified in Supplementary Information S2. Although the transmission might be triggered by few undetected index cases associated with traveling, further investigation is limited due to lack of information. Given the information of seed cases associated with traveling network dataset, our analytic framework can be extended to a more comprehensive context.

Data Sharing Statement

All data used in this work were collected from the Centre for Health Protection (CHP),[1–3] the government of Hong Kong, and the Hong Kong International Airport (HKIA).[4] All data sources were publicly available.

Ethics Approval and Consent to Participate

The measles cases data in this work were collected via public domains,[1,2] and thus the ethical approval or individual consent was not applicable.

Author Contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Disclosure

Shi Zhao, Xiujuan Tang and Xue Liang should be considered as joint first authors. Daihai He is supported by an Alibaba (China)-Hong Kong Polytechnic University Collaborative Research project. Maggie H Wang is a shareholder of Beth Bioinformatics Ltd. The authors report no other conflicts of interest in this work.

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