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The city-wide full-scale interactive application of sewage surveillance programme for assisting real-time COVID-19 pandemic control – A case study in Hong Kong

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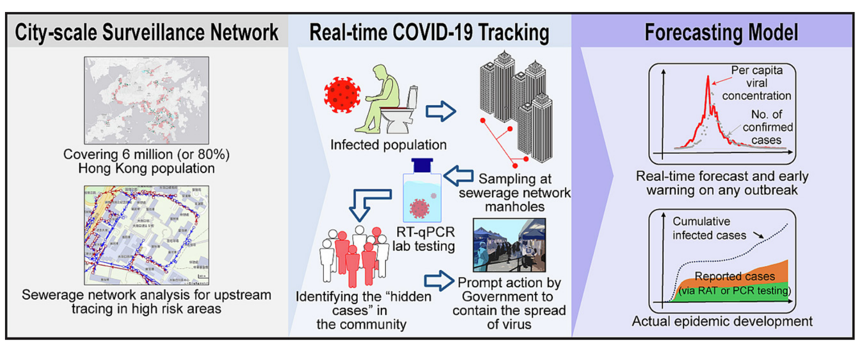
HIGHLIGHTS

- Hong Kong successfully applied Sewage Surveillance for real-time COVID-19 tracking.
- The success came from the synergy among government, academic and private sectors.
- Sewage data provided early warning with 2–4 days lead time to enhance preparedness.
- Robust regression models were developed to estimate actual infection numbers.
- City-scale sewage data informed planning of preventive measures to combat COVID-19.

GRAPHICAL ABSTRACT



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ABSTRACT

The paper discusses the implementation of Hong Kong's tailor-made sewage surveillance programme led by the Government, which has demonstrated how an efficient and well-organized sewage surveillance system can complement conventional epidemiological surveillance to facilitate the planning of intervention strategies and actions for combating COVID-19 pandemic in real-time. This included the setting up of a comprehensive sewerage network-based SARS-CoV-2 virus surveillance programme with 154 stationary sites covering 6 million people (or 80 % of the total population), and employing an intensive monitoring programme to take samples from each stationary site every 2 days. From 1 January to 22 May 2022, the daily confirmed case count started with 17 cases per day on 1 January to a maximum of 76,991 cases on 3 March and dropped to 237 cases on 22 May. During this period, a total of 270 "Restriction-Testing Declaration" (RTD) operations at high-risk residential areas were conducted based on the sewage virus testing results, where over 26,500 confirmed cases were detected with a majority being asymptomatic. In addition, Compulsory Testing Notices (CTN) were issued to residents, and the distribution of Rapid Antigen Test kits was adopted as alternatives

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to RTD operations in areas of moderate risk. These measures formulated a tiered and cost-effective approach to combat the disease in the local setting. Some ongoing and future enhancement efforts to improve efficacy are discussed from the perspective of wastewater-based epidemiology. Forecast models on case counts based on sewage virus testing results were also developed with R^2 of 0.9669–0.9775, which estimated that up to 22 May 2022, around 2,000,000 people (~67 % higher than the total number of 1,200,000 reported to the health authority, due to various constraints or limitations) had potentially contracted the disease, which is believed to be reflecting the real situation occurring in a highly urbanized metropolis like Hong Kong.

1. Introduction

The COVID-19 pandemic, one of the most serious public health crises in recent decades, has resulted in 600 million cumulative cases and more than 6 million deaths in less than 3 years (World Health Organization, 2022a). To control the spread of COVID-19, jurisdictions around the world have implemented various non-pharmaceutical interventions (e.g. social distancing, business closure, mask-on requirements, travel restrictions, quarantining), and most have been reported to be effective to different extents (Bo et al., 2021; Lai et al., 2020; Liu et al., 2022). While these measures have to be carefully planned according to the local epidemic situation, scientific and cost-effective tools to keep track of the epidemic are essential to inform policy formulation (Paterson and Durrheim, 2022). Conventional population-scale clinical diagnostics (i.e. polymerase chain reaction (PCR) tests through the collection of deep throat saliva and/or nasal swab) plays a critical role in addressing the COVID-19 pandemic. However, the huge financial burden to the community coupled with inherent limitations (e.g. active test avoidance due to privacy, invasiveness, and uncomfortable feeling, as well as passive test avoidance from asymptomatic carriers, etc.) has urged policymakers to explore alternative solutions (Betancourt et al., 2021).

Wastewater surveillance can complement epidemic surveillance by providing monitoring at the population scale as a low-cost, efficient, and non-intrusive approach. It can also help shed light on prevalence rates ‘hidden’ by asymptomatic infections, poor health-seeking behaviour as well as in settings with low individual diagnostic capacity (Lodder and de Roda Husman, 2020). Since the global outbreak of SARS-CoV-2, there is an increasingly large body of publications showing sewage surveillance being tested as a promising strategy to combat the pandemic, and being applied in more than 60 countries (Naughton et al., 2021). The World Health Organization published interim guideline in April 2022 to provide globally applicable advice on environmental surveillance for SARS-CoV-2 to complement public health surveillance (World Health Organization, 2022b). A literature study conducted in 2021 revealed that surveillance programmes collected sewage samples largely from wastewater treatment plants, only with a few from septic tanks or manholes, and the programmes being reviewed were largely of smaller scales with smaller community coverage (e.g. hospitals, dormitories/campuses, airports, cruise ships), thus a relatively small number of sampling points ranging from 1 to 33 (Bonanno Ferraro et al., 2021).

At the same time, large-scale surveillance programmes have also been strongly encouraged to be implemented at the city or national level, though successful examples are rarely reported. The European Commission issued its final recommendation in March 2021, suggesting its member states put in place a national surveillance system for large cities by October 2021 (European Commission, 2021). A notable example was the intensive wastewater monitoring program for COVID-19 across the four nations in the United Kingdom, which has well demonstrated its importance to protect public health at the national level, and provided an account of the approaches adopted to manage uncertainties in wastewater monitoring that are more tractable (Wade et al., 2022). The Netherlands has set up a national sewage monitoring programme for a daily sampling of 352 municipal wastewater treatment plants to cover all 17 million people in the country (Centers for Disease Control and Prevention, 2019). A National Wastewater Surveillance System has been developed in the United States by the Centers for Disease Control and Prevention in September 2020 to coordinate the programmes implemented by state, tribal, local, and territorial health departments to act as a data portal for centralised and standardized data to support pandemic response, and also to assist in sharing best practices and building laboratory capacity among health departments (Kirby et al., 2021). In Asia, the National Environmental Agency of Singapore commenced a wastewater surveillance programme for COVID-19 in April 2020, and its surveillance coverage has been expanded from 200 sites in 2021 to over 400 sites in 2022 with a weekly testing capacity of about 4000 upon the development of high-throughput testing protocol including polyethylene glycol (PEG) precipitation and ultrafiltration methods for RNA enrichment (Ahmed et al., 2020; Mailepessov et al., 2022). China also released a standardized manual in March 2022 for providing guidelines on the choice of sewage testing methodology for all city governments to consider (National Health Commission of the PRC, 2022).

Hong Kong, as an international city and transportation hub, was unavoidably impacted by COVID-19. Yet the city managed to maintain a low infection rate in the first three waves of COVID-19 (1st wave: January – February 2020, 2nd wave: March – April 2020, 3rd wave: July – September 2020), largely attributed to strong public awareness of personal hygiene despite the crowded living environment and the adequate implementation of general non-pharmaceutical intervention measures at city level (e.g. social distancing and travel ban). During the 4th wave which impacted Hong Kong for a longer duration (November 2020 – April 2021), the Hong Kong Special Administrative Region (HKSAR) Government (hereafter referred to as “the Government”) explored the application of sewage surveillance as a holistic and non-intrusive approach for epidemic monitoring and collaborated with The University of Hong Kong (HKU) to develop a sewerage network-based sewage surveillance programme (Deng et al., 2022a; Xu et al., 2021). Due to the limited analytical capacity of only up to 24 samples per day during the early stage of the programme (i.e. 14 December 2020–4 March 2021), the major target of applying this proof-of-concept “practical prototype” was to identify specific areas to uncover previously unsuspected patients through the issuance of Compulsory Testing Notices (CTN)[1] (*https://www.coronavirus.gov.hk/eng/compulsory-testing.html#compulsory-testing*) and Restriction-Testing Declarations (RTD)[2] (https://www.coronavirus.gov.hk/eng/compulsory-testing.html#Restriction-testing-declaration), achieving Hong Kong's primary anti-epidemic goal of “early identification, early isolation, and early treatment”. The study achieved a sensitivity of 54 % and a specificity of 95 % for identifying a previously unsuspected patient within a sewershed (Deng et al., 2022b), and was demonstrated to be successful in detecting

[1] If persons who are subject to compulsory testing have symptoms, they should seek medical attention immediately and undergo testing as instructed by a medical professional. They should not attend the ad-hoc mobile specimen collection stations or Community Testing Centres/Stations. Furthermore, persons who are subject to testing should, as far as reasonably practicable, take appropriate personal disease prevention measures including wearing a mask and maintaining hand hygiene; and unless for the purpose of undergoing the specified test, stay at their place of residence or private premises and avoid going to their workplace until the test result is ascertained as far as possible.

[2] Subject to the epidemic development and the need for infection control, the Government will delineate **restricted areas** and make a “restriction-testing declaration”. Persons within the areas are required to stay in their premises and undergo compulsory testing in accordance with the arrangement by the Government, and can only leave after the relevant test results are mostly ascertained. All premises within the restricted areas, whether or not confirmed cases were found therein, would be included in the compulsory testing notice. Any person who had been present in the restricted area for more than two hours in the past 7 days (including but not limited to visitors, residents and workers) have to also undergo compulsory testing.

silent COVID-19 transmission through several illustrative cases in the residential areas of Kowloon. However, there was still no full-scale application of sewage surveillance to assist the epidemic control (Olesen et al., 2021; Polo et al., 2020).

Following a "Practically-Zero Cases" period in the local community during May – November 2021, the epidemic rebounded in Hong Kong in late December 2021 (the 5th wave), and reached a peak level in early March 2022 with over 76,000 cases per day. The highly transmissible Omicron B.1.1.529/BA.2 was the predominant variant rendering social distancing and personal protective measures much less effective. Since the start of the 5th wave, the sewage surveillance programme, already proved in the 4th wave as an effective method to serve as an "early warning system" to monitor trends of SARS-CoV-2 transmission for providing un-interrupted epidemic tracing (Xu et al., 2021), was scaled up significantly with major objectives to (1) provide early warning through real-time nowcast and forecast of city-wide epidemic trend; (2) assist in policy formulation to facilitate informed decisions to relax/tighten intervention and other social distancing measures; (3) identify hotspots through risk assessment for real-time anti-epidemic actions and resources deployment; and (4) enumerate the asymptomatic COVID-19 patients in defined communities.

This paper introduces what the Government has done to develop, evolve, optimise, and put into practice, from a "practical prototype" to a "city-wide approach", a sewerage network-based SARS-CoV-2 surveillance system tailor-made for Hong Kong covering 80 % of the city's population, which has helped contain the COVID-19 epidemic in a scientific and efficient manner based on real-time prediction of case counts in the territory. More importantly, it demonstrated how the programme can be fully utilized by the Government to inform the planning and subsequent assessment of the intervention strategies by providing hindcasting and forecasting of the epidemic situation at different phases of the epidemic, which has constituted a useful case example overcoming the analytical challenges commonly faced by many applications owing to the short timescale for the outbreak, e.g. correlation with and predictions of case counts. The result of this study will provide an example of how to combat COVID-19 epidemic in a densely populated world-class metropolis using full-scale sewerage network-based SARS-CoV-2 surveillance in real-time.

2. Methods

2.1. Field sampling strategy: site selection and sample collection

Hong Kong has a comprehensive public sewerage system with centralised sewage treatment works covering 93 % of its population. About 95 % of the sewage collected is transferred to six large sewage treatment works with flow rates of 100,000–2000,000 m^3/day. This centralised system has rendered sewage surveillance at sewage treatment works alone, i.e. the most common approach reported in the literature, insufficient. Correspondingly, the Government adopted a city-wide sewerage network-based sewage surveillance programme which could better capture the spatial distribution of SARS-CoV-2 signals across the territory.

2.1.1. Site selection

Through sewerage network analysis, representative manholes were identified as sampling sites (i.e. stationary sites) for sewage collection to detect the presence of SARS-CoV-2. Manholes located at the entrance of shops and malls, or those on busy roads where temporary traffic arrangements would be inevitable for sampling, were avoided as far as practicable. Key hospitals with COVID-19 patients or quarantine facilities were also excluded from the stationary sites to avoid background contamination of the sewage samples collected from the community. Site investigations and trials were then conducted to ascertain sampling suitability. Each stationary site represented an average population of 40,000 (range 10,000–260,000), a size manageable for the Government to detect positive signals and conduct upstream tracing, if deemed necessary, for identifying hidden cases. The number of stationary sites was progressively increased from 26 during the initial pilot sewage surveillance in October 2020, to 64 for larger coverage in early 2021, and then to 154 during the 5th wave of COVID-19. The population coverage was also increased from 2 to 4 million, and finally to 6 million, equivalent to 80 % of Hong Kong's population.

2.1.2. Sampling frequency

The sampling frequency was increased from a 5-day cycle (i.e. all stationary sites were sampled once every 5 days) in early 2021 to a 2-day cycle during the 5th wave to capture the short incubation period (about 3 days) of the prevailing Omicron variant (Tanaka et al., 2022, Wu et al., 2022). The daily sampling capacity was also increased from 40 samples per day in mid-2021, progressively to 84 in February 2022 (i.e. the onset of the 5th wave) and then to a stable 100 since mid-March 2022. Up to the end of May 2022, a total of 10,081 sewage samples were collected from the stationary sites.

2.1.3. Sampling instrument

During each sampling occasion, 1 L of composite sewage samples were collected from the manholes at a 15-min interval for three hours between 7 and 10 am to capture the morning flush. To reduce the manpower requirement for sewage sample collection, in-manhole auto-samplers developed by HKU and the Government were adopted (Patent number: HK30057398) if the manholes' conditions permitted (i.e. manholes with negative head < -9.8 m, since the auto-samplers use peristaltic pumps to take sewage samples from sewers with a suction lift up to 9.8 m of negative head). The in-manhole auto-samplers were specially designed and equipped with a timer to automatically collect sewage samples at pre-set periods and intervals, and mounted beneath a manhole to minimize equipment footprint and traffic impact. The setup of the in-manhole auto-sampler is illustrated in Fig. 1. All samples were kept on ice upon collection and immediately delivered to the laboratories for analysis before 1 pm each day.

2.1.4. Logistics arrangement

A list of sampling sites was finalised by midnight before sampling in the next morning. Labelled sample bottles were prepared and distributed to the sampling teams before sampling. Communications among the coordinators of the management, sampling, delivery, and laboratory teams were ensured through a common sampling digital tracking platform to deal with unexpected site conditions. The platform recorded all key information about the sampling and delivery procedures, which served as a useful quality assurance tool.

2.2. Sewage laboratory testing method

During the first phase of the programme before March 2021, sewage samples were delivered to HKU for RT-qPCR analysis of N1 and E genes using the ultracentrifuge method as reported by Deng et al. (2022a). A reagent blank (200 μL of RNase-free water in the extraction kit) was used as a negative control for RNA extraction and RT-qPCR quantification steps. To increase the testing capacity, three commercial laboratories were invited after March 2021 to participate in the sewage surveillance programme. In March 2022, the magnetic binding bead method for RNA enrichment (MagMAX Wastewater Ultra Nucleic Acid Isolation Kit with Virus Enrichment, Thermo Fisher Scientific) was introduced which increased the daily total testing capacity from 84 to 156. The theoretical detection limit (i.e. one copy per reaction) of the ultracentrifuge method and the magnetic beads method was 333 copies/L and 2500 copies/L, respectively. While studies have shown that different sewage testing methods have their own merits and demerits (Ahmed et al., 2020) and may achieve different virus recovery rates, to ensure data integrity between different testing methods, a parallel test was conducted to analyze over 100 sewage samples using both the ultracentrifuge method and magnetic beads method, and the results obtained by both methods were directly compared for data alignment.

All participating laboratories were required to obtain accreditation for their sewage testing methods and to regularly participate in international proficiency tests. Since March 2022, an inter-laboratory comparison programme, developed with reference to ISO 13528 and 17,043, had also

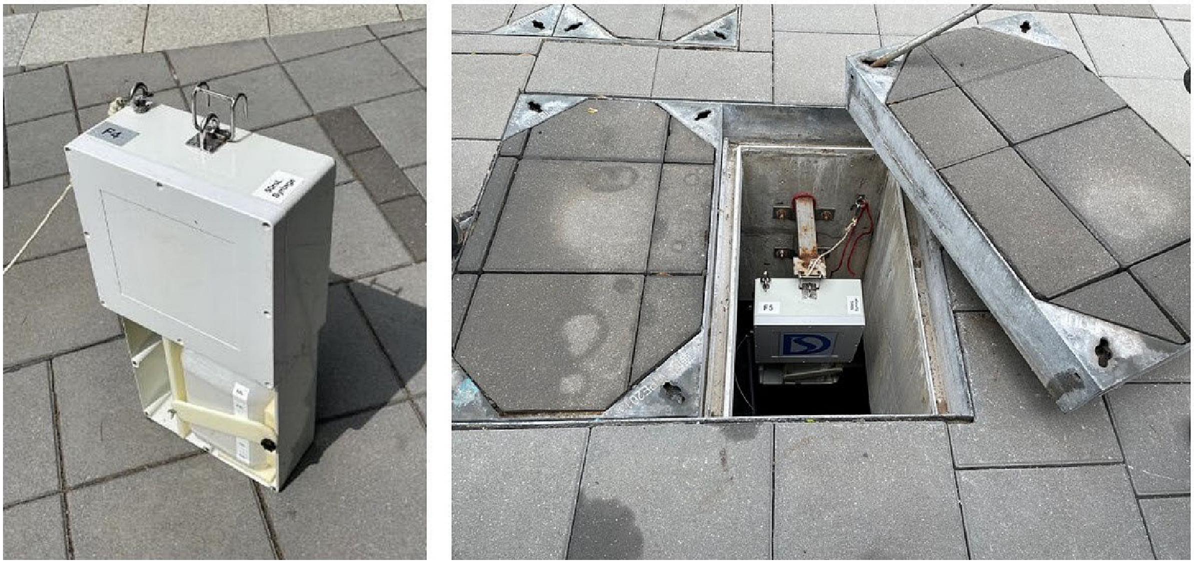

Fig. 1. Setup of in-manhole automatic sampler.

been adopted to assess at bi-weekly intervals the laboratories' performances in terms of recovery, repeatability, and stability of the testing methods using sewage samples spiked with known concentrations of N1 and E genes.

2.3. Sewage and epidemiology data

Cycle threshold (Ct) values and the corresponding concentrations of N1 and E genes (in copy/L) of the sewage samples were both submitted by the commercial laboratories by 10 pm on the same day of sampling to facilitate immediate follow-up actions by the Government. A sewage sample would be classified as "positive" only if the Ct values of both the N1 and E genes were below 40, and its corresponding viral concentration was defined as the maximum of the N1 and E gene concentrations (Deng et al., 2022a; Xu et al., 2021).

For easy comparison of the change in the epidemic situation, per capita viral concentration, V_t (in copy/L) for entire Hong Kong on a particular day "t" was subsequently calculated using the following equation:

$$V_t = \frac{\Sigma V_{i,t} \times P_i}{P_{Total}}$$

where $V_{i,\,t}$ = per capita viral concentration at the stationary site "i" on the day "t", P_i = population covered by the stationary site "i", and P_{Total} = total population covered by all the stationary sites sampled on the day "i".

The number of "confirmed cases" was made public by the Centre for Health Protection (CHP) of the Government (https://chp-dashboard.geodata.gov.hk/covid-19/en.html). Before 26 February 2022, all reported cases were confirmed by positive PCR results. To enhance the monitoring of case count, the Government announced that positive results obtained by Rapid Antigen Tests (RAT) since 26 February 2022 were also considered as confirmed cases without the need for confirmatory PCR testing. "Confirmed cases" by these two different diagnostic methods were both included in this study.

2.4. Development of forecast model for epidemic trend

The Government had been relying on PCR and RAT (since 26 February 2022) to identify the "confirmed cases". This study attempted to apply the extensive amount of sewage data (i.e. per capita viral concentration) to forecast the epidemic trend, using the number of "confirmed cases" as the dependent variable. In light of the differences in the availability and response time of the data, individual models were developed through linear regression for "confirmed cases" reported by positive PCR and RAT results (i.e. PCR and RAT models, respectively). The calibration periods for the PCR model were 22 January – 8 March 2022 while that for the RAT model were 13 March – 15 April 2022. The PCR and RAT models were then put into real-time use for validation starting on 9 March and 16 April, respectively. RAT data collected between 27 February and 12 March 2022 were not used for model calibration but for trend analysis due to large fluctuations and uncertainties of the practices in public at the initial phase of implementation.

Before developing the forecast models, cross correlation analysis, a measurement to track the movement of two sets of time series data relative to each other, was conducted to study the relationship between the per capita viral concentration and the number of "confirmed cases", and to confirm if there exists a specific time lag between the two variables to inform the choice of the independent variable for model development.

PCR and RAT model performances of calibration period and validation period were quantitatively evaluated using the statistical metrics including Root Mean Square Error (RMSE), the Pearson's correlation coefficient (R) and the index of agreement (IOA). The root mean squared errors (RMSE) is the square root of the mean squared error between the forecasted and reported number of cases. IOA and R values represent the degrees of coincidence and the correlation of the two datasets, respectively. IOA has a range between 0 and 1 while R has a range between −1 to +1, and the closer the value of these two metrics is to 1, the better match between the forecasted and actual number of cases is.

$$\text{RMSE} = \sqrt{\frac{\Sigma_{i=1}^{n}(O_i - F_i)^2}{n}}$$

$$\text{R} = \frac{\Sigma_{i=1}^{n}\left(O_i - \overline{O}\right)\left(F_i - \overline{F}\right)}{\sqrt{\Sigma_{i=1}^{n}\left(O_i - \overline{O}\right)^2}\sqrt{\Sigma_{i=1}^{n}\left(F_i - \overline{F}\right)^2}}$$

$$\text{IOA} = 1 - \frac{\Sigma_{i=1}^{n}(O_i - F)^2}{\Sigma_{i=1}^{n}\left(\left|F_i - \overline{O}\right| + \left|O_i - \overline{O}\right|\right)^2}$$

where O_i is the reported number of cases, F_i is the forecasted number of case, $\overline{O}$ is the average of reported number of cases and $\overline{F}$ is the average of forecasted number of cases.

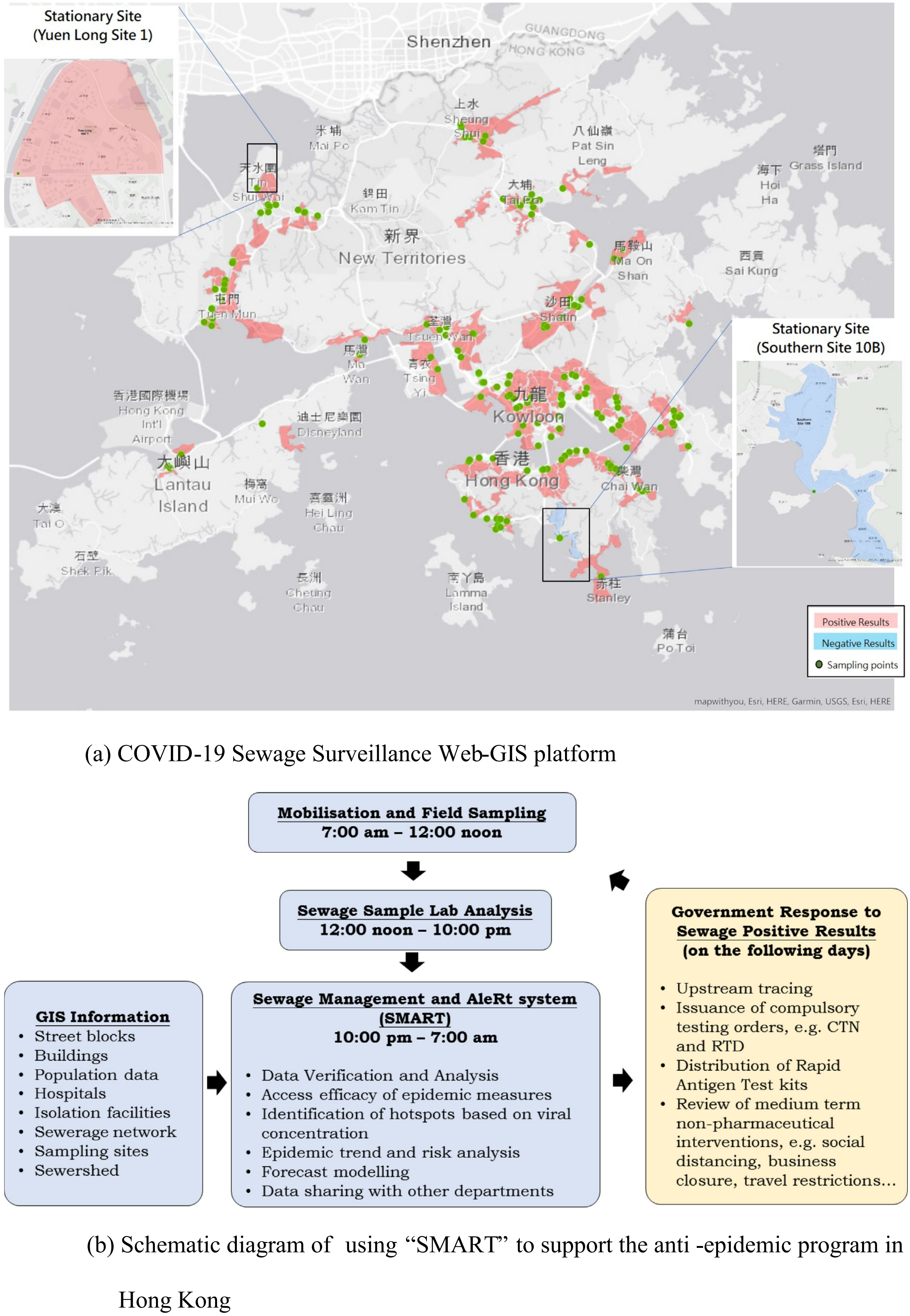

Fig. 2. (a) COVID-19 Sewage Surveillance Web-GIS platform
b) Schematic diagram of using "SMART" to support the anti-epidemic program in Hong Kong.

2.5. Development of the innovative sewage management and AleRt SysTem (SMART)

To enable immediate follow-up actions by various departments, the Government also developed the SMART with HKU, which is a real-time, interactive spatio-temporal database with statistical and analytical functions developed using the Geographic Information System (GIS) platform (ArcGIS Pro 2.9, ESRI) and Business Intelligence (BI) technology (Power BI, Microsoft) to assist in the management and analysis of the mass quantity of information (Fig. 2a and b). All the epidemiology data (i.e. spatial distribution of "confirmed cases") and sewage testing data (i.e. viral concentration) were instantly uploaded to the system once available through a self-developed data synchronization module for automatic data integration and visualization. The SMART enables detailed data analysis alongside other geographical information such as building information, population data, sewerage system information, as well as operational data including locations of designated COVID-19 hospitals, community isolation facilities, quarantine hotels, etc. which might affect data assessment due to potential presence of COVID-19 viruses in sewage discharged from these facilities.

A Web GIS approach was adopted to provide a user-friendly visual presentation tool for the sewage data through a range of colours assigned to sampling sites in points and sewersheds in polygons. The spatial data enabled the tracing of positive signals via the sewerage network and the associated population with a higher risk of infection based on the viral concentration level. The analysis would then be followed up by a revision of the sampling plan in the following days, as well as the implementation of various intervention measures to contain the disease.

In response to the sewage surveillance results, the Government established an inter-departmental working team involving the Drainage Services Department to carry out the sewage sampling, the Environmental Protection Department to analyze the sewage data, and the Health Bureau and CHP to implement district-level intervention measures (such as compulsory testing and distribution of RAT kits) in a smaller community to identify COVID-19 cases for timely isolation and contact tracing, complementing the general non-pharmaceutical intervention measures enacted across the city (e.g. social distancing and travel ban). Each day before midnight, the stationary sites were listed in descending order of their per capita viral concentrations. For sites appearing at the top of the list, the Government would issue compulsory testing orders to the residents in the sewersheds, at scales making reference to the types, locations, designs, and densities of the residential developments, as well as records of recent operations in those areas and the corresponding outcomes. Further upstream tracing for more targeted follow-up actions might also be warranted if any particular site was found to have consistently high viral concentrations over a period of time. For areas of moderate risk (i.e. areas with positive signals but relatively low viral concentration), the Government would distribute RAT kits to the residents, cleaning workers, and property management staff for their voluntary testing to identify virus carriers as early as possible. The efficacy of these sewage-related measures was subsequently assessed through the monitoring of the viral concentration before and after the implementation of these district-level measures.

3. Results

3.1. Parallel test results

Fig. 3 shows the scatter plot between the results, i.e. N1 gene and E gene concentrations in copy/L, obtained by the ultracentrifuge method and magnetic beads method during the parallel test, both in logarithmic scale. A wide range of concentrations between 3000 and 60,000,000 copies/L was covered by this parallel test. The linear regression lines passing through the origin were also plotted with the following equations:

$$\text{N1 gene}: y = 0.929\times\left(R^2 = 0.78\right)$$

$$\text{E gene}: y = 0.910\times\left(R^2 = 0.74\right)$$

where x = concentrations obtained by magnetic beads method and y = concentrations obtained by ultracentrifuge method.

The high R^2 values (0.78 for the N1 gene and 0.74 for the E gene) indicated that a good linear agreement could be maintained even after the introduction of the magnetic beads method. It was also noted that both regression lines had a slope smaller than 1 (0.929 and 0.910, respectively), suggesting that the magnetic beads method generally yielded higher

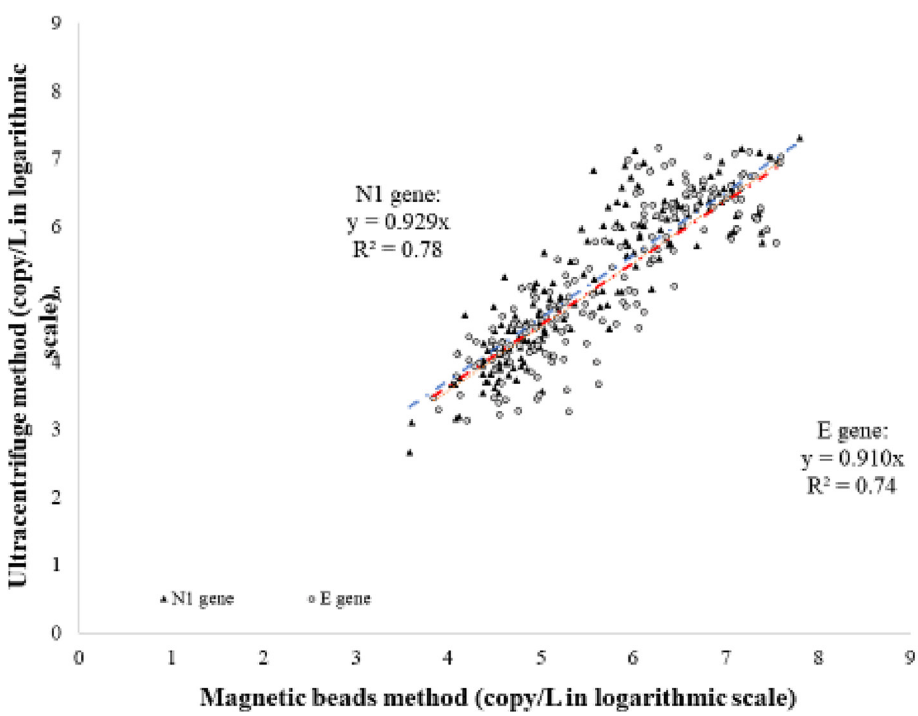

Fig. 3. Scatter plot between the results obtained by ultracentrifuge method and magnetic beads method obtained during the parallel test for N1 gene and E gene concentrations (copy/L in logarithmic scale).

concentrations when compared to the ultracentrifuge method. For data alignment to ensure unbiased data interpretation, N1 gene and E gene concentrations reported by the magnetic beads method were first adjusted with the adjustment factor of 0.929 and 0.910, respectively, before they were utilized for further analysis.

3.2. Epidemic trend in Hong Kong

During the study period between January and May 2022, the number of “confirmed cases” in Hong Kong has reached the peak in early March 2022 and then started to decrease gradually and returned to a relatively low level in May 2022, as a result of the tightening of social distance as well as anti-epidemic interventions. Fig. 4(a) shows the time series of the 2-day (i.e. day “t” and its previous day) running geometric mean of per capita viral concentration ($V_{g,t}$) and the number of confirmed cases (by PCR and RAT) during the study period; $V_{g,t}$ was adopted because it exhibited the highest correlation with the number of “confirmed cases”. An exponential increase in viral concentration was observed since late January and until late February, reaching a maximum per capita concentration of 4,560,000 copies/L. The peak was immediately followed by a rapid decaying trend, with some fluctuations observed in mid-March, until the per capita viral concentration decreased to below 10,000 copies/L in May (i.e. 99.9 % reduction from the peak). When the per capita viral concentration was further transformed into a logarithmic scale (Fig. 4(b)), a three-phase pattern was clearly observed: the per capita viral concentration followed a doubling time of 2 days during 1 and 13 February (R^2 = 0.966 when fitted with a model of 2-day doubling time), then slowed down to 5 days between 14 and 27 Feb (R^2 = 0.945), and started to decrease from 28 February until 4 May 2022 with a half-life of 8 days (R^2 = 0.973). The pattern also matched well with the number of “confirmed cases” in the logarithmic scale. Fig. 4(c) shows the percentage of positive sewage samples during the 5th wave, which exhibited a similar pattern as the per capital viral concentration but with a flatter plateau instead of a sharp peak, i.e. climbing from 18 % in late January to 99 % between 12 February and 8 April, and progressively dropped back to below 30 % towards the end of May 2022.

3.3. PCR and RAT models

It was noted in Fig. 4(a) and (b) that the trend of $V_{g,t}$ resembled well with the daily number of “confirmed cases” with a lead time. Previous studies reported that sewage testing could pick up signals 4–10 days earlier than the actual report of cases due to the time required for individual cases to go for testing after contracting the virus, and the time required for the laboratories to complete and report the testing result (Kaplan et al., 2021; Peccia et al., 2020). Cross correlation analysis conducted in this study (Fig. 5) revealed that the lead times with the highest correlation of $V_{g,t}$ to PCR results and RAT results were 4 days (correlation coefficient = 0.696) and 2 days (correlation coefficient = 0.590), respectively. The correlations were considered to be significant when the absolute value is greater than $\frac{2}{\sqrt{n-|k|}}$, where n is the number of observations and k is the lag. For PCR results,

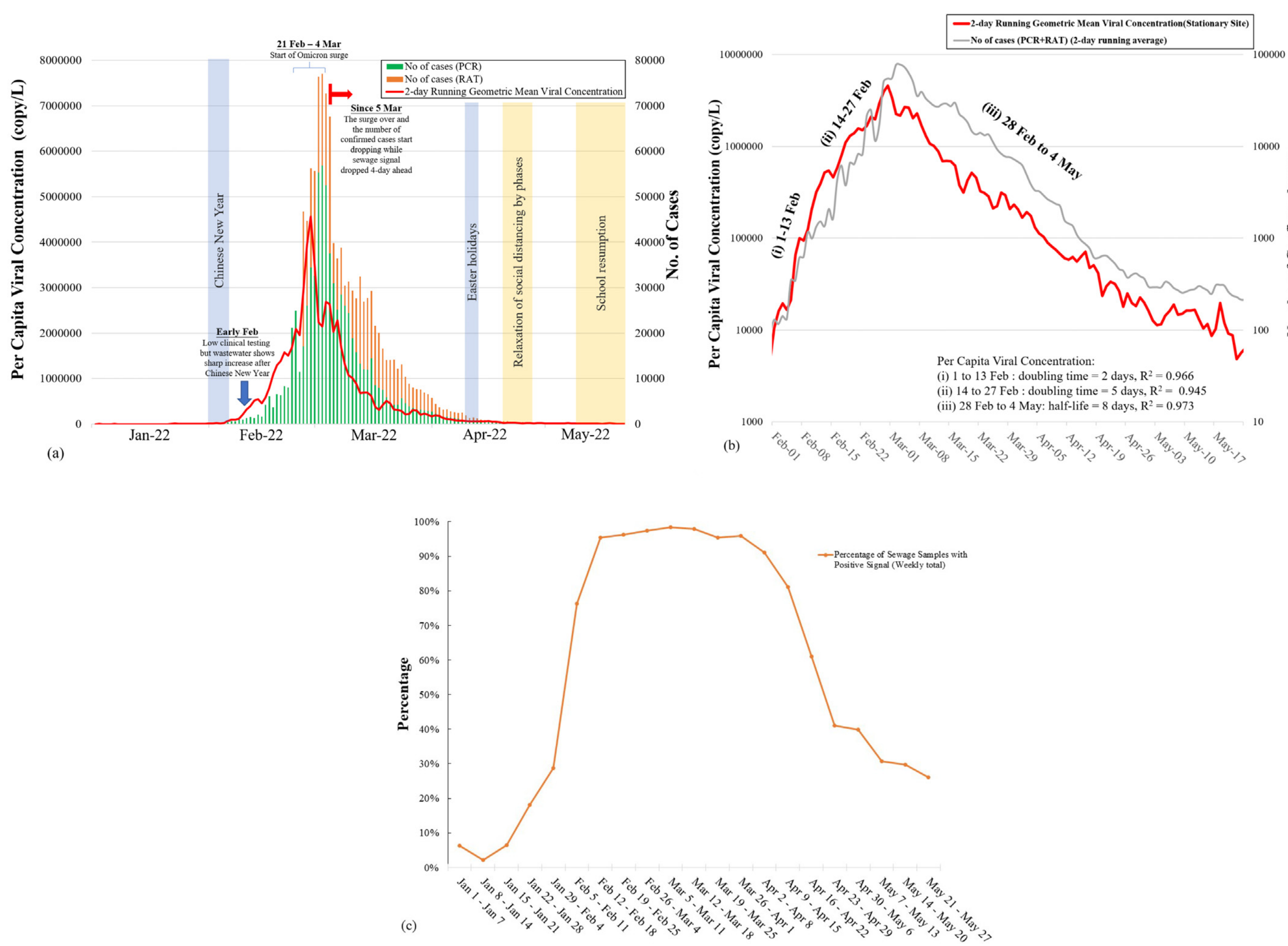

Fig. 4. (a) Comparison of the 2-day running geometric mean of per capita viral concentration and number of “confirmed cases”
(b) Trend of the 2-day running geometric mean of per capita viral concentration and number of “confirmed cases” in logarithmic scale
(c) Percentage of positive sewage samples.

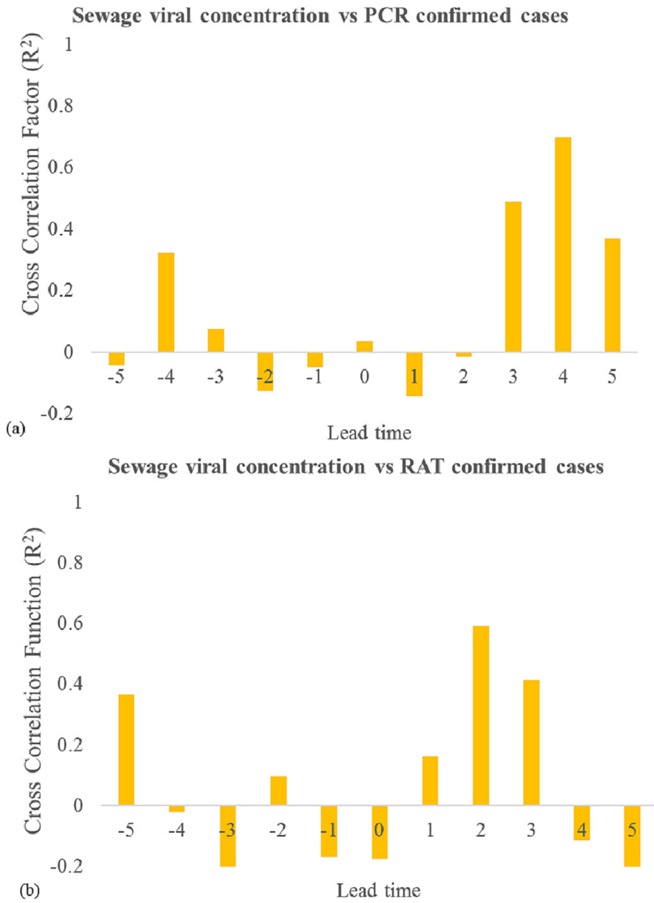

Fig. 5. Cross Correlation Factors (CCF) plot between the per capita viral concentration and number of "confirmed case" (a) under PCR and (b) RAT test.

the correlation was significant as $0.696 > \frac{2}{\sqrt{46 - |4|}} = 0.3086$. For RAT results, the correlation was significant as $0.590 > \frac{2}{\sqrt{34 - |2|}} = 0.3536$. As further illustrated in Fig. 6, among the PCR models developed to predict the number of "confirmed cases" using $V_{g,t}$ of different lead days (0 to 5 days), the 4-day lead model also yielded the highest R^2 of 0.9775, which was in line with the cross correlation analysis results, and this model was therefore adopted for subsequent analysis. A similar comparison for the RAT models was conducted to confirm the 2-day lead as suggested by the cross correlation analysis.

Correspondingly, the PCR and RAT models were developed using the 2-day running geometric mean of per capita viral concentration with a 4-day lead ($V_{g,t-4}$) and a 2-day lead ($V_{g,t-2}$), respectively. Due to the already high correlation between the per capita viral concentration in arithmetic mean and the number of "confirmed cases", the per capita viral concentration was not log-transformed before model development. The best-fit linear models obtained were:

$$PCR_t = 0.0131 \times V_{g,t-4}$$

and

$$RAT_t = 0.0192 \times V_{g,t-2}$$

The R^2 values of the PCR model and the RAT model were 0.9775 and 0.9669, respectively, indicating that both models could explain a very large portion of the variance of the dependent variable, i.e. the number of "confirmed cases". Fig. 7 shows the comparison between the time series of actual and model forecasted number of "confirmed cases" (in a 2-day running average) for (a) PCR and (b) RAT. The performance metrics for the models during both calibration and validation periods are presented in Table 1. As reflected through trend observations supported by the performance metrics, the PCR model yielded a very good match with the observed number during both the calibration period and real-time application period, while the RAT model also reasonably captured the overall decreasing trend during both periods.

Subsequently, the actual total number of COVID-19 "infected cases" in Hong Kong during the study period was estimated using these two developed models through hindcast. Fig. 8 shows the comparison of the cumulative number of "confirmed cases" reported to CHP and forecasted by the models. The forecast models estimated that, up to 22 May 2022, there was a total of about 2,000,000 (i.e. 1,200,000 from the PCR model and 800,000 from the RAT model) "infected cases", equivalent to about 27 % of Hong Kong's population. This figure was around 67 % higher than the total number of 1,200,000 "confirmed cases" as reported to CHP.

4. Discussion

4.1. Sewage surveillance programme in Hong Kong led by the government

During the 5th wave, the highly contagious Omicron variants were reported to be prevailing, and according to the local epidemiology data, only about 0.5 % of the total cases were associated with the Delta variants. Compared to the previous four waves, the extremely high transmission rate in the 5th wave was unexpected. A large number of infected patients and the corresponding demand surge in PCR testing services for COVID-19 had overloaded the local testing capacity, leading to possible delays or even failure in identifying infected patients in a timely manner. In comparison, the high-density sewage surveillance conducted in the same period provided an unbiased analysis of the viral concentration in the community, and the Government considered it as a useful management and administrative tool for tracking the epidemic development.

The inter-departmental working team established within the Government has implemented the sewage surveillance programme round the clock since December 2020, with sewage sampling starting from 7:00 am daily, followed by laboratory testing, data analysis, and production of a GIS-based report by 7:00 am on the next day. This enabled a centralised management approach to make direct reference to the sewage data to formulate follow-up plans, such as issuance of compulsory testing orders and distribution of RAT kits. While the Government assumed a leading management role in the programme, assistance was acquired from the academic and private sectors through work decentralization to provide scientific backup to the programme (e.g. to develop the testing protocol) and to rapidly boost up the testing capacity to increase sampling frequency and population coverage. At the same time, the Government adopted various measures strategically, including the parallel tests and inter-laboratory comparison programme, to ensure data integrity. Daily processing of this large quantity of data was also made possible through the development of the innovative and powerful SMART by the Government, such that thorough analysis could be carried out using GIS and data analytics tools to reach information-driven decisions more efficiently (Fig. 2). The successful implementation of the sewage surveillance programme to help Hong Kong tide over the sudden arrival of a peak wave of the epidemic has demonstrated strong synergy through cooperation among different sectors.

4.2. Essence of applying the forecast models

The positive rate of sewage samples remained close to 100 % for an extended period when the epidemic peaked. This single parameter alone could not help identify whether the trend was still increasing or indeed starting to decrease in the midst of this critical period. Correspondingly, the per capita viral concentration, a directly quantification of the situation with actual measurements, became crucial to epidemic tracking. The presentation of sewage surveillance data in terms of the daily per capita concentration also allowed meaningful comparisons between cities in different geographic locations (Hata et al., 2020).

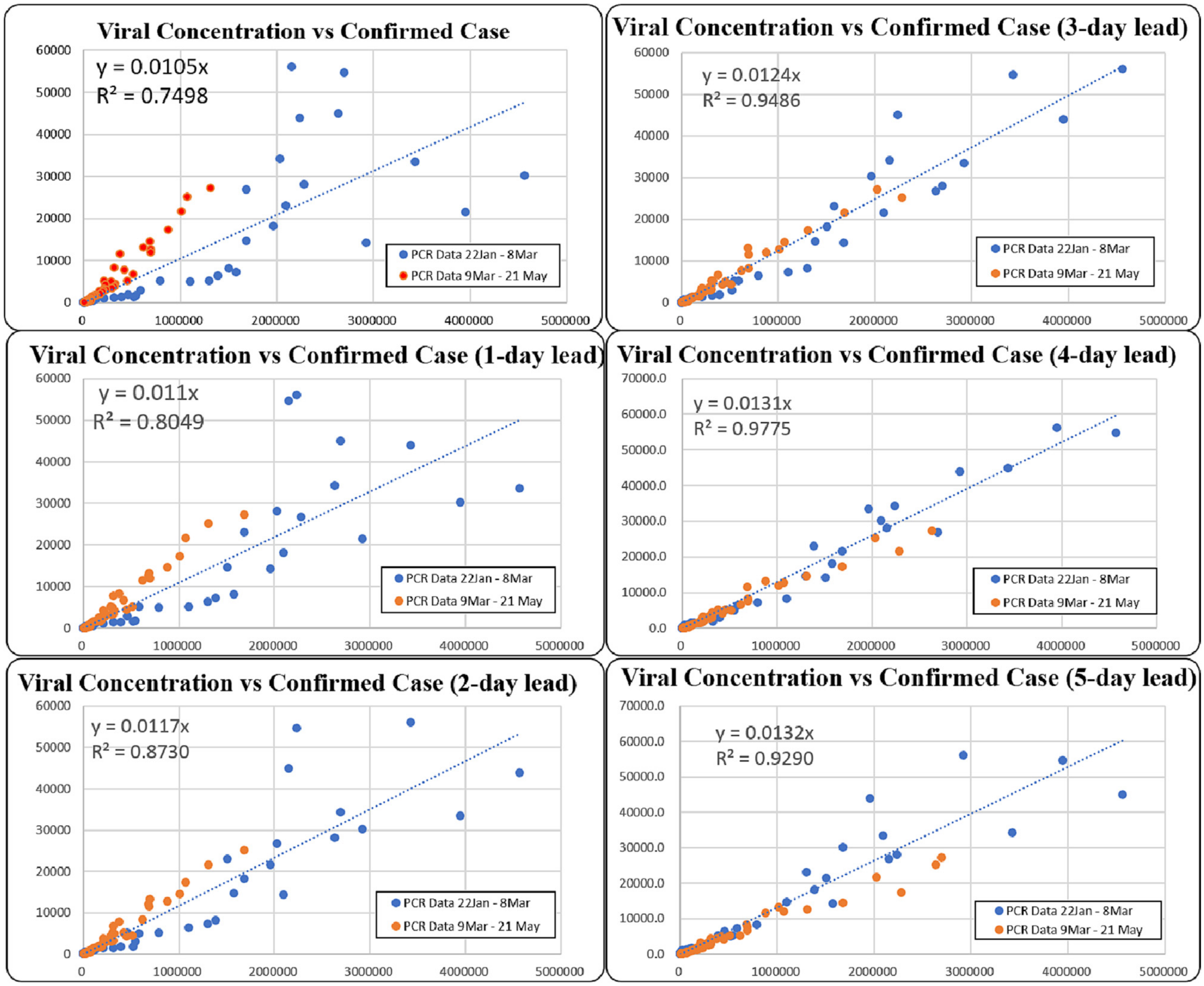

Fig. 6. Comparison of PCR models developed using $V_{g,t}$ of different lead days (0 to 5 days). (X-axis - per capital viral concentration (copy/L); Y-axis - number of "confirmed" cases).

To further utilize this important set of data, real-time forecast models were developed using the viral concentration data as the independent variable to predict the actual number of "infected cases". It is noteworthy that there existed no direct correlation between population sizes and viral concentrations due to different virus-shedding load that could be associated with different factors such as age and sex of the patients, disease severity, number of days since the patients got infected, types of variants, etc. (Badu et al., 2021; Puhach et al., 2022) as well as the fact that only about 50 % of the infected cases would shed viruses in the excreta (Gupta et al., 2020). Furthermore, there were other inherent uncertainties categorically associated with the viral concentration, in particular, the sampling randomness and the representativeness of the sewage samples to the actual condition that were collected at each of the stationary sites during the 3-h morning flush surge.

Notwithstanding the above, since the choice of the independent variable $V_{g,t}$ could have largely averaged out the uncertainties by just making reference to the running trend across the whole city, instead of looking into the more fluctuating daily variations and spatial distribution, an exceptionally strong correlation could still be obtained between the per capita viral concentration and the number of "confirmed cases", with R^2 values of the PCR and RAT models being as high as 0.9775 and 0.9669 respectively, enabling the establishment of a reliable forecast model to facilitate real-time tracking of the epidemic, even in a densely populated city like Hong Kong with the complicated sewerage system.

In our study, the linear regression model, the simplest parametric model, was found to be a highly tenable tool in forecasting the epidemic trend. After all, a simple model, if proven to be reliable enough for forecasting purposes, could be an ideal solution from the Government's perspective in handling the epidemic. It is cautioned however that one might obtain different outcomes in other cities with different population characteristics, sewerage network arrangements, and epidemic situations. Therefore, detailed analysis of sewage data and epidemiology information is always a prerequisite for jurisdictions to develop a suitable model for epidemic forecasting.

The Government accepted "positive cases" by both PCR and RAT, and the latter method was only accepted in late February 2022 as aforementioned. Inherent uncertainties were associated with both types of epidemiology data: cases reported by PCR, though reliable, were limited by its testing capacity during the epidemic peak and thus could have underestimated the number of confirmed cases; cases reported by RAT, though simple and rapidly done, was limited by the low sensitivity.

Correspondingly, this study developed two separate forecast models for confirmed cases by PCR and RAT. Despite the high uncertainties, the forecast models gave a good estimation of the actual infection numbers that could not be accurately reflected by the limited clinical testing capacity. One major finding from the forecast models was that a total of 2,000,000 "infected cases" were estimated, 67 % higher than the actual reported numbers of "confirmed cases". With a total population of 7,500,000 people in

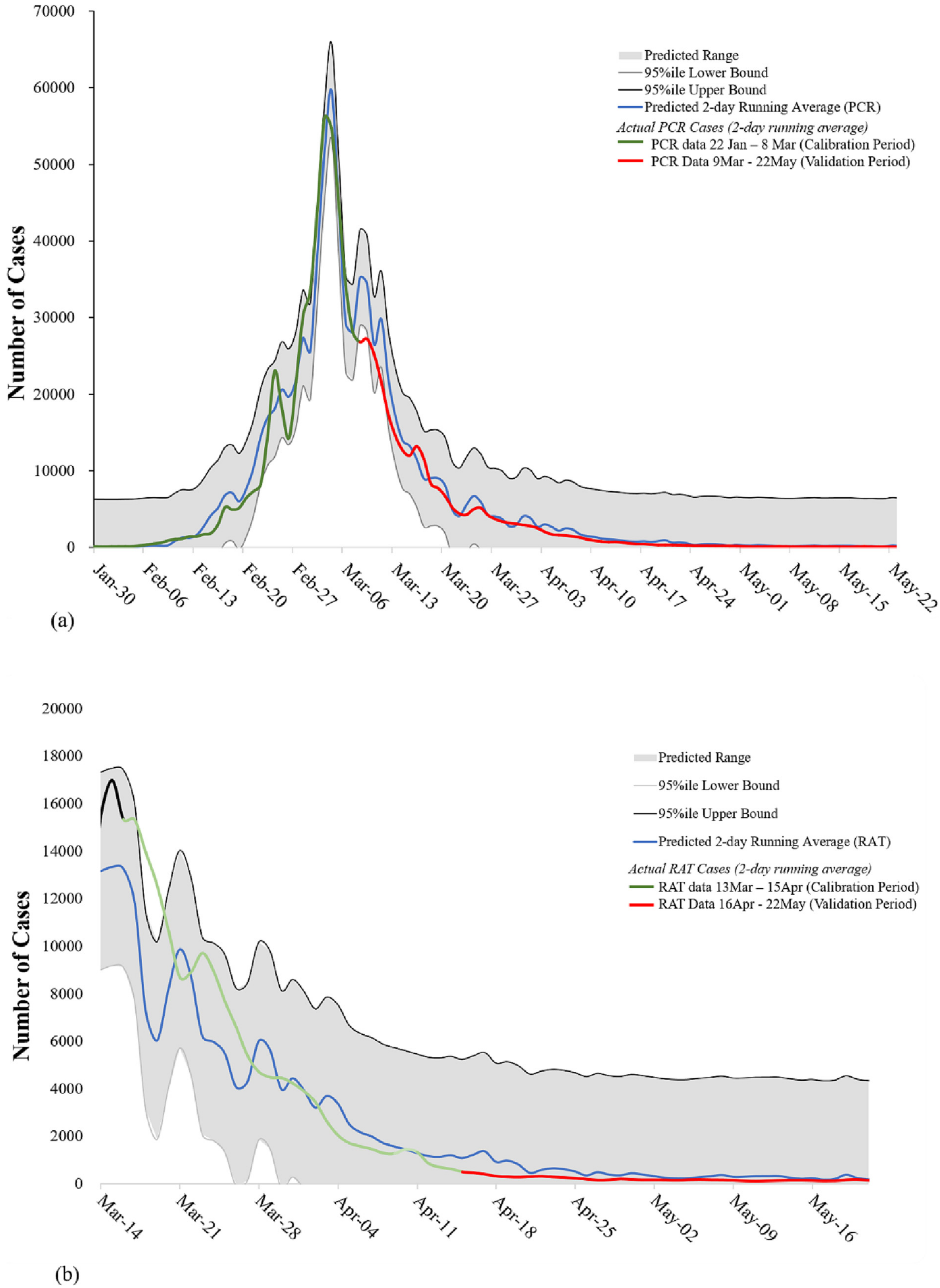

Fig. 7. Comparison of forecasted number of cases with (a) actual PCR cases and (b) actual RAT cases.

Hong Kong, this represented an overall cumulative infection rate of 27 %. Though surprising, the result was not unreasonable in view of overloaded clinical diagnostic services during the peak wave of the epidemic. We believe the differences could come from (1) infected persons (especially asymptomatic or mildly symptomatic persons) who recovered without receiving any PCR or RAT tests, (2) RAT positive cases conducted before 26

Table 1
Statistical evaluation of the forecasting models in calibration and validation period.

	RMSE	Index of Agreement (IOA)	Pearson's Correlation (R)
PCR model (calibration period)	2869.55	0.991	0.9835
PCR model (validation period)	1545.93	0.985	0.9877
RAT model (calibration period)	1408.50	0.979	0.9628
RAT model (validation period)	352.12	0.386	0.8503

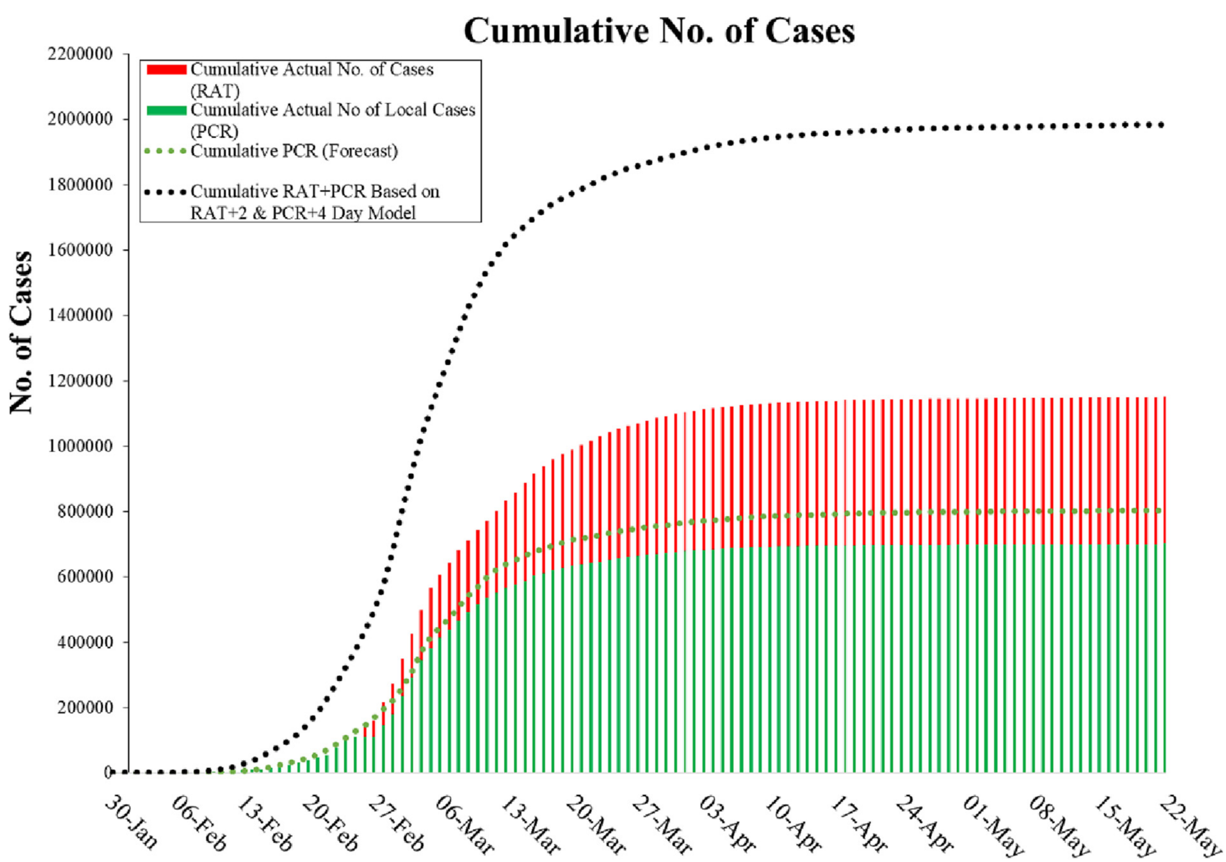

Fig. 8. Comparison of the reported and forecasted cumulative number of "confirmed cases".

February without subsequent PCR testing; or (3) RAT positive cases who did not report their results to the Government. In fact, the model results were indirectly validated against some reported statistics of the Government and were found to be highly accurate. On 14 March 2022, the Government announced that out of the 190,000 civil servants, 90,000 employees of the Hospital Authority, and 20,000 employees of the MTR Corporation, the infectious rates were 17 %, 20 %, and 20 %, respectively. The PCR and RAT models predicted an overall cumulative 1,770,000 infected persons (i.e. 23.6 %) as at 14 March 2022, indicating a very close description of the real situation in terms of the infection rates.

4.3. Synergy of sewage surveillance programme and intervention strategy implementation

At present, there has been a lack of consistent guidance on the definition of a positive wastewater result, either based on a significantly high viral concentration cut-off value and/or a consecutive number of days with wastewater sampling tested positive (Shah et al., 2022). In our study, the sewage data and forecast results with a lead time of 2–4 days to the actual report time of "confirmed cases" have well demonstrated the usefulness of sewage surveillance in providing territory-wide information to allow for sufficient and precious time for the Government to formulate preventive measures and intervention strategies such as social distancing and travel ban; and the surveillance results also became a basis to review the effectiveness of strategies following a certain period of their implementation. This is particularly important when the availability of diagnostic testing cannot meet the demand, and the number of confirmed cases is rising exponentially with a doubling time of 2–3 days (Fig. 3(b)) causing unforeseeable public anxiety.

The explosive spread of the 5th wave since January 2022 was originated from a transmission event in a designated quarantine hotel: an inbound traveler was infected with the Omicron sub-variant BA.2 towards the end of her compulsory 21-day quarantine by an imported case staying in the neighboring room, suspected to be via airborne transmission. The case later infected a household member, who further transmitted the virus to a cleaner of a densely populated estate (i.e. the first super-spreader), leading to more than 400 "confirmed cases" in one single estate over 10 days, and this surge of cases was also picked up by the sewage surveillance.

In view of the exponential increase in viral concentration since late January 2022, the Government quickly responded by implementing a range of stringent non-pharmaceutical interventions on 10 February 2022, including a special work arrangement to allow Government employees to work from home on a roster basis, travel bans and more stringent social distancing measures, etc. The follow-up actions resulted in an immediate containment in transmission since 13 February as revealed by the viral concentration, i.e. the per capita viral concentration doubling time decreased from 2 days during 1–13 February 2022 to 5 days during 14–27 February 2022 as shown in Fig. 3(b). While the decrease in the number of confirmed cases was observed only after the peak on 4 March 2022, the decreasing trend was actually first observed through sewage surveillance on 28 February 2022. This piece of information was extremely useful for the Government at that moment due to the limited PCR testing capacity, the high number of reported cases, the public anxiety generated, and the increasing pressure on the local healthcare system. The decreasing trend was further verified upon the implementation of a city-wide voluntary daily RAT campaign between 8 and 10 April (i.e. all Hong Kong residents were provided with RAT kits and encouraged to conduct the tests every day during these three days), during which a rebound of "confirmed cases" was not observed, demonstrating the effectiveness of the intervention strategies being implemented.

In light of the steadily decreasing number of confirmed cases as well as the per capita viral concentration, the Government gradually relaxed the social distancing measures since 21 April 2022, including the extension of dine-in hours for restaurants, and the reopening of premises such as gyms, sports venues and cinemas. Although some fluctuations in the viral concentration was observed since then, the general decreasing trend provided valuable insights to support the Government's plan to continue the relaxation of other intervention measures.

In parallel with the territory-wide epidemic tracking at stationary sites, the Government also made reference to the sewage surveillance to dynamically identify areas of high risks through upstream tracing. Once very high viral concentrations were consistently detected in any of the 154 stationary sites, the Government would also trace its upstream manholes (i.e. ad-hoc sites) for additional sewage collection to narrow down the area of concern from a large sewershed to a city block or even a single building, such that more focused follow-up actions could be taken only at the hotspots of higher risks, minimising unnecessary disturbances to other low-risk areas. By the end of May 2022, more than 2000 ad-hoc sites had already been identified for sampling when necessary.

Through upstream tracing, a total of 270 RTD operations at these city blocks or buildings of high risks had been conducted – in an RTD operation, the Government exercised its power under which people within the specific "restricted area" were required to stay in their premises and undergo compulsory testing until all people have completed the test. Such arrangement also helped relieve the burden on clinical diagnostics through prioritization of limited resources to those at higher risk as revealed by sewage surveillance. Through the RTD operations, over 26,500 confirmed cases were detected although the number did not contribute a high percentage relative to the total number of confirmed cases in the 5th wave, these cases were essentially asymptomatic that could otherwise not be detected, and could still contribute to COVID-19 transmission if left undiagnosed; in fact, some of these RTD operations were conducted at sites with originally zero or very low reported "confirmed cases". Other measures, such as the issuance of CTN to demand any person to receive PCR test within 3-days and the distribution of RAT kits, were also adopted as alternatives to RTD operations at other areas of moderate risk, formulating a tiered approach to combat the disease. These measures effectively helped the identification of hidden cases, lowered the transmission rate of the disease, and reduced the pressure on the local healthcare system, which eventually helped Hong Kong to tide over the 5th wave.

4.4. Future development

The sewage surveillance programme evolution is a continuous process to further streamline the sampling and testing procedures. Some ongoing enhancements include (1) the introduction of narrowband Internet of things (NB-IoT) technique to facilitate real-time communication with the in-manhole auto-samplers to enhance their sampling efficiency, (2) the commencement of routine detection of variants, (3) the invitation of more active participation from academic and private sectors to explore innovative solutions to further bring down sampling and testing cost and enhance efficiency (e.g. trial application of passive sampling), and (4) evaluation of spatio-temporal variation of effective reproductive number (R_t), a critical indicator to monitor disease dynamics, through incorporating sewage data into the Susceptible-Infectious-Recovered (SIR) model for district-based risk assessment (Calvetti et al., 2020). At the same time, the Government is devoted to staying responsive and versatile, and to keeping the sewage surveillance programme flexible yet scientifically solid to prepare for all possible scenarios of epidemic development. The Government will also keep abreast of the latest development of wastewater-based epidemiology, and explore every opportunity to advance the programme with state-of-the-art technology and innovative ideas.

5. Conclusions

Accurate and reliable information on the status of the local epidemic situation is extremely important for the Government in making the right decision to fight the virus. The successful implementation and expansion of the city-wide high-density sewerage network-based surveillance programme in Hong Kong during a peak wave of COVID-19 well illustrated the importance of a strong partnering relationship among different sectors, and set an example for cities in other places to make reference to. Despite the limitations of sewage surveillance which does not provide a means to identify the hidden case directly, advantages remain clear when it is applied as an integrated risk assessment tool to facilitate early warning and effective planning with all-round consideration of exposure risks and other management factors (e.g. time and cost of programme implementation), also avoiding any potential biases of epidemiological indicators arising from limited diagnostic testing capacity, etc. This study also demonstrated that relative to downstream monitoring at sewage treatment plants, upstream monitoring directly at the sewerage network could be an option for densely populated cities with centralised wastewater treatment facilities and complicated sewerage networks, which can reveal both the general trend across the territory and identify districts/city blocks with higher risks, facilitating information-driven and tiered management strategies to maximize resource utilization through prioritization with time (during peak periods) and space (at hotspots).

CRediT authorship contribution statement

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Wai Thoe: Conceptualization, Methodology, Writing, Visualization.
Ron R. Yang: Conceptualization, Methodology, Writing.
Wai-ping Cheung: Methodology, Data analysis.
Che-kong Chen: Conceptualization, Methodology, Project administration and Supervision.
King-ho To: Methodology, software.
Kan-ming Pak: Methodology, Reviewing and Editing.
Hon-wan Leung: Methodology.
Wai-kwan Lai: Methodology.
Tsz-kin Wong: Methodology.
Tat-kwong Lau: Methodology.
Ka-wing Au: Methodology, Reviewing and Editing.
Xiao-qing Xu: Methodology.
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Ho-kwong Chui: Conceptualization, Methodology, Data analysis, Writing, Project administration and Supervision.

Data availability

The data that has been used is confidential.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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