Parallel Session 3: Preparedness for the Next Pandemic

T3a - Grid Monitoring of SARS-CoV-2 in Sewage for an Early-warning Sign of Community Outbreak

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Introduction and Project Objectives: Sewage surveillance, which tests the collection of faecal samples in a given sewershed, could offer a scalable, cost-effective strategy for measuring population-level infections. This project objectives are to test SARS-CoV-2 virus in community sewage collected from various sites of Hong Kong using methods established by the HKU team, to provide early-warning signals for the re-emergence of COVID-19 in local communities as a supplementary part for the clinical tests.

Methods: Sewage testing method for SARS-CoV-2 includes three steps: virus concentration, viral genetic material (RNA) extraction and quantification via Reverse transcription qPCR.

Results: The initial trial was conducted in early October 2020 as a response to an infection cluster at Kwai Chung. Initial findings of the trial indicated that sewage testing data were largely consistent with the clinical tests, and the sewage test was a useful tool to provide additional information for assessing the risk associated with outbreak in an area. We then applied our approach to monitor the re-emergence of SARS-CoV-2 circulation in local community by testing sewage samples collected from 26 stationary sites in Hong Kong. The sewage surveillance in this stage has effectively caught the rising trend of clinical cases in the fourth wave starting from the middle of November 2020.

From December 2020 to February 2021, routine sewage analysis at the 26 stationary sties were shifted to the monitoring of estates with infection clusters. Sewage testing results provided a basis for statutory public health action in identifying buildings and places for compulsory testing operations to uncover the infected individuals in local community. More than 50 confirmed cases were found, cutting off hidden transmission chains in these communities.

As the fourth wave of COVID-19 in Hong Kong begun to subside from February 2021, we resumed the routine monitoring of the 26 stationary sties for this HMRF project. Sewage testing results at this stage indicated the downward trend of the fourth outbreak.

Conclusion: The above results about sewage surveillance for SARS-CoV-2 in Hong Kong have demonstrated that the sewage surveillance could be used for the following purposes: (1) Providing early warning signals for COVID-19 outbreak; (2) Tracking the development trend of community outbreak; and (3) Complementing the monitoring of estates with infection clusters.

Since December 2020, daily sewage testing results have been incorporated into local monitoring scheme as an essential part of the whole control strategy of COVID-19. The systematic routine sewage monitoring programme now covers over 112 stationary sampling sites in Hong Kong, providing early warning signal of COVID-19 re-emergence for over 5.4 million people.

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T3b - Molecular Epidemiological Study of COVID-19 Cases in Hong Kong

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Introduction/Objectives: Molecular epidemiology can track the spread of epidemics. As a WHO COVID-19 Reference Laboratory, we attempted to use next generation sequence (NGS) technology to understand the viral dynamic of SARS-CoV-2 in Hong Kong. Findings from our analyses were reported to the Hong Kong Government on a weekly basis to inform field investigations, epidemiological studies and public health response.

Methods: We obtained SARS-CoV-2 positive respiratory samples from Centre for Health Protection and deduced full-length viral genomes using various NGS platforms (Illumina and Nanopore).

Results and Discussion: Hong Kong has experienced 4 major waves of COVID-19. Thus far, we have sequenced about 25% of all COVID-19 cases in Hong Kong. Although there were numerous importations of SARS-CoV-2 variants, including variants of concern (VOC), only three variant introductions were responsible for 90% of locally acquired cases. We also demonstrated that SARS-CoV-2 transmission patterns in these waves were very different from each others. In addition, we observed that non-adherence to prolonged preventative measures may lead to sustained local transmission in Hong Kong. We will discuss a few representative super-spreading events as examples.

We provided genetic evidence to demonstrate the world's first reverse zoonotic transmission (humans to pets), SARS-CoV-2 reinfection, and inflight transmission. We also identified certain settings (e.g., hotels and airport) and environmental conditions (e.g., poor ventilation) are potential hotspots for SARS-CoV-2 transmission. Our investigations also revealed possible virus sources, previously unknown transmission chains and misdiagnosed cases. These findings helped to develop or refine evidence-based control policy against COVID-19.

We also studied a substantial number of imported cases, thereby identifying countries seriously affected by VOC. Such information is critical to policy makers for revising travel restriction policy on incoming travellers. We also reasoned that travel hubs like Hong Kong can be used as surveillance sites to monitor SARS-CoV-2 sequence diversity at regional level.

In addition to local impacts, we used our experiences to draft WHO guidelines for genomic surveillance of SARS-CoV-2 and use our sequencing pipelines to analysis cases for overseas countries.

Conclusion: Hong Kong uses an elimination strategy to control COVID-19 and a close monitoring of SARS-CoV-2 sequence dynamic within Hong Kong is one of the essential components to achieve this. Our work has provided scientific underpinning to develop COVID-19 control strategies.

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T3c - Whole-genome Sequencing of COVID-19 Cases in Hong Kong: Development of a Geophylogenetic Database and Characterisation of SARS-CoV-2 Variants Circulating in the Community

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Background: In spite of stringent public health measures, Hong Kong experienced four epidemic waves of COVID-19, resulting in 12,348 infected cases and 213 deaths as of October 2021. Our team established Nanopore GridION and Illumina Miseq platform for whole-genome sequencing of SARS-CoV-2 at the early stage of the pandemic (in February 2020).

Objective: We aim to develop a phylogenomic database coupled with geospatial information system to unveil the transmission linkage of COVID-19 cases in Hong Kong.

Result: Phylogenomic analysis enabled us to identify an asymptomatic patient as the source of the first superspreading event of COVID-19 (Buddhist worship hall cluster) happened in late February 2020. After months of relative quiescence, a large COVID-19 outbreak (third wave) occurred in Hong Kong in July 2020. The phylogeny of some early cases indicated that the outbreak was attributed to a single lineage B.1.1.63, which was identical to viral genomes isolated from marine crew and aircrew who were exempted from mandatory quarantine.

In early October 2020, before the onset of the fourth wave, we identified a novel viral genome (lineage B.1.36.27) among local cases, which was most closely related to imported cases from Nepal. We highlighted flaws in hotel quarantine arrangements, under which travellers could still receive visitors. The Government later implemented the policy that inbound travellers should be quarantined at designated hotels and not be allowed visitors.

In December 2020, the United Christian Hospital experienced a large outbreak of SARS-CoV-2 in a palliative care and medicine ward. Later in January 2021, two healthcare workers from North District Hospital tested positive after taking care of COVID-19 patients. In both cases, we conducted phylogenomic analysis, enabling the hospitals to trace the transmission chain and prevent further cases.

In April 2021, we used rapid phylogenomic analysis to identify the transmission link between Filipino domestic helpers and an Indian businessman who had travelled from Dubai and tested positive for a SARS-CoV-2 VOC Beta. The genomic data enabled us to trace the entire transmission chain and their close contacts. Eventually, we identified an inbound traveller, who had stayed in the adjacent hotel room to the Indian businessman during quarantine, was the source of the transmission.

Recently we developed a phylogeographical information system which integrated the genomic, epidemiological, spatial and temporal information of COVID-19 cases in Hong Kong. Data visualizations are combined with the cartographic display to yield a clear view of the genomic diversity of SARS-CoV-2 variants and their distributions across Hong Kong districts, with a focus on the clustering of cases based on phylogenetic proximity.

Conclusion: Continued genomic surveillance of the imported cases is pivotal in detecting novel lineages that enters Hong Kong.

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T3d - Community Based Sero-epidemiological Study of COVID19 to Provide Data in Real Time on Age-stratified Infection Attack Rates, Disease Severity and Population-immunity, for Guiding Intervention Policy

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Introduction and Project Objectives: During an epidemic, diagnosed cases represent a tip-of-the-iceberg of infection taking place in the community. Sero-epidemiological studies provide an effective means to assess true infection attack rates in a community to inform control strategies. The aim of the study was to define infection attack rates, development and duration of population immunity to SARS-CoV-2 through population based serial cross sectional and longitudinal sero-epidemiology studies.

Methods: Venous blood samples were collected from volunteers from four study cohorts chosen to provide different levels of exposure risk and one of RT-PCR confirmed cases. These were Cohort A) Community-based longitudinal cohort; Cohort B) Serial age-stratified cross-sectional sampling of blood donors; Cohort C) Individuals working in occupations associated with increased social contacts who are at increased risk of infection; Cohort D) Individuals discharged from quarantine. Cohort E: Cohort E) was a longitudinal follow up of a cohort of RT-PCR confirmed COVID-19 infections to define the duration of immunity following natural infection. Sera were tested by for SARS-CoV-2 specific antibody and a subset tested for T cell responses.

Results: Total numbers of sera collected from Cohorts A, B, C and D as of end of August 2021 was 4599, 13,968, 2,066 and 4,296 respectively. Virus neutralization confirmed sero-prevalence in the unvaccinated individuals in the four cohorts were 1.3% (95% CI 0.9-1.9), 0.12% (95% CI 0.06-0.19), C 0.16% (95% CI 0.02-0.57) and 9.92% (95% CI 8.92-10.9) respectively. Cohort A is the most representative cohort for estimating population sero-prevalence. From this data we estimate a total of 61,000 (95% CI 18,000 to 128,000) infections which is age-adjusted incidence of 0.8%. Thus, case detection captured 29 % of overall infections occurring in Hong Kong. Blood donors under-estimated population sero-prevalence, likely because blood-donors are a more "health conscious" subgroup of the population and because blood donation is deferred for 180 days for anyone with confirmed COVID-19, likely excluding most of those with known infection.

Follow up of RT-PCR confirmed SARS-CoV infections showed that neutralizing antibody will remain detectable for around 1,717 days after symptom onset and that levels conferring 50% protection will be maintained for around 990 days post-symptom onset, in symptomatic patients. PRNT titres wane faster in children.

Discussion and Conclusion: Population based infection attack rate in the community remains low and 29% of infections are detected. Symptomatic COVID-19 disease is followed by relatively long-lived protection from re-infection by antigenically similar viruses.

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T3e - Investigation of Hong Kong's Early Detection, Assessment and Response (S-EDAR) System to the New Emerging Infectious Disease Outbreak COVID-19

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Introduction and Project Objectives: Our study aims to inform policy makers how Hong Kong's system of early detection, assessment and response (S-EDAR) to COVID-19 can be enhanced for control during the course of the pandemic at different transmission scenarios, and to inform future preparedness and response plans.

Methods: Relevant documents from WHO and other international public health organizations and scoping review of the international literature are used to evaluate the effectiveness and implementation of S-EDAR in Hong Kong with input from policy-makers and relevant stakeholders and comparative case study of government responses to provide real-time input for adjustments in pandemic control (Stage 1); and for an enhanced S-EDAR informed by international and local experts, and a Delphi survey for the feasibility and applicability (Stage 2). Inputs from:
- Comparative case studies of government responses in Hong Kong, Japan, Malaysia, South Korea, Shanghai, and Singapore;
- 35 local key informants including policy-makers, healthcare administrators and professionals in public and private sectors, business organizations, and general public/patients;
- 17 local and international experts;
- Analysis of infection surveillance and control data from Centre of Health Protection and Hospital Authority, and assessing effectiveness of screening strategies for inbound travellers

Results:
1. Comparative case studies
    The key lessons from the six jurisdictions highlighted the need for an on-going surveillance system, broaden screening, comprehensive preparedness plans and regular drills, information technology, capacity for testing, contact tracing, isolation and quarantine. Measures should be proportionate to the stages of the outbreak to reduce socio-economic impacts. Relaxation of measures should be based on risk assessment stratified by environmental settings, implemented in stages, and reversible when needed.

2. System dynamics modelling
    The simulation suggested that both PCR-polymerase chain reaction test (with a 7-day quarantine) and rapid antigen test screening for inbound travelers is insufficient to control local transmissions at travel volumes in 2019. However, travel volumes at the lower level 1 month before the entry ban of all countries can be controlled.

3. Development of an Enhanced S-EDAR for Hong Kong
    From findings of key informant interviews and expert workshops, an Enhanced three component S-EDAR has been developed 1) "Preparedness plan and resilience system", 2) "Readiness system" to mobilize resources, enhance surge capacities and scale-up response, and 3) "Response system" with implementation strategies at government, healthcare and community levels for response actions to be taken by different sectors.

Conclusion: The Enhanced S-EDAR will be a robust evolutionary system to enable preparedness, readiness and timely response to the rapidly changing transmission scenarios and dynamic context in the control of COVID-19 and emerging infectious diseases. Its feasibility and applicability will be scrutinized in the Delphi survey of local experts.

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