

# **Nosocomial outbreak of COVID-19 by possible airborne transmission leading to a superspreading event**

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**Summary:** A superspreading event due to possible airborne transmission demonstrated the need for stringent SARS-CoV-2 screening at admission to healthcare facilities and better architectural design of the ventilation system to prevent such outbreaks.

Accepted Manuscript

## **Abstract**

**Background:** Nosocomial outbreaks with superspreading of COVID-19 due to a possible airborne transmission has not been reported.

**Methods:** Epidemiological analysis, environmental samplings, and whole genome sequencing (WGS) were performed for a hospital outbreak.

**Results:** A superspreading event involving 12 patients and 9 healthcare workers (HCWs) occurred within 4 days in 3 of 6 cubicles at an old-fashioned general ward with no air exhaust built within the cubicles. The environmental contamination by SARS-CoV-2 RNA was significantly higher in air grilles (>2m from patients' head and not reachable by hands) than high-touch clinical surfaces (36.4%, 8/22 vs 3.4%, 1/29,  $p=0.003$ ). Six (66.7%) of 9 contaminated air exhaust grilles were located outside patient cubicle. The clinical attack rate of patients was significantly higher than HCWs (15.4%, 12/78 exposed-patients vs 4.6%, 9/195 exposed-HCWs,  $p=0.005$ ). Moreover, clinical attack rate of ward-based HCWs was significantly higher than non-ward-based HCWs (8.1%, 7/68 vs 1.8%, 2/109,  $p=0.045$ ). The episodes (mean  $\pm$  S.D) of patient-care duty assignment in the cubicles was significantly higher among infected ward-based HCWs than non-infected ward-based HCWs (6.0 $\pm$ 2.4 vs 3.0 $\pm$ 2.9,  $p=0.012$ ) during the outbreak period. The outbreak strains belong to SARS-CoV-2 lineage, B.1.36.27 (GISAID Clade GH) with the unique S-T470N mutation on WGS.

**Conclusion:** This nosocomial point source superspreading due to possible airborne transmission demonstrated the need for stringent SARS-CoV-2 screening at admission to healthcare facilities and better architectural design of the ventilation system to prevent such outbreaks. Portable high-efficiency particulate filters were installed in each cubicle to improve ventilation before resumption of clinical service.

## INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the most devastating emerging infectious disease in the 21<sup>st</sup> century, resulting in >116 million infections with >2.5 million deaths globally as of March 7, 2021[1]. Despite public health measures including universal masking, social distancing, school closure, working from home, territorial lock down, quarantining and testing international travelers, isolating confirmed cases, and quarantining close contacts, the pandemic remains uncontrolled in many parts of the world. Based on our experience from the SARS outbreak in 2003, universal masking in the community and enhancement of infection control measures were immediately implemented in Hong Kong soon after the official announcement of a cluster of community-acquired pneumonia related to a wet market in Wuhan, Hubei Province, China on December 31, 2019 (day 1 of our epidemic response)[2,3]. With these control measures, the number of COVID-19 patients per million population in Hong Kong was kept at a low level compared with neighboring areas with comparable social-economic characteristics. We also achieved zero hospital-acquired SARS-CoV-2 infection among healthcare workers (HCWs) during the three epidemic waves of COVID-19 in the first 300 day of our local epidemic combat[4,5].

However, when the fourth wave of COVID-19 started in early November 2020, the increasing number of cases in the community, especially asymptomatic cases, posed such a high epidemic pressure on the healthcare setting that the first nosocomial outbreak occurred on day 358 of our epidemic response. Although nosocomial outbreaks of COVID-19 have been reported in the hospitals and long-term care facilities, the risk factors of nosocomial acquisition of COVID-19 and information on genomic epidemiology was limited[6]. Here, we described a nosocomial outbreak of COVID-19 with a SARS-CoV-2 lineage B.1.36.27 carrying a distinct mutation, T470N, in Spike (S) protein.

## METHODS

### *Epidemiological investigation for COVID-19 outbreak*

In response to the third wave of COVID-19 in Hong Kong, universal screening for SARS-CoV-2 by reverse transcription polymerase chain reaction(RT-PCR) for all patients upon admission was adopted in all public hospitals under the governance of Hospital Authority since September 9, 2020(day 254). An outbreak investigation was initiated in a medical and palliative ward(2D) of United Christian Hospital(UCH), after a 91-year-old female patient(P1) was readmitted one day after discharge and confirmed SARS-CoV-2 positive by admission screening on December 22, 2020(day 358). The case definition for this outbreak investigation was any patients or HCWs with SARS-CoV-2 RT-PCR positive after any exposure at ward 2D. The time of exposure to ward 2D was initially defined as 14 days before and after December 22, 2020(the date of initiation of outbreak investigation with isolation of confirmed or exposed patients). The onset time was subsequently revised to December 18, 2020 when the index case was identified. Epidemiological investigation and contact tracing were conducted to identify the potential source of infection and the close contact among hospitalized patients and HCWs. For patients, a close contact is generally defined as one having face-to-face contact for >15 minutes or staying in the same cubicle for >2 hours with the confirmed case, regardless of their protection by surgical masks. For HCWs, a close contact is defined as one who carries out aerosol generating procedures for the confirmed COVID-19 case without wearing appropriate personal protective equipment (PPE) including surgical respirator, cap, face shield, isolation gown, and gloves, because these PPE are mandated for aerosol generating procedures in all clinical areas. COVID-19 screening test by RT-PCR was offered to all close contacts and non-close contacts in ward 2D, as well as HCWs in UCH who did not attend ward 2D as a precautionary measure. Infection control experts from local University, Hospital Authority, and Centre for Health Protection reviewed the preliminary data, performed on-site visit and investigation and made recommendation on control measures on December 26, 2020(day 362).

### ***Environmental investigation and disinfection***

Swab samples from the patient's bedside environment and the air grilles(10 cm x 120 cm in size at the ceiling height of 2.35m at the corridor and at 2.6m in the cubicle) of the air ventilation system in ward 2D were taken for SARS-CoV-2 by RT-PCR before and after terminal disinfection as we previously described[3,7]. For the patients' bedside environment, six high-touch surfaces including bedside rails, bedside table, bedside locker, monkey pull, call bell, and bed control panel were collected.

The heating, ventilation, and air conditioning(HVAC) system of ward 2D was assessed by hospital engineers to determine the direction of air flow and air-changes-per-hour(ACH). Environmental cleaning and disinfection were performed twice daily by sodium hypochlorite solution(1,000 ppm) with disposable wipes.

### ***Laboratory diagnosis and whole genome sequencing***

The nasopharyngeal flocced swab or deep throat saliva of patients and HCWs, and environmental samples were tested for SARS-CoV-2 by RT-PCR[3,7], and whole genome sequencing by Illumina or nanopore technology was performed as we previously described[8,9] for all the virus strains from patients and HCWs of this nosocomial outbreak, and other locally-acquired(n=68) and imported COVID-19 cases(n=9) reported within the study period(December 18, 2020  $\pm$  14 days) in Hong Kong.

### ***Phylogeographic analysis***

Maximum-likelihood whole genome phylogenetic tree was constructed using IQ-TREE2[10], with the generalized time reversible substitution model TIM2+F as the best predicted model by BIC. The option -czb was used to mask unrelated substructure of the tree with branch length representing mutation count of less than 1. The ultrafast bootstrap option was used with 100 replicates. The geographic distributions of the cases were displayed on Hong Kong map using ArcGIS Pro v.2.7.1

according to the coordinates of their residential addresses retrieved from the publicly accessible website[11]. This study was approved by the Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Hospital Cluster.

### ***Statistical Analysis***

The  $\chi^2$  and Fisher exact test, and t-Test were used as appropriate. A p value of  $<0.05$  was considered statistically significant.

## **RESULTS**

### ***Epidemiological investigation of COVID-19 outbreak***

On December 22, 2020 (day 358), a 91-year-old lady (P1) with underlying carcinoma of colon, was found to have COVID-19 upon readmission for shortness of breath. P1 was therefore isolated in the airborne infection isolation room (AIIR) per protocol[3]. Contact tracing identified 6 patient contacts staying in the same cubicle (cubicle F) with P1 during her incubation period. Two patients (P2 and P3) were COVID-19 test positive (Figure 1). Since P2 was transferred from intensive care unit after stabilization of her diabetic ketoacidosis to cubicle F, bed 35 on December 18, 2020, and transferred to cubicle D, bed 26 on December 21, 2020, further contact tracing of other close contact for SARS-CoV-2 testing on baseline, day 3, day 7, and day 12 thereafter and quarantine in AIIR .

The index case of this outbreak was identified to be P2, who could epidemiologically link up with the remaining hospital-acquired COVID-19 patients (HCAPs). The outbreak period was defined as the length of stay of P2 in ward 2D (December 18 to December 22, 2020). A total of 12 HCAPs, stayed in cubicle D, E, and F of ward 2D, were infected in this outbreak (Table 1). Aerosol generating procedures were not performed on these 12 HCAPs. The clinical attack rate was 15.4% (12 HCAPs out of 78 quarantined patients). Except for 2 ambulatory patients, the remaining 10 HCAPs were either chair-bound or bed-bound. Of these 12 HCAPs, the median age was 84 years (range: 20-92), nine (75%)

had either malignancies or chronic illnesses, and six (50%) were asymptomatic for COVID-19. Three of 6 symptomatic HACPs died 3 to 7 days after diagnosis. Except for P4, P11, and P12, the remaining 9 HACPs stayed in cubicle D and F during their entire hospitalization before the onset of this outbreak (Figure 2). The average length of stay within the same cubicle by the index and HACPs was 2 days (range: 1-3). P4 and P11 were infected after staying in a temporary bed, 39E, placed in the corridor outside cubicle F for 1 day, and P12 stayed in cubicle E all along and exposed to the other HACPs in the same ward for 4 days (Figure 2).

There were 86 ward-based HCWs working in ward 2D, including 54 nurses, 11 doctors, and 21 supporting and clerical staff. A total of 9 HCWs were found to be infected with COVID-19 (Table 2). Except for S1, who was a phlebotomist and have collected blood from the index case 3 days before symptom onset, and S4, a non-ward-based cleaning staff, 7 (8.1%) of 86 ward-based HCWs were infected. The mean episodes ( $\pm$  standard deviation) of duty assignment to care for patients in cubicle D to F was significantly higher among infected ward-based HCWs than the non-infected ward-based HCWs ( $6.0 \pm 2.4$  vs  $3.0 \pm 2.9$ ,  $p=0.012$ ) during the outbreak period. Of 109 non-ward-based HCWs who had visited ward 2D during the outbreak period, only two (S1 and S4) (1.8%) of 109 non-ward-based HCWs were tested positive. The clinical attack rate of ward-based HCWs was significantly higher than that of non-ward-based HCWs (8.1% vs 1.8%,  $p=0.045$ ). The clinical attack rate of HCWs was significantly lower than that of the patients (4.6%, 9 infected HCWs/195 HCWs exposed at ward 2D vs 15.4%, 12 HACPs/78 patients,  $p=0.005$ ). In addition to 86 ward-based and 109 non-ward based HCWs, another 5,481 HCWs without epidemiological link with this outbreak were voluntarily tested but negative for SARS-CoV-2. In total, 5,676 (92%) of 6,143 HCWs in UCH were tested in this outbreak investigation.

After isolation of SARS-CoV-2 infected patients and HCWs in AIIRs, quarantine of exposed patients and HCWs, and terminal disinfection, ward 2D was reopened on January 15, 2021. Portable high-efficiency-particulate air filters were installed in each cubicle. The outbreak formally ended on January 27, 2021 when there was no new COVID-19 case for 28 days since the last confirmed case.



### ***Environmental investigation and disinfection***

Of 52 environmental samples collected for SARS-CoV-2 RT-PCR in ward 2D, 23 samples were collected from clinical surfaces, which could be touched by patients and HCWs. Another 29 samples were collected from the air grilles of the heating, ventilation, and air conditioning (HVAC) system, which were housed at the ceiling of ward (>2m from the patients' head and not reachable by hands of patients or HCWs) (Table 3). The environmental contamination rate by SARS-CoV-2 RNA was significantly higher in the air grilles as compared with the clinical surfaces (36.4%, 8/22 vs 3.4%, 1/29,  $p=0.003$ ). Six (66.7%) of 9 air exhaust grilles and 2 (15.4%) of 13 air supply grilles were contaminated with SARS-CoV-2 RNA. The air grilles of HVAC system in the ward 2C with no COVID-19 patients has comparable design to ward 2D were chosen as control. The contamination rate of the air grilles in ward 2D was significantly higher than that in the control ward 2C (36.4%, 8/22 vs 0%, 0/35,  $p<0.001$ ). In all non-AIIR wards, the ACH was 6 (4 re-circulation and 2 fresh air) with air supply from patient cubicles and air exhausted to the corridors.

### ***Whole genome phylogenetic analysis***

Whole genome sequencing revealed that the nosocomial outbreak was attributed to a SARS-CoV-2 lineage, B.1.36.27(GISAID Clade GH), which is predominant in the fourth wave of COVID-19 in Hong Kong[12]. Compared to the reported genomes of this lineage, all 21 outbreak cases harbored an additional mutation, 22971c>a, leading to an amino acid substitution, T470N, in S protein. Phylogenetic analysis was conducted to illustrate the genomic relationship between the outbreak cases and other locally-acquired( $n=68$ ) and imported COVID-19 cases( $n=9$ ) reported within this study period (Figure 3). Sixteen locally-acquired cases were found to harbor T470N and were clustered with the 21 outbreak cases. The map with geographical distribution illustrated that those cases were aggregated within the catchment area of UCH (Figure 3). This finding indicated that a SARS-CoV-2 strain that harbored S-T470N was already disseminating in the surrounding districts of UCH in mid-December, 2020 and eventually led to the nosocomial outbreak.

## Discussion

With the bitter experience of 2003 SARS resulting in 386 infected HCWs with 8 deaths in Hong Kong, our top priority is to protect our HCWs by minimizing the risk of nosocomial transmission of COVID-19. With the implementation of multi-pronged infection control strategy in all hospitals under Hospital Authority, we have successfully prevent hospital-acquired COVID-19 among HCWs from pre-pandemic phase to pandemic phase[4,5,13,14] till this first nosocomial COVID-19 outbreak at day 358 since December 31, 2020. A thorough outbreak investigation for the root cause was therefore conducted to understand if lapses in infection control measures during patient care practices or unusual environmental factors have contributed to this outbreak.

Universal admission screening was considered by the United States and others as an additional measure for prevention of nosocomial outbreak[15,16]. However, false negative results may occur if the patients were tested when the viral load is low. Our index case failed to be picked up at admission and stayed in the non-AIIR ward. To address this limitation, repeated testing for SARS-CoV-2 is required in patients with unexplained respiratory symptoms or pulmonary infiltrates in the chest-radiograph.

The design of HVAC system, floor plan, and ceiling height of ward 2D were postulated to be important contributing factors in this nosocomial outbreak. There were no air exhaust grilles inside the semi-enclosed patient cubicles with unusually low ceiling height, which might increase the density of virus laden aerosol as evidenced by the finding that two-third of air exhaust grilles were contaminated with SARS-CoV-2 RNA. When the index patient was transferred to cubicle F, all patients in this 6-bed cubicle became infected. Since the air exhaust grilles were located in the corridor outside patient cubicles, which had an even lower ceiling height of 2.35 m, it may explain why two patients (P4 and P11) were infected when they sequentially stayed in bed 39E which was directly located underneath the air exhaust grille at the corridor outside cubicle F.

In contrast to our previous findings of undetectable SARS-CoV-2 RNA in the newly built airborne infection isolation rooms with standard ceiling height of 2.7m, 12 ACH with negative pressure,

and equipped with both air supply and exhaust grilles to allow unidirectional airflow inside the room[3,7], the cause of this nosocomial outbreak in the old-fashion general ward could be possibly attributed to airborne transmission. In the experience of SARS-CoV-1, possible airborne transmission is usually associated with the performance of aerosol generating procedures. In fact, potential airborne transmission of COVID-19 through the ventilation system in restaurant and public transport[17,18]. Viable SARS-CoV-2 was isolated from air samples collected 2 to 4.8 m away from the patients housed in a hospital room with 6 ACH[19]. Further research on airborne transmission in the hospital setting is warranted[20,21].

In addition to the environmental factors, the patients might have acquired SARS-CoV-2 from HCWs during patient care procedures by contact and respiratory droplets; especially when 83% of HACPs were either chair-bound or bed-bound. If the major cause of SARS-CoV-2 transmission was related to the suboptimal hand hygiene among HCWs or contamination of high-touch surfaces, cases should be found in all 6 cubicles, instead of HACPs found only in two cubicles (cubicle D and F). Our hand hygiene compliance has actually increased during the COVID-19 pandemic[22]. Furthermore, the extent of contamination by SARS-CoV-2 RNA was significantly higher in the air grilles than the ward environmental surfaces. As the air grilles of the ventilation system are always >2m from the head of patients and not reachable by hands of patients or HCWs, the presence of SARS-CoV-2 RNA in these air grilles cannot be coming from respiratory droplets but from airborne aerosols which constitutes an indirect evidence that this outbreak is possibly due to airborne transmission.

The mode of acquisition of COVID-19 by HCWs is difficult to ascertain. The infected HCWs had significantly more episodes of assignment to care for HACPs. These HCWs had more exposure to the cubicles and the outside corridor where the air grilles were contaminated by SARS-CoV-2 RNA. All HCWs worn surgical mask of ASTM (American Society of Testing and Materials) level 1 standard, of which the bacterial filtration efficiency for particle of 3 microns in size was  $\geq 95\%$ , and our hospitalized patients also worn these masks during the COVID-19 pandemic[23]. However, our HCWs may be at higher risk of exposure when they were required to care for unrecognized COVID-19 patients, especially during patients' mask-off activities such as mouth washing and oral feeding. Mask-off

activities was shown to have increased risk of COVID-19 transmission in the community[2], whereas universal masking could reduce the exhalation of virus-containing respiratory droplets or airborne aerosol[24]. Therefore, we have subsequently enhanced our staff protection with eye protection such as eye shields, face shields or goggles while caring patients during their mask-off time.

The present outbreak was a SSE because a total of 20 secondary infected cases were diagnosed within 9 days[25]. SSE was arbitrarily defined when an index patient transmitted to >8 other persons at the time of SARS[26]. The hospital environment may have facilitated transmission from the index patient to a larger number of cases. When case prevalence is very high in the community, SSE as suggested by epidemiological analysis cannot be confirmed if whole genome sequencing is not performed[27]. Notably the SSE of our present outbreak was also confirmed by whole genome sequencing that S-T470N, which has not been found in other sequences publicly available at GISAID, was found in all patients and HCWs in this outbreak. Further genomic investigation for other locally-acquired cases revealed that SARS-CoV-2 lineage B.1.36.27 carrying S-T470N mutation have recently emerged in Hong Kong and had been disseminating in the geographical vicinity of UCH shortly before the nosocomial outbreak.

Although nosocomial outbreaks of COVID-19 had been reported in many parts of the world (Supplementary Table), our report was the only one with findings in environmental surveillance which suggest the mechanism of possible airborne transmission leading to SSE. This proposition was further confirmed by whole genome sequencing. Our study is limited by the lack of air sampling during the outbreak, because by the time of on-site investigation, all patients and contacts were isolated and quarantined. Despite this limitation, many of the air grille samples were still RT-PCR positive. Better architectural design of the healthcare ventilation system is important to prevent such outbreaks.

## **NOTES**

### **Contributors**

VC-CC, S-CW, and K-YY had roles in study design, data analysis, literature search, and writing up of the manuscript. VC-CC, KS-CF, S-CW, LS-KC, K-YC, W-SC, and K-YY had roles in outbreak investigation. GK-HS, DCL, HT, and KK-WT had roles in whole genome sequencing and phylogenetic analysis. L-KL, W-MC, JS-LL, AW-HC, KK-GT, JDI, KS-SL, and KKL had roles in laboratory work. M-SW had role in spatial geographic analysis. All authors reviewed and approved the final version of the manuscript.

### **Acknowledgement**

We thank our frontline staff and management team of United Christian Hospital, Hospital Authority to facilitate this study.

### **Financial support**

This study was partially supported by the Health and Medical Research Fund (HMRF) Commissioned Research on Control of Infectious Disease (Phase IV), CID-HKU1-2 and CID-HKU1-16, and HMRF Commissioned Research on COVID-19, COVID190204, Food and Health Bureau, Hong Kong SAR Government.

### **Potential conflicts of interest**

The No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

## References

1. Weekly epidemiological update - 9 March 2021. World Health Organization. <https://www.who.int/publications/m/item/weekly-epidemiological-update---10-march-2021> Published March 9, 2021. Accessed March 11, 2021.
2. Cheng VC, Wong SC, Chuang VW, et al. The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2. *J Infect* **2020**;81:107-114.
3. Cheng VCC, Wong SC, Chen JHK, et al. Escalating infection control response to the rapidly evolving epidemiology of the coronavirus disease 2019 (COVID-19) due to SARS-CoV-2 in Hong Kong. *Infect Control Hosp Epidemiol* **2020**;41:493-498.
4. Cheng VCC, Wong SC, Chuang VWM, et al. Absence of nosocomial transmission of coronavirus disease 2019 (COVID-19) due to SARS-CoV-2 in the pre-pandemic phase in Hong Kong. *Am J Infect Control* **2020**;48:890-896.
5. Cheng VC, Wong SC, Tong DW, et al. Multi-pronged infection control strategy to achieve zero nosocomial COVID-19 infection among Hong Kong healthcare workers in the first 300 days of combat. *Infect Control Hosp Epidemiol* **2021**;doi: 10.1017/ice.2021.119.
6. Abbas M, Robalo Nunes T, Martischang R, et al. Nosocomial transmission and outbreaks of coronavirus disease 2019: the need to protect both patients and healthcare workers. *Antimicrob Resist Infect Control* **2021**;10:7.
7. Cheng VC, Wong SC, Chan VW, et al. Air and environmental sampling for SARS-CoV-2 around hospitalized patients with coronavirus disease 2019 (COVID-19). *Infect Control Hosp Epidemiol* **2020**;41:1258-1265.
8. To KK, Chan WM, Ip JD, et al. Unique SARS-CoV-2 clusters causing a large COVID-19 outbreak in Hong Kong. *Clin Infect Dis* **2020**;doi:10.1093/cid/ciaa1119
9. Leung KS, Ng TT, Wu AK, et al. Territorywide Study of Early Coronavirus Disease Outbreak, Hong Kong, China. *Emerg Infect Dis* **2021**;27:196-204.
10. Minh BQ, Schmidt HA, Chernomor O, et al. IQ-TREE 2: New Models and Efficient Methods for Phylogenetic Inference in the Genomic Era. *Mol Biol Evol* **2020**;37:1530-1534.
11. Archives of List of buildings with confirmed / probable cases of COVID-19. Centre for Health Protection. Department of Health. The Government of the Hong Kong Special Administrative Region. <https://www.chp.gov.hk/en/features/102991.html> Accessed February 9, 2021.
12. Siu GK, Lee LK, Leung KS, et al. Will a new clade of SARS-CoV-2 imported into the community spark a fourth wave of the COVID-19 outbreak in Hong Kong? *Emerg Microbes Infect* **2020**;9:2497-2500.
13. Wong SC, Leung M, Lee LL, Chung KL, Cheng VC. Infection control challenge in setting up a temporary test centre at Hong Kong International Airport for rapid diagnosis of COVID-19 due to SARS-CoV-2. *J Hosp Infect* **2020**;105:571-573.
14. Wong SC, Leung M, Tong DW, et al. Infection control challenges in setting up community isolation and treatment facilities for patients with coronavirus disease 2019 (COVID-19): implementation of directly-observed environmental disinfection. *Infect Control Hosp Epidemiol* **2020**:1-29. doi:10.1017/ice.2020.1355
15. Interim infection prevention and control recommendations for healthcare personnel during the coronavirus disease 2019 (COVID-19) pandemic. 2020 Centers for Disease Control and Prevention. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html> Updated February 23, 2021. Accessed March 1, 2021.

16. Scheier T, Schibli A, Eich G, et al. Universal Admission Screening for SARS-CoV-2 Infections among Hospitalized Patients, Switzerland, 2020. *Emerg Infect Dis* **2021**;27:404-410.
17. Lu J, Gu J, Li K, et al. COVID-19 Outbreak Associated with Air Conditioning in Restaurant, Guangzhou, China, 2020. *Emerg Infect Dis* **2020**;26:1628-1631.
18. Shen Y, Li C, Dong H, et al. Community Outbreak Investigation of SARS-CoV-2 Transmission Among Bus Riders in Eastern China. *JAMA Intern Med* **2020**;180:1665-1671.
19. Lednicky JA, Lauzardo M, Fan ZH, et al. Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients. *Int J Infect Dis* **2020**;100:476-482.
20. Chia PY, Coleman KK, Tan YK, et al. Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients. *Nat Commun* **2020**;11:2800.
21. Nissen K, Krambrich J, Akaberi D, et al. Long-distance airborne dispersal of SARS-CoV-2 in COVID-19 wards. *Sci Rep* **2020**;10:19589.
22. Wong SC, AuYeung CH, Lam GK, et al. Is it possible to achieve 100 percent hand hygiene compliance during the coronavirus disease 2019 (COVID-19) pandemic? *J Hosp Infect* **2020**;105:779-781.
23. Wong SC, Lam GK, AuYeung CH, et al. Absence of nosocomial influenza and respiratory syncytial virus infection in the coronavirus disease 2019 (COVID-19) era: Implication of universal masking in hospitals. *Infect Control Hosp Epidemiol* **2021**;42:218-221.
24. Brooks JT, Butler JC. Effectiveness of Mask Wearing to Control Community Spread of SARS-CoV-2. *JAMA* **2021**;doi:10.1001/jama.2021.1505
25. Transmission of SARS-CoV-2: implications for infection prevention precautions. World Health Organization. <https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions>. Published July 9, 2020. Accessed February 12, 2021.
26. Shen Z, Ning F, Zhou W, et al. Superspreading SARS events, Beijing, 2003. *Emerg Infect Dis* **2004**;10:256-60.
27. Voeten H, Sikkema RS, Damen M, et al. Unravelling the modes of transmission of SARS-CoV-2 during a nursing home outbreak: looking beyond the church super-spread event. *Clin Infect Dis* **2020**;doi:10.1093/cid/ciaa1664

Table 1. Epidemiological characteristics patients infected with coronavirus disease 2019 (COVID-19) in the medical and palliative ward (2D), United Christian Hospital

Case no.	Sex / age	Underlying disease <sup>a</sup> (acute presentation) / hospitalization, d, before staying with the index case <sup>b</sup> [maximum duration, d, of stay with the index case in the same cubicle]	Positive test: date / specimen (CT value) <sup>c</sup>	Clinical symptoms of COVID-19	Outcome / duration, d, of hospitalization after admission and [diagnosis of COVID-19]
P1	F/91 <sup>d</sup>	CA colon (SOB) / 17 d [cubicle F, 3 d]	Dec 22, 2020 / DTS (14.5) <sup>e</sup>	SOB, at dx	Recovered / 66 d [45 d]
P2	F/84 <sup>f</sup>	DM (DKA) / cubicle F, 3 d & cubicle D, 1 d <sup>b</sup>	Dec 22, 2020 / NPS (12.5) <sup>g</sup>	Asymptomatic	Remained hospitalized
P3	F/71 <sup>d</sup>	CA vagina (PVB) / 108 d [cubicle F, 3 d]	Dec 22, 2020 / NPS (24.1) <sup>g</sup>	Fever, 1 d post-dx	Death / 119 d [7 d]
P4	F/83 <sup>h</sup>	Nil (suspected DVT) / 0 d [cubicle F corridor, 1 d] <sup>i</sup>	Dec 24, 2020 / DTS (13.4) <sup>j</sup>	Cough, 3 d pre-dx	Recovered / 45 d [39 d]
P5	F/74 <sup>d</sup>	CA lung (SOB) / 2 d [cubicle F, 3 d]	Dec 25, 2020 / DTS (15.3) <sup>k</sup>	Fever, at dx	Death / 12 d [3 d]
P6	F/92 <sup>d</sup>	CHF (SOB) / 0 d [cubicle D, 1 d]	Dec 25, 2020 / NPS (10.6) <sup>k</sup>	Fever, at dx	Recovered / 21 d [17 d]
P7	F/89 <sup>d</sup>	CHF (SOB) / 11 d [cubicle F, 3 d]	Dec 25, 2020 / NPS (27.3) <sup>k</sup>	SOB, 3 d pre-dx	Death / 23 d [5 d]
P8	F/87 <sup>d</sup>	CA cervix (PVB) / 49 d [cubicle F, 3 d]	Dec 25, 2020 / DTS (15.2) <sup>k</sup>	Asymptomatic	Recovered / 93 d [37 d]
P9	F/73 <sup>d</sup>	Nil (ARF) / 5 d [cubicle D, 1 d]	Dec 25, 2020 / NPS (12.0) <sup>k</sup>	Asymptomatic	Recovered / 51 d [42 d]
P10	F/84 <sup>d</sup>	MDS (acute cholecystitis) / 7 d [cubicle D, 1 d]	Dec 25, 2020 / DTS (24.9) <sup>k</sup>	Asymptomatic	Death / 48 d [37 d]
P11	F/20 <sup>h</sup>	Nil (acute tonsillitis) / 0 d [cubicle F corridor, 1 d] <sup>i</sup>	Dec 26, 2020 / DTS (40.6) <sup>l</sup>	Asymptomatic	Recovered / 17 d [11 d]
P12	F/90 <sup>d</sup>	CA colon (UTI) / 9 d [same ward, 4 d] <sup>m</sup>	Dec 26, 2020 / NPS (22.3) <sup>l</sup>	Asymptomatic	Remained hospitalized

Note. ARF, acute renal failure; CA, carcinoma; CHF, congestive heart failure; CT, cycle threshold value of reverse transcription polymerase chain reaction for SARS-CoV-2 RNA detection; d, day; DM, diabetes mellitus; DKA, diabetic ketoacidosis; DTS, deep throat saliva; DVT; deep vein thrombosis; dx, diagnosis; IO, intestinal obstruction; MDS, myelodysplastic syndrome; NPS, nasopharyngeal swab; PVB; per vaginal bleeding; SOB, shortness of breath; UTI, urinary tract infection.

<sup>a</sup> The principle diagnosis was presented; <sup>b</sup> the index case was considered as a superspreader, patient P2 staying in ward 2D cubicle F (bed 35) from December 18, 2020 to December 21, 2020 and transferring to ward 2D cubicle D (bed 26) from December 21, 2020 to December 22, 2020; <sup>c</sup> DTS or NPS was collected for reverse transcription polymerase chain reaction for SARS-CoV-2 RNA detection upon admission and during contact tracing for potential secondary cases;

<sup>d</sup> chair-bound patient; <sup>e</sup> P1 was diagnosed by admission screening. Since P1 was just discharged from ward 2D of United Christian Hospital 1 day (December



21, 2020) before readmission (December 22, 2020), P1 was defined as hospital-acquired COVID-19 and contact tracing was performed to identify the source of infection as well as other potential secondary cases; <sup>f</sup> bed-bound patient; <sup>g</sup> COVID-19 was diagnosed in the first round of contact tracing; <sup>h</sup> ambulatory patient; <sup>i</sup> this patient bed (bed 39E) was directly underneath the exhaust vent of air ventilation system; <sup>j</sup> P4 was tested in outpatient setting because of the onset of cough 3 days after discharge from ward 2D of United Christian Hospital; <sup>k</sup> the first round of COVID-19 screening was undetectable for SARS-CoV-2 RNA on December 22, 2020, and SARS-CoV-2 RNA was detected by the second round of COVID-19 screening on December 25, 2020; <sup>l</sup> the first round of COVID-19 screening was undetectable for SARS-CoV-2 RNA on December 22, 2020, and SARS-CoV-2 RNA was detected by the second round of COVID-19 screening on December 26, 2020; <sup>m</sup> P12 stayed in cubicle E, where it was located between cubicle F and cubicle D, and did not stay in the same cubicle with the index case.

Table 2. Epidemiological investigation of coronavirus disease 2019 (COVID-19)-infected healthcare workers (HCWs) in the medical and palliative ward (2D), United Christian Hospital

Case no.	Sex / age	Rank <sup>a</sup> / epidemiological analysis of HCWs exposure to the index case <sup>b</sup>	Symptoms (d of symptom onset after last / first exposure to index case <sup>b</sup> )	Positive test: date / specimen (CT value)	Hospitalization (d) <sup>c</sup>
S1	F/52	Phlebotomist <sup>c</sup> / blood taking to the index case <sup>d</sup>	Fever (3 d) <sup>e</sup>	Dec 24, 2020 / DTS (30.3)	17
S2	F/51	Nurse / oral care for the index case daily	Cough (4 d / 8 d)	Dec 25, 2020 / DTS (19.9)	16
S3	F/29	Nurse / RT to the index case daily	Fever, headache (2 d / 6 d)	Dec 26, 2020 / NPS (27.3)	11
S4	F/49	Cleaning staff <sup>d</sup> / performing terminal disinfection in ward 2D <sup>f</sup>	Asymptomatic	Dec 26, 2020 / DTS (27.7)	11
S5	F/32	Nurse / Insertion to Ryle's tube to the index case	Sore throat (4 d / 8 d)	Dec 26, 2020 / NPS (24.4)	11
S6	F/48	Nurse / team leader without direct care for the index case <sup>g</sup>	Headache (2 d / 6 d) <sup>h</sup>	Dec 26, 2020 / DTS (23.1)	10
S7	F/62	PCA / feeding medication, turning patients in ward <sup>i</sup>	Fever, cough, RN (3 d / 7 d)	Dec 26, 2020 / NPS (27.3)	10
S8	F/22	Nurse / feeding medication & RT, turning patients in ward <sup>i</sup>	Cough, RN (5 d / 9 d)	Dec 29, 2020 / DTS (26.7)	10
S9	F/38	PCA / feeding medication & meal, turning patients in ward <sup>i</sup>	Fever, sore throat, cough (6 d / 10 d)	Dec 30, 2020 / DTS (27.8)	8

Note. CT, cycle threshold value of reverse transcription polymerase chain reaction for SARS-CoV-2 RNA detection; d, day; DTS, deep throat saliva; NPS, nasopharyngeal swab; PCA, patient care assistant; RN, running nose; RT, Ryle's tube feeding.

<sup>a</sup> Ward-based HCWs in ward 2D unless specified. Ward-based HCWs were stationed in the ward during their work shift; <sup>b</sup> the index case was considered as a superspreader, patient P2 staying in ward 2D from December 18, 2020 to December 22, 2020; <sup>c</sup> all infected healthcare workers were in stable condition and recovered; <sup>d</sup> non-ward-based HCWs in ward 2D; <sup>e</sup> exposure to index case on December 21, 2020; <sup>f</sup> terminal disinfection performed on December 21 and December 25, 2020; <sup>g</sup> deliver medication to another unrecognized COVID-19 patient, patient P9; <sup>h</sup> day of symptom onset based on the exposure to patient P10; <sup>i</sup> including index case, P2.

Table 3. Environmental surveillance of high-touched surfaces, hand washing basins, and air grilles for SARS-CoV-2 RNA by RT-PCR in the medical and palliative ward (2D), United Christian Hospital

Location <sup>a</sup>	Number of positive / number of surfaces being sampled [% of positive]	CT value (if positive)
High-touch surfaces <sup>b</sup>		
Bed 33	0 / 6	NA
Bed 34	0 / 6	NA
Bed 37	0 / 6	NA
Bed 38	0 / 6	NA
Patient privacy curtain <sup>b</sup>		
Bed 33	0 / 1	NA
Hand washing basins <sup>c</sup>		
Washing basin in cubicle D	0 / 1	NA
Water taps in cubicle D	1 / 1	35.8
Washing basin in cubicle F	0 / 1	NA
Water taps in cubicle D	0 / 1	NA
Areas touched by patients and HCWs (subtotal)	1 / 29 [3.4%]	NA
Air grilles of HVAC system <sup>d</sup>		
Air supply air grilles to		
Single room bed 1	0 / 1	NA
Single room bed 2	0 / 1	NA
Cubicle A	0 / 1	NA
Cubicle B	0 / 1	NA
Cubicle C	0 / 1	NA
Cubicle D	1 / 1	34.4
Cubicle E	1 / 1	38.0
Cubicle F	0 / 1	NA
Cubicle G	0 / 1	NA
Single room bed 45	0 / 1	NA
Nurse station (central)	0 / 1	NA
Nurse station (near cubicle A)	0 / 1	NA
Nurse station (near cubicle F)	0 / 1	NA
Air exhaust air grilles from		
Corridor outside female toilet	1 / 1	36.4
Corridor outside male toilet	1 / 1	33.2
Corridor outside cubicle D & E	1 / 1	34.1
Corridor outside cubicle F	1 / 1	33.6
Corridor outside cubicle G	1 / 1	37.6
Corridor outside single room bed 45	0 / 1	NA

Nurse station (central)	1 / 1	34.6
Nurse station (near cubicle A)	0 / 1	NA
Nurse station (near cubicle F)	0 / 1	NA
Areas non-touched by persons (subtotal)	8 / 22 [36.4%]	NA

CT, cycle threshold value of reverse transcription polymerase chain reaction for SARS-CoV-2 RNA detection; HCWs, healthcare workers; HVAC, heat, ventilation, and air conditioning; NA, not applicable.

<sup>a</sup> The geographic location the items of ward 2D can be referred to Figure 2; <sup>b</sup> six high-touch surfaces included bedside rails, bedside table, bedside locker, monkey pull, call bell, and bed control panel. The environmental samples were collected on December 22, 2020; <sup>c</sup> the environmental samples were collected on December 26, 2020; <sup>d</sup> the environmental samples were collected on December 29 to December 31, 2020.

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## Figure Legend

### Figure 1.

Timeline of the epidemiological investigation for COVID-19 outbreak in a medical and palliative ward (ward 2D) in United Christian Hospital, Hong Kong

Note. AICU, adult intensive care unit; DKA, diabetic ketoacidosis; NPS: nasopharyngeal swab; PCA, patient care assistant; SOB, shortness of breath.

# denoted the recognition of a hospital-acquired COVID-19 case and the commencement of outbreak investigation on December 22, 2020.

P1 to P12 denoted the 12 hospital-acquired COVID-19 patients and S1 to S9 denoted the 9 hospital-acquired COVID-19 healthcare workers.

### Figure 2.

Layout of the medical and palliative ward (ward 2D) with nosocomial outbreak of COVID-19

Note. It is a mixed ward to care for patients with general medical problems and terminal illnesses. The size of cubicle is 43.56 square meter (6.6m x 6.6m) and the walls go up to the top that separate each cubicle completely. P1 to P12 denoted the 12 hospital-acquired COVID-19 patients. The dotted line denoted movement of P2 who stayed in cubicle F (bed 35) from December 18, 2020 to December 21, 2020 and transferred to cubicle D (bed 26) from December 21, 2020 to December 22, 2020. Bed 39E was a temporary bed and was directly underneath the exhaust vent of air ventilation system. Two patients (P4 & P11) with hospital-acquired COVID-19 stayed in bed 39E.

### Figure 3.

Phylogeographic analysis of the genomic and spatial relationship between the COVID-19 cases involving in the nosocomial outbreak, locally-acquired and imported COVID-19 cases in Hong Kong during the study period (i.e. December 18, 2020  $\pm$ 14 days).

Note. The tree was constructed by maximum likelihood method. The reference genome Wuhan-Hu-1 (GenBank accession number MN908947.3) was used as the root of the tree. P and S represented patient and healthcare workers isolates of SARS-CoV-2 in the nosocomial outbreak in United Christian Hospital (UCH), respectively. L and Imp represented isolates of SARS-CoV-2 from locally acquired and imported COVID-19 cases which were subjected to whole genome sequencing.

On the geographic map, the residential location of patients and healthcare workers in the nosocomial outbreak were denoted as green and yellow dots respectively. All harbored S-T470N mutation. Sixteen locally-acquired cases that were not fulfilled the case definition of this nosocomial outbreak were found to harbor S-T470N. These cases were denoted as pink dots. Other locally-acquired cases that did not have S-T470N were denoted as blue dots. For extensive link analysis, all cases (n=2,428) reported within the study period were also included. Each grey dot represents the residential location of a case. The darkness is directly proportional to the number of confirmed cases in that location.

Figure 1

### Timeline of the epidemiological investigation for COVID-19 outbreak

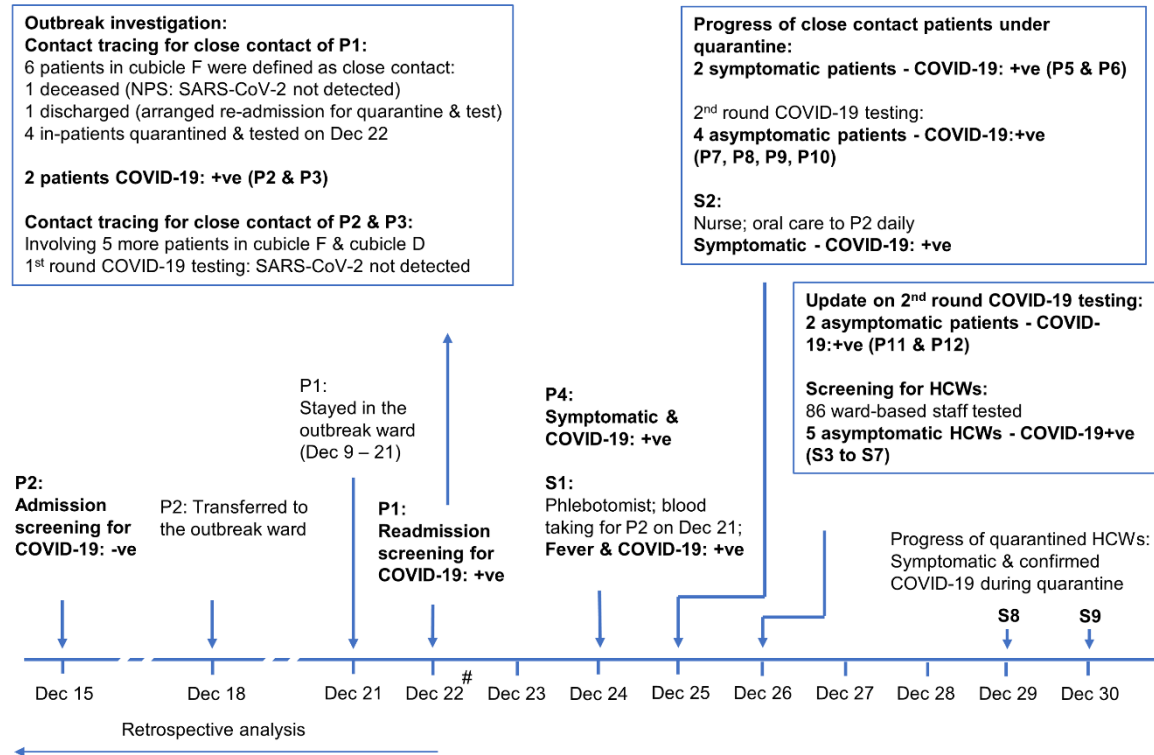
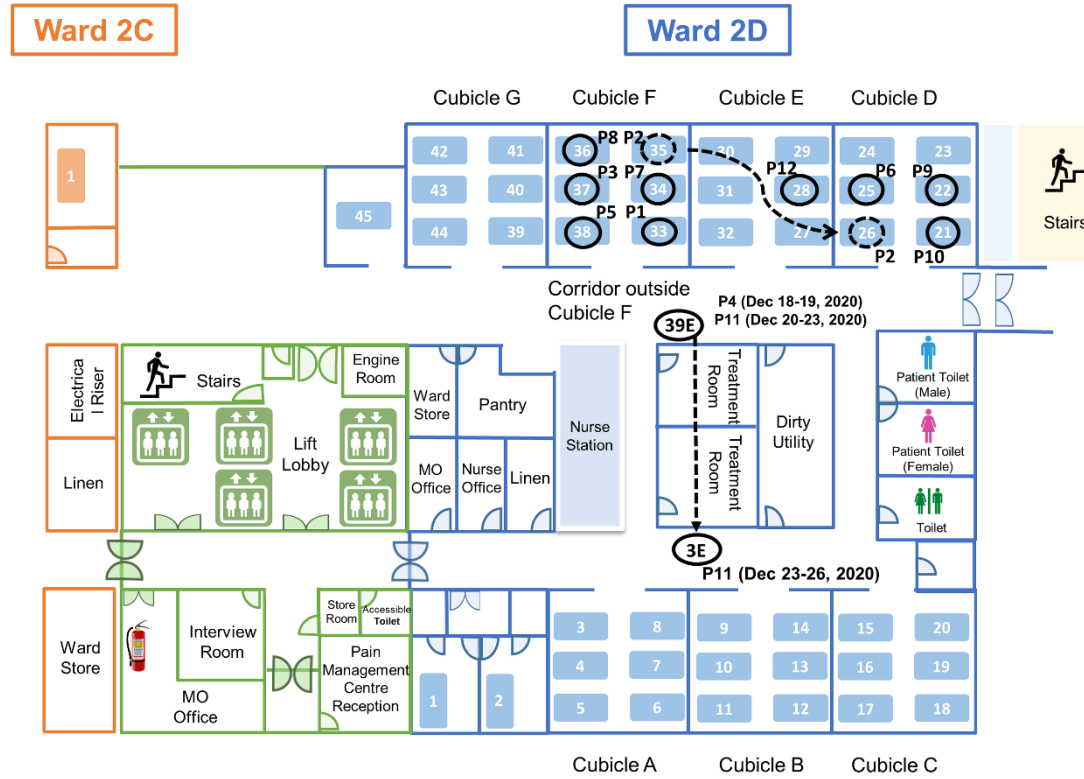


Figure 2



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Figure 3

