

A COVID-19 nursing home cluster linked to a household transmission: An epidemiological, clinical and phylogenetic investigation.

Junxiong Pang*, Huei Nuo Tan*^, Tze Minn Mak, Sophie Octavia, Sebastian Maurer-Stroh, Fernanda L Sirota, Mark Peng Chew Chan, Ian Yi Onn Leong, Valerie TJ Koh, Peng Lim Ooi, Shawn Vasoo, Dale Fisher, Lin Cui, Heidi Rafman, Jeffery Cutter, Vernon J Lee^

*These authors contributed equally

^Corresponding authors:

Huei Nuo Tan

Tan Tock Seng Hospital

Email: huei_nuo_tan@ttsh.com.sg

Vernon J Lee

Communicable Diseases Division

Ministry of Health, Singapore

12 College Road, Singapore 169852

Email: Vernon_LEE@moh.gov.sg

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Author's Name	Highest Degree	Affiliation/ Institution	Email Address
Junxiong Pang	PhD	Ministry of Health, Singapore; Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore	vincent_pang@moh.gov.sg
Huei Nuo Tan	MBBS	Department of Geriatric Medicine, Tan Tock Seng Hospital	huei_nuo_tan@ttsh.com.sg
Tze Minn Mak	PhD	National Public Health Laboratory, National Centre for Infectious Diseases, Singapore	mak_tze_minn@moh.gov.sg
Sophie Octavia	PhD	National Public Health Laboratory, National Centre for Infectious Diseases, Singapore	Sophie_octavia@moh.gov.sg
Sebastian Maurer-Stroh	PhD	Bioinformatics Institute, Agency for Science, Technology and Research, Singapore; Department of Biological Sciences, National University of Singapore, Singapore; National Public Health Laboratory, National Centre for Infectious Diseases, Singapore	sebastianms@bii.a-star.edu.sg
Fernanda L Sirota	PhD	Bioinformatics Institute, Agency for Science, Technology and Research, Singapore	fernanda@bii.a-star.edu.sg
Mark Peng Chew Chan	MBBS	Department of Geriatric Medicine, Tan Tock Seng Hospital	peng_chew_chan@ttsh.com.sg
Ian Yi Onn Leong	MBBS	Division of Central Health, Tan Tock Seng Hospital	ian_leong@ttsh.com.sg
Valerie TJ Koh	MPH	Ministry of Health, Singapore	valerie_tj_koh@moh.gov.sg
Steven Peng Lim Ooi	MBBS	Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore; National	steven_pl_ooi@ncid.sg

		Centre for Infectious Diseases, Singapore	
Shawn Vasoo	MBBS	National Centre for Infectious Diseases, Singapore	shawn_vasoo@ncid.sg
Dale Fisher	MBBS	National University Hospital and National University Health System, Singapore	mdcfda@nus.edu.sg
Lin Cui	PhD	National Public Health Laboratory, National Centre for Infectious Diseases, Singapore	cui_lin@moh.gov.sg
Heidi Rafman	MBA	Agency for Integrated Care, Singapore	heidi.rafman@aic.sg
Jeffery Cutter	MBBS	Ministry of Health, Singapore; National Centre for Infectious Diseases, Singapore	jeffery_cutter@moh.gov.sg
Vernon Jian Ming Lee	PhD	Ministry of Health, Singapore; Saw Swee Hock School of Public Health, Singapore	vernon_lee@moh.gov.sg

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Abstract (221/250 words)

Background

Residents in nursing homes are at risk of high morbidity and mortality due to coronavirus disease 2019 (COVID-19). We report the first nursing home COVID-19 outbreak in Singapore and its clinical, epidemiological, laboratory and phylogenetic investigations.

Methods

Serial point prevalence testing was conducted among the residents and staff following identification of the index case (a symptomatic resident) with SARS-CoV-2 infection. Active contact tracing, screening of close contacts, whole genome sequencing and phylogenetic analysis were conducted to identify the source and extent of the outbreak.

Results

Among the 108 residents and 56 healthcare workers (HCW) in the nursing home, 14 (13%) residents and two (3.6%) HCW were diagnosed with COVID-19, with case fatality rate of 28.6% (4/14) among the residents. Five residents were symptomatic (35.7%) and the others were asymptomatic (64.3%) before the point prevalence survey. The genomic virus typing in this nursing home outbreak was lineage B.6 which is rare among other GISAID clades globally but common regionally. Among the family contacts of the two infected healthcare workers, only one member was infected and had recent travel history.

Conclusion

The COVID-19 outbreak in a nursing home in Singapore was contained through prompt epidemiological investigations, active case finding and containment, and infection prevention and control measures.

Research in Context

Evidence before this study

Residents in nursing homes are at risk of high morbidity and mortality due to coronavirus disease 2019. The identification of potential source/s of infection and understanding of the transmission pattern are challenging.

Added value of this study

This study identified that the case-fatality rate (28.6%) is as high as nursing homes in other countries even though active infection prevention and control measures were implemented promptly. Majority (64.3%) of the resident cases were asymptomatic cases which is challenging for surveillance and investigation. The use of clinical, epidemiological and phylogenetic analysis identified the likely introduction of SAR-CoV-2 from a household transmission of an infected nursing staff, who stays outside the nursing home.

Implications of all the available evidence

Strict cohorting of staffs to designated wards, monitoring of staffs' health status before work and increasing staffs' residential capacity in the nursing home are likely to prevent and reduce the spread of SARS-CoV-2 transmission in the nursing home facility.

Introduction (2594/2500 words)

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus resulted in the coronavirus disease 2019 (COVID-19) pandemic as declared by the World Health Organization on 11 March 2020. Singapore reported the first imported and local COVID-19 case on January 23 and February 1, 2020, respectively. Among the different risk groups for spread and severity of COVID-19 infection, nursing homes have been associated with high mortality and morbidity in many countries¹⁻⁴. Nursing homes are communal living facilities with a vulnerable population that requires rendered care, tends to be older, and has multiple comorbidities, cognitive and physical disabilities. They are a hotbed for large outbreaks because of difficulties in detection and implementation of safe distancing and infection control measures^{5,6}.

Nursing homes in Singapore are long-term care facilities catering to those who require skilled nursing care, medical care, and rehabilitative services. In this study we report the first nursing home outbreak in Singapore and the measures implemented to contain it. We performed serial point-prevalence survey (PPS) among the residents to assess the extent of transmission. In the course of this investigation, we have identified the source of infection, asymptomatic infections and pre-symptomatic transmission through a combination of clinical, epidemiological, laboratory and phylogenetic investigations.

Methods

Outbreak Investigation and Response

The facility had a 111-bed capacity with 55 female residents, 53 male residents and 56 health care workers (HCW) at the time of the outbreak. The facility is housed across 3 single-level blocks – block A housed both males and females in two separate wings, block B housed male

residents only and block C female residents only (Figure 1). Each block consists of 3 to 5 cubicles with 4 to 18 beds in each cubicle and the resident areas had natural ventilation with fans. Approximately 20% of the residents were ambulant. The remainder were non-ambulant or required assistance.

On March 30, 2020, an 86-year-old female resident who had developed fever on March 21 was conveyed to an acute hospital after she deteriorated despite having received treatment for presumed aspiration pneumonia and was diagnosed with COVID-19 on March 31. Active surveillance at the facility and enhanced infection prevention and control practices (IPC) were implemented. The activities and contact tracing of each case in the last 14 days were performed to obtain information on the nature and duration of all possible exposure to the index case during the infectious period among the staff, visitors and female residents using a standardized institutional contact tracing template. Possible epidemiological links between cases and their household members were also derived and analyzed from interviews with nursing home staff and affected household members. An imported case is defined as a laboratory-confirmed case identified in Singapore with travel history from COVID-19 affected countries in the last 14 days before onset of symptoms. All epidemiological investigations were implemented under the Infectious Diseases Act and this included the use of data for analysis to guide public health interventions to control outbreaks.

The premises and floor plan of the facility and staff workflows were surveyed on site on the same day the index case was identified as a confirmed case. We also ascertained the ambulatory status and baseline cognitive function of all the residents, and determined the accommodation arrangements for the HCW to assess the risk of staff cross-infection. In

accordance with national policy enacted since February 2020, HCW in the facility were segregated into different care teams based on the different blocks.

Case Detection and Epidemiological Analysis

For the initial point prevalence survey, nasopharyngeal swabs were performed on all residents of the facility and HCW who were symptomatic. The swabs for residents were performed on-site by a mobile team for polymerase chain reaction (PCR) testing for SARS-CoV-2, which were completed by April 1. Thereafter, weekly point-prevalence surveys for asymptomatic residents were performed on April 6, 13, 20, 24. In between, residents and HCW who were symptomatic were conveyed to an acute hospital for further evaluation to rule out COVID-19. Individuals who had a positive swab PCR results were immediately admitted to hospital for isolation and further management.

Remaining residents of some of the affected wards were isolated in a vacant nursing home temporarily, after the second round of test to minimize on-going transmission. Other residents chosen to be isolated were ambulant individuals with cognitive impairment who could not comply with movement restriction (Figure 1). New admission or transfer of returning residents was suspended, except for returning residents who recovered from COVID-19 infection and were non-infectious.

Infection Prevention and Control

With the identification of the index case, personal protective equipment (PPE) was stepped up in patient care areas to add gloves and gowns, in addition to the pre-existing requirement for surgical masks. N95 masks and eye protection were used when performing aerosol-generating procedures (including suctioning and nasopharyngeal swabs) and when caring for

residents with symptoms of acute respiratory infection. Alcohol-based hand sanitizers were strategically placed and PPE donning and doffing locations were identified. The frequency of environmental cleaning of high-touch areas was increased. Nursing practice was changed to minimize the risk of cross-contamination from commonly used items, equipment and supplies.

Laboratory COVID-19 Diagnosis

All primary samples tested PCR positive for SARS-CoV-2 by RT-PCR at diagnostic laboratories were forwarded to the National Public Health Laboratory, under the provisions of the Infectious Diseases Act in Singapore for testing and validation using an in-house method as previously described⁷.

Sequencing and phylogenetic analysis

Residual RNA were subjected to tiled amplicon PCR using ARTIC nCoV-2019 version 3 panel⁸, where One-Step RT-PCR was performed using the SuperScript™ III One-Step RT-PCR System with Platinum™ *Taq* DNA Polymerase (ThermoFisher Scientific). Sequencing libraries were prepared using the Nextera XT and sequenced on MiSeq (Illumina) to generate 300bp paired-end reads. The reads were subjected to a hard-trim of 50 bp on each side to remove primer artifacts using BBMap prior to consensus sequence generation by Burrows-Wheeler Aligner-MEM v0.7.17, with default settings⁹. The generated consensus sequences were shared via GISAID¹⁰. Closely related representative strains from other countries (99.99% identity and matching the time window) were identified in the GISAID database using BLASTN¹¹. Due the epidemiological context of travel from Sri Lanka for one case, the three phylogenetically closest sequences in GISAID from Sri Lanka were included. All sequences were aligned using MAFFT (v7.427)¹², with hCoV-19/Wuhan/WIV04/2019

(accession: EPI_ISL_402124) as a reference together with CoV-19/Singapore/1/2020 (EPI_ISL_406973) to root the tree. The alignment was manually inspected and trimmed using Jalview¹³. IQ-TREE v1.6.1¹⁴ was used with ModelFinder¹⁵ and 1000 step ultrafast bootstrapping¹⁶ to create a maximum likelihood phylogenetic tree with zero length branches collapsed.

Results

Demographic and clinical characteristics of the cases

Among the 108 residents and 56 HCW in the nursing home, 14 (13%) residents and two (3.6%) HCW were diagnosed with COVID-19, corresponding to an attack rate of 9.8% (16/164). The median age of the infected residents was 86.5 (IQR 78.5 to 88) and 85.7% were female. Table 1 shows the characteristics of the infected residents and HCW. Nine residents and two HCW (S1 and S2), excluding the index case, were diagnosed within the first 2 days of the outbreak. The two HCW (S1 and S2) were female, of Indian nationality, were 43 and 32 years of age and were taking care of the female wards. Three other residents were diagnosed on April 6 and 1 resident, R14, was diagnosed on April 20 (Figure 2). The last diagnosed resident had been transferred to an acute hospital on Day 10 (April 9) of the outbreak for non-respiratory symptoms and was isolated throughout the whole hospitalization. He was asymptomatic prior to being diagnosed on April 20. Other than the index case, four other residents were symptomatic (35.7%) and the rest were asymptomatic (64.3%) before the time of the tests (Figure 2). However, four residents were found to be febrile on the day of admission (range 37.6 to 38.2 ° C) and 2 others developed fever after the admission. Two infected residents had poor oral intake and hypoactive delirium with no respiratory symptoms. Eight of the infected residents were non-ambulant.

The cubicle with the highest number of cases was in block C (Figure 1). This cubicle had residents who were ambulant and had shouting behavior. Four residents, including the index case, died from COVID-19, resulting in a case-fatality rate of 28.6%. They were 80, 85, 86 and 96 years old, and died between 9 to 25 days from date of diagnosis. All the others only had mild illness. The outbreak was declared closed on April 24, 14 days after the last affected case had been transferred out of the facility.

Among the staff, 18 lived in the on-site dormitory while 38 staff lived outside the facility in their own homes. As there was free social interaction between staff, all staff were regarded as potential contacts and were placed on 14 days quarantine from the start of the outbreak. No visitors were found to be in close contact with the index case in the last 14 days before the onset of symptoms.

Source of Infection and Phylogenetic Linkages

The primary case of the nursing home is likely to be one of the infected HCW, Nurse S1, who had onset of symptom (headache; an atypical symptoms for COVID-19) on March 17 while at work, and had fever (38.2° C) on March 18 (Figure 4). She was on sick leave between March 18 and 24. She did not have any recent travel history nor any known exposure to positive cases in the last 14 days before first symptom onset. Notably, her husband (H1) had travelled to Sri Lanka on February 26 and had arrived back to Singapore on March 14. Her husband (H1) recalled that his first symptom onset was only on March 30. Both Nurse S1 and her husband (H1) were diagnosed with COVID-19 on April 1 (Figure 2). All other nine household contacts of the two infected HCW were quarantined and were not reported to be COVID-19 positive.

With the exception of R14, phylogenetic analysis of SARS-CoV-2 genome sequences obtained from all cases, including H1, grouped into a single cluster (Figure 3, labelled in blue), supported by a single mutation (T27588A) not found in other sequences in the database before the nursing home outbreak. In contrast, R14 bore a C23185T mutation which was absent in the other nursing home cases but was common among B.6 lineage sequences circulating in Singapore. This suggests that there might be more than one introduction of different strains of SARS-CoV-2 in this nursing home outbreak. However, definitive evidence was not available from our investigation, as only the symptomatic HCW were screened and the full genomic sequences of R3, who was residing beside R14 in the same ward (Figure 1), was not successfully sequenced for comparison.

The nursing home outbreak sequences belonged to pangolin B.6 lineage (part of other GISAID clades not common globally), which predominantly circulated in Asia (primarily in India with 41% of all submitted strains between March and April 2020 classified as B.6, Malaysia 74% and Singapore 61% compared to only 1% globally). The extent of B.6 viruses circulating in Sri Lanka is unknown due to limited Sri Lanka sequences submitted into GISAID (14 as of 7th September) even though the outbreak in Sri Lanka was identified since 9th March. The phylogenetically closest strains from Sri Lanka in the database are classified as lineage B.4 and share a common ancestor with lineage B.6 characterized by variant G11083T. It is possible but not genetically proven that B.6 lineage strains also circulated in Sri Lanka during the relevant time period.

As such, there are two possibilities of transmission in the household. First, the Nurse S1 had acquired the infection from her husband H1 pre-symptomatically, albeit less likely as her symptom onset was 13 days earlier than her husband and in view of the lack of other

epidemiological exposure or contact with other confirmed cases (Figure 4). Second, the Nurse S1 might have transmitted the virus to her husband (H1) after her onset of symptoms on the 17th April (Figure 4).

Discussion

The first COVID-19 outbreak in a nursing home in Singapore had an attack rate of 13% (14/108) and case fatality rate (CFR) of 28.6% (4/14) among its residents. The CFR is significantly higher than the national rate of 0.1%, as of August 2020, and this is similar to nursing home outbreaks in Canada¹⁷ and USA⁴. Residents residing in nursing home tend to be frail, have multiple comorbidities and impairment in function and cognition, which would have limited their ability to report symptoms accurately or they tend to have atypical presentation¹⁸. The transmission rate may also increase if cognitively impaired residents continue to wander around the facility. By pre-emptively transferring these residents out of the facility for isolation, further transmission was effectively curtailed.

Studies of other clusters have established pre-symptomatic and asymptomatic transmission of SARS-CoV-2² and this is biologically plausible¹⁹. Such transmissions pose challenges to early detection and containment of outbreaks. Serial PPS, if resources permit, may allow for early detection of asymptomatic and pre-symptomatic patients to suppress transmission^{2,3,20}. Undetected infections have been shown to cause larger outbreaks in some clusters and mass screening rather than symptom-based testing is now widely accepted as the preferred strategy for management of nursing home outbreaks^{21,22}. Strict compliance to IPC is critical as it may minimize the risk of pre-symptomatic transmission from HCW to residents.

This outbreak only had 2 infected male residents compared to 12 female residents. The relative protection among the male wards was likely attributable to two infected HCW who were managing the female wards, and the strategy of team segregation and cohorting which has been shown to be effective in limiting spread²³. However, this staff segregation needs to be maintained not only at work but also during mealtimes and social activities, and among the staff residential living arrangement. Otherwise, inherent risks for cross infection will be present. Reducing the risk of infection among staff members has been associated with decreasing risk of mortality among the residents¹⁷.

Based on the epidemiological analysis, the HCW is potentially the source of transmission in this nursing home outbreak, despite adhering to PPE guidelines and taking sick leave. HCW who mingle in the community and engage in social interactions outside of work are a potential weak link in the prevention of outbreaks in nursing home, especially when community spread is prevalent in the population. From May 2 to Jun 1, when community transmissions were evident in Singapore, MOH implemented additional supportive measures to lodge most HCW who were providing direct care to nursing home residents in hotels or dormitories on-site to minimize their exposure to infections in the community. HCW also underwent stringent health status checks and were required to declare family travel history as part of active surveillance. In addition, with effect from May 8, all healthcare staff and residents at the nursing homes who developed acute respiratory symptoms were required to undergo testing for COVID-19. Strict implementation of infection prevention and control practices²⁴, improving air flow²⁵, active case finding through contact tracing with early detection and isolation of close contacts and positive cases²⁶ as well as staff and associated households segregation plans can significantly reduce the morbidity and mortality of

residents in a nursing home outbreak. Since this outbreak, Singapore has seen only one other nursing home outbreaks of a smaller scale.

There are some limitations in this investigation. The activities in the last 14 days and onset of symptoms of the detected cases were based on recall and hence, there was potential recall bias. However, the shift work of nursing staff and activities of residents as well as travel history were well-documented. As only symptomatic HCW were screened, the possibility of more than one introduction of SARS-CoV-2 cannot be completely excluded. However, the likelihood is low as infection prevention and control measures were further strengthened after the index case was identified. Point prevalence survey was only done on all residents and only symptomatic HCW and seroprevalence was not performed to assess the overall COVID-19 positivity rate of the nursing home, hence, there is a potential underestimation of attack rate and overestimation of case fatality rate. The incomplete whole genome sequences of the two HCW cases and the limited submission of genetic sequences from Sri Lanka potentially underestimates the likelihood of the phylogenetic linkages between Sri Lanka and the nursing home outbreak.

Conclusion

Nursing home are vulnerable to external sources of SARS-CoV-2 and key preventive strategies should include measures to minimise risk of pathogen introduction and good infection control and prevention practices.

351 **References**

- 352 1. Graham NSN, Junghans C, Downes R, et al. SARS-CoV-2 infection, clinical features and
353 outcome of COVID-19 in United Kingdom nursing homes. *The Journal of infection* 2020;81:411-9.
- 354 2. Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 Infections and
355 Transmission in a Skilled Nursing Facility. *N Engl J Med* 2020;382:2081-90.
- 356 3. Patel MC, Chaisson LH, Borgetti S, et al. Asymptomatic SARS-CoV-2 infection and COVID-19
357 mortality during an outbreak investigation in a skilled nursing facility. *Clinical infectious diseases* : an
358 official publication of the Infectious Diseases Society of America 2020.
- 359 4. McMichael TM, Currie DW, Clark S, et al. Epidemiology of Covid-19 in a Long-Term Care
360 Facility in King County, Washington. *N Engl J Med* 2020;382:2005-11.
- 361 5. Lester PE, Holahan T, Siskind D, Healy E. Policy Recommendations Regarding Skilled Nursing
362 Facility Management of Coronavirus 19 (COVID-19): Lessons from New York State. *J Am Med Dir*
363 Assoc 2020;21:888-92.
- 364 6. Pillemer K, Subramanian L, Hupert N. The Importance of Long-term Care Populations in
365 Models of COVID-19. *Jama* 2020;324:25-6.
- 366 7. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic Features and Clinical Course of
367 Patients Infected With SARS-CoV-2 in Singapore. *Jama* 2020;323:1488-94.
- 368 8. Tyson JR, James P, Stoddart D, et al. Improvements to the ARTIC multiplex PCR method for
369 SARS-CoV-2 genome sequencing using nanopore. *bioRxiv* 2020.
- 370 9. Deng X, Gu W, Federman S, et al. Genomic surveillance reveals multiple introductions of
371 SARS-CoV-2 into Northern California. *Science* 2020;369:582-7.
- 372 10. Shu Y, McCauley J. GISAID: Global initiative on sharing all influenza data - from vision to
373 reality. *Euro surveillance* : bulletin Europeen sur les maladies transmissibles = European
374 communicable disease bulletin 2017;22.
- 375 11. Altschul SF, Madden TL, Schaffer AA, et al. Gapped BLAST and PSI-BLAST: a new generation
376 of protein database search programs. *Nucleic Acids Res* 1997;25:3389-402.
- 377 12. Katoh K, Standley DM. MAFFT multiple sequence alignment software version 7:
378 improvements in performance and usability. *Mol Biol Evol* 2013;30:772-80.
- 379 13. Waterhouse AM, Procter JB, Martin DM, Clamp M, Barton GJ. Jalview Version 2--a multiple
380 sequence alignment editor and analysis workbench. *Bioinformatics* 2009;25:1189-91.
- 381 14. Nguyen LT, Schmidt HA, von Haeseler A, Minh BQ. IQ-TREE: a fast and effective stochastic
382 algorithm for estimating maximum-likelihood phylogenies. *Mol Biol Evol* 2015;32:268-74.
- 383 15. Kalyaanamoorthy S, Minh BQ, Wong TKF, von Haeseler A, Jermiin LS. ModelFinder: fast
384 model selection for accurate phylogenetic estimates. *Nat Methods* 2017;14:587-9.
- 385 16. Hoang DT, Chernomor O, von Haeseler A, Minh BQ, Vinh LS. UFBoot2: Improving the
386 Ultrafast Bootstrap Approximation. *Mol Biol Evol* 2018;35:518-22.
- 387 17. Fisman DN, Bogoch I, Lapointe-Shaw L, McCready J, Tuite AR. Risk Factors Associated With
388 Mortality Among Residents With Coronavirus Disease 2019 (COVID-19) in Long-term Care Facilities in
389 Ontario, Canada. *JAMA Netw Open* 2020;3:e2015957.
- 390 18. Norman RE, Stall NM, Sinha SK. Typically Atypical: COVID-19 Presenting as a Fall in an Older
391 Adult. *J Am Geriatr Soc* 2020;68:E36-E7.
- 392 19. Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of
393 Infected Patients. *N Engl J Med* 2020;382:1177-9.
- 394 20. Roxby AC, Greninger AL, Hatfield KM, et al. Outbreak Investigation of COVID-19 Among
395 Residents and Staff of an Independent and Assisted Living Community for Older Adults in Seattle,
396 Washington. *JAMA internal medicine* 2020.
- 397 21. Dora AV, Winnett A, Jatt LP, et al. Universal and Serial Laboratory Testing for SARS-CoV-2 at
398 a Long-Term Care Skilled Nursing Facility for Veterans - Los Angeles, California, 2020. *MMWR*
399 Morbidity and mortality weekly report 2020;69:651-5.

22. Team EPHE, Danis K, Fonteneau L, et al. High impact of COVID-19 in long-term care facilities, suggestion for monitoring in the EU/EEA, May 2020. Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin 2020;25.
23. Yen MY, Schwartz J, King CC, et al. Recommendations for protecting against and mitigating the COVID-19 pandemic in long-term care facilities. J Microbiol Immunol Infect 2020;53:447-53.
24. The Global Handwashing Partnership (Accessed 31 October 2019, 2019, at <https://globalhandwashing.org/about-handwashing/why-handwashing/health/>)
25. Lynch RM, Goring R. Practical Steps to Improve Air Flow in Long-Term Care Resident Rooms to Reduce COVID-19 Infection Risk. J Am Med Dir Assoc 2020;21:893-4.
26. Singh H, Popli T. Stopping the SARS-CoV-2 surge in the USA-CDC recommendations and ground realities. Adv Respir Med 2020;88:173-5.

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Declaration of conflict

The authors declared no conflict of interest.

Authors' contributions

HNT conceived the study. JP and HNT led the study, collected, analysed and interpreted the data as well as drafted the manuscript. LC, TMM and SO collected the samples, performed the whole genome sequencing and analyzed the sequencing data. SMS and FLS performed the bioinformatics and phylogenetic analysis. MPCC, IYOL, VTJK, PLO, SV, DF, HR, JC, VJL were involved in data collection, analysis, interpretation, and critical editing of the manuscript.

Role of funding source

No funding

Ethics committee approval

Data were collected under the Infectious Disease Act for outbreak investigation and approved
by Ministry of Health, Singapore.

Captions

Figure 1. Spot Map of Facility

Schematic diagram of the facility (not drawn to scale) showing the spot map of infected cases and date of diagnosis; residents who were moved out of the facility on day 8 (April 7) of the outbreak.

Figure 2. Epicurve and Characteristics of COVID-19 Cases

Epicurve was charted based on onset of symptoms and swab positives notification from the serial point-prevalence survey. Gender, age, ethnicity (C-Chinese; M-Malay; I-Indian), symptomatic status, date of PCR test, admission and fatality were highlighted. The index and primary cases of the nursing home outbreak is R1 and S1, respectively. H1 is the household member of S1.

Figure 3. Phylogenetic Tree of Nursing Home and the Associated Household Member.

The whole genome sequences of the cases from the nursing home (highlighted in blue) were closely clustered together, except for R14 (highlighted in orange). H1, the whole genome sequence of the husband of nursing staff S1 was genetically similar to the cases of the nursing home cluster and the India sequence. Viral quantity and quality were not high enough to conduct the whole genome sequencing for R3, R10, S1 and S2 successfully.

Figure 4. Epidemiological Transmission and Linkages between a Household Cluster and Nursing Home Cluster.

Presymptomatic household transmission occurred from H1 (husband of S1; travel history to Sri Lanka and returned on 14 March) to S1 (wife of H1; Staff Nurse of nursing home). This led to the introduction of the SARS-CoV-2 transmission within the nursing home.

506 **Figure 1.**

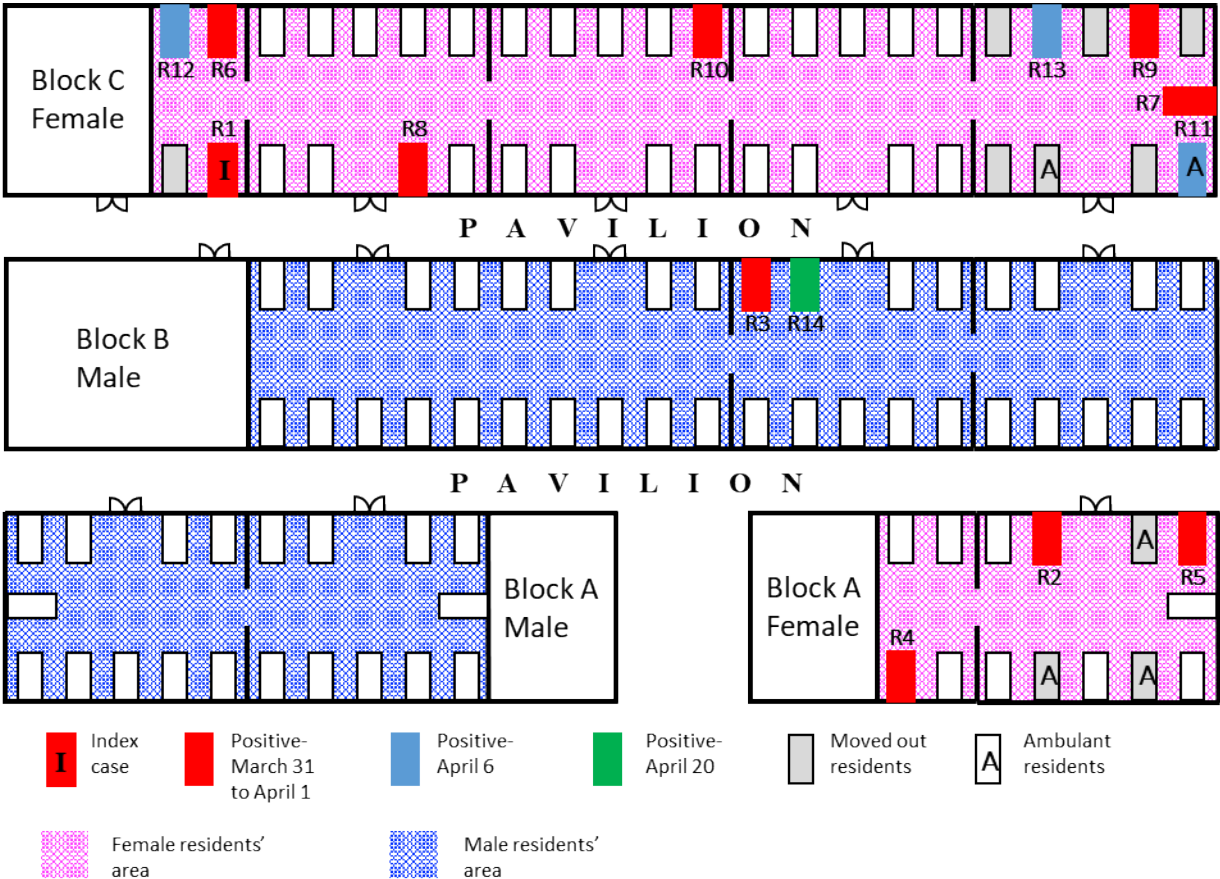
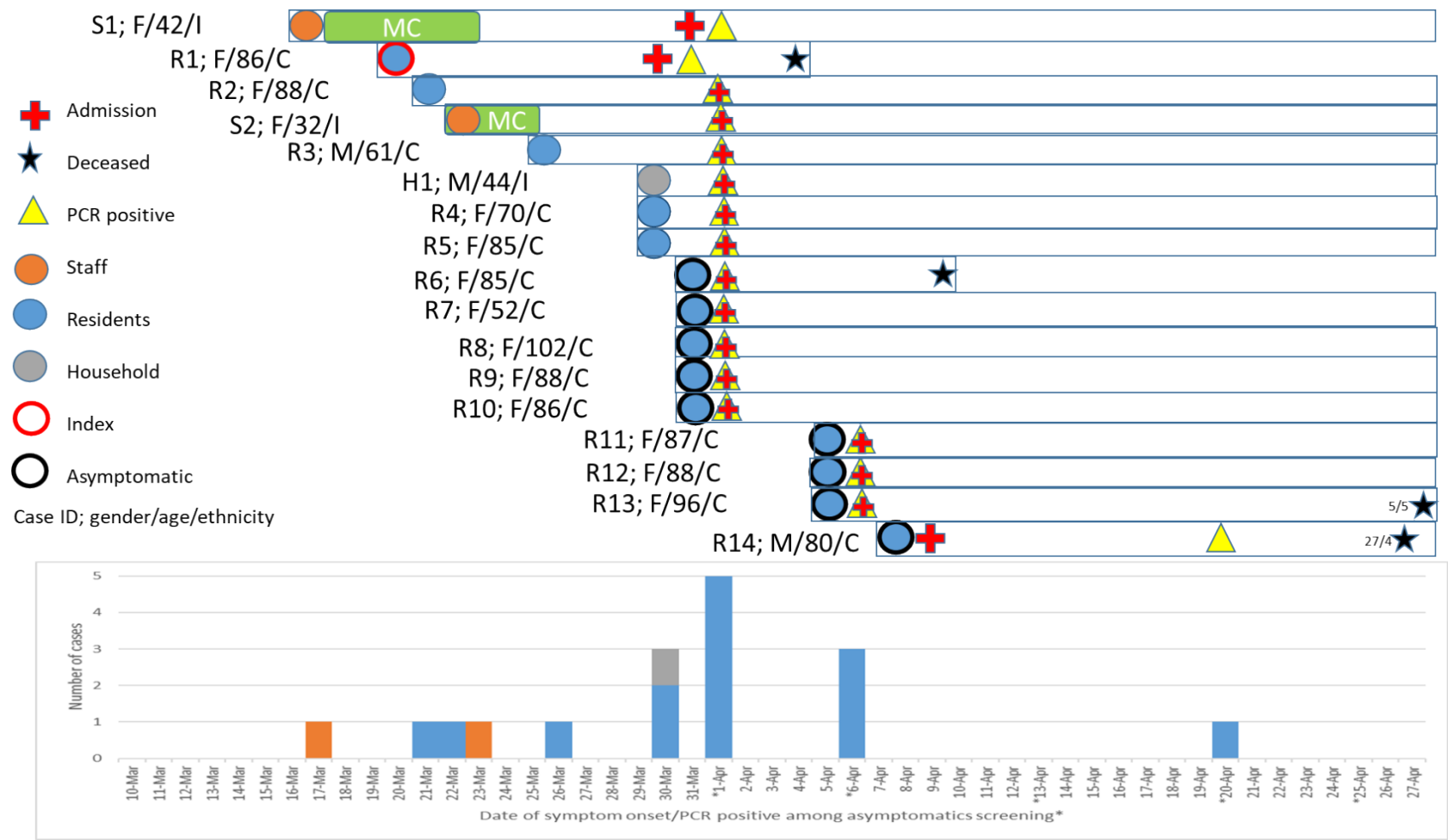


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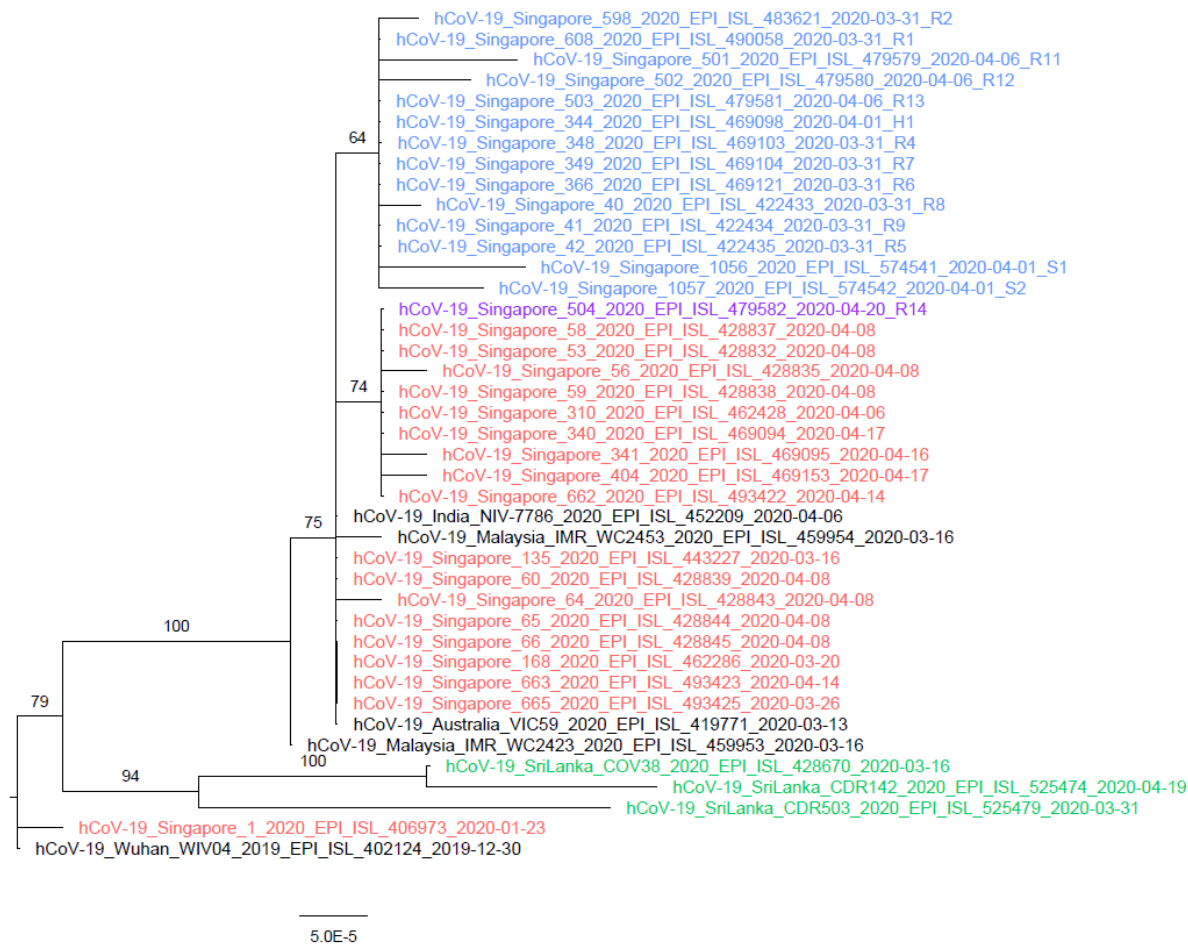
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517 **Figure 2.**

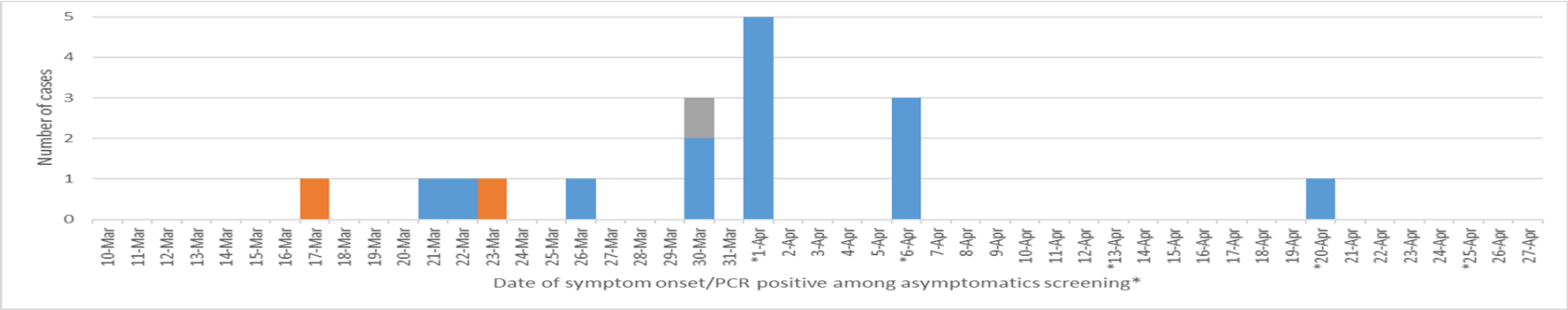
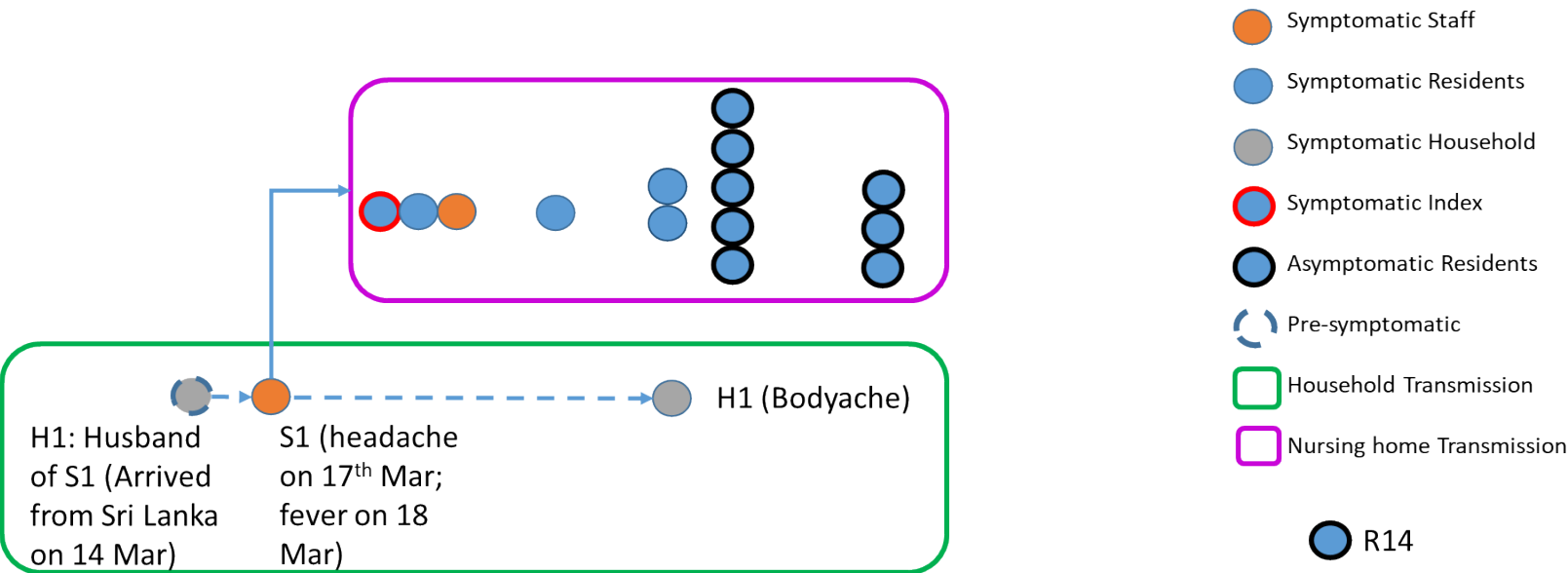


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Figure 3.



530 **Figure 4.**



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533 **Table 1. Characteristics of Nursing Home Residents and HCW with COVID-19**

	Residents			HCW
	Survivor (n=10)	Non-survivor (n=4)	All (n=14)	(n=2; S1, S2)
Demographics				
Age, median (IQR) years	86.5 (67.8-88)	85.5 (81.3-93.5)	86 (77.5-88)	(42, 32)
Female, No. (%)	9 (90)	3 (75)	12 (85.7)	2 (100)
Comorbidities & Function				
Hypertension	3 (30)	3 (75)	6 (42.9)	0
Diabetes Mellitus	0	0	0	0
Coronary Heart Disease	0	0	0	0
Cerebrovascular Disease	2 (20)	0	2 (14.3)	0
Chronic Respiratory Disease	0	0	0	0
Chronic Renal Disease	2 (20)	1 (33.3)	3 (21.4)	0
Cognitive impairment	6 (60)	3 (75)	9 (64.3)	0
Ambulant	1 (10)	0	1 (7.1)	2 (100)
Outcome				
Symptomatic	4 (40)	1 (25)	5 (35.7)	2 (100)
Duration of admission, median (range) days	21 (12-31)	14 (5-25)	19.5 (12.8-28.3)	(9, 5)

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All Submitters of data may be contacted directly via www.gisaid.org

Accession ID	Originating Laboratory	Submitting Laboratory	Authors
EPI_ISL_402124 EPI_ISL_406973 EPI_ISL_419771	Wuhan Jinyintan Hospital Singapore General Hospital Victorian Infectious Diseases Reference Laboratory (VIDRL)	Wuhan Institute of Virology, Chinese Academy of Sciences National Public Health Laboratory Victorian Infectious Diseases Reference Laboratory and Microbiological Diagnostic Unit Public Health Laboratory, Doherty Institute	Peng Zhou, Xing-Lou Yang, Ding-Yu Zhang, Lei Zhang, Yan Zhu, Hao-Rui Si, Zhengli Shi Mak, TM; Octavia S; Chavatte JM; Zhou, ZY; Cui, L; Lin, RTP Caly L., Seemann T., Sait, M., Schultz M., Druce J., Sherry, N.
EPI_ISL_422433, EPI_ISL_422434, EPI_ISL_422435 EPI_ISL_428670	National Public Health Laboratory, National Centre for Infectious Diseases Centre for Dengue Research	National Public Health Laboratory, National Centre for Infectious Diseases Centre for Dengue Research	Mak TM, Octavia S, Cui L, Lin RTP Chandima Jeewandara, Dinuka Ariyaratne, Laksiri Gomes, Deshni Jayathilaka, Ananda Wijewickrama, Eranga Narangoda, Damayanthi Idampitiya, Neelika Malaige Mak TM, Octavia S, Chavatte JM, Cui L, Lin RTP
EPI_ISL_428832, EPI_ISL_428835, EPI_ISL_428837, EPI_ISL_428838, EPI_ISL_428839, EPI_ISL_428843, EPI_ISL_428844, EPI_ISL_428845 EPI_ISL_443227 EPI_ISL_452209 EPI_ISL_459953 EPI_ISL_459954	National Public Health Laboratory, National Centre for Infectious Diseases National Public Health Laboratory, National Centre for Infectious Diseases Institute for Medical Research, Infectious Disease Research Centre, National Institutes of Health, Ministry of Health Malaysia Institute for Medical Research, Infectious Disease Research Centre, National Institutes of Health, Ministry of Health Malaysia National Public Health Laboratory, National Centre for Infectious Diseases	National Public Health Laboratory, National Centre for Infectious Diseases National Public Health Laboratory, National Centre for Infectious Diseases Institute for Medical Research Infectious Disease Research Centre, National Institutes of Health, Ministry of Health Malaysia Institute for Medical Research, Infectious Disease Research Centre, National Institutes of Health, Ministry of Health Malaysia National Public Health Laboratory, National Centre for Infectious Diseases	Mak Tze Minn, Octavia Sophie, Chavatte Jean-Marc, Cui Lin, Lin Raymond Tzer Pin Potdar V Suppliah J, Mohd-Zawawi Z, Kamel KA, Eilan K, Kalyanasundram J, Mohd-Zain R, Thayan R Suppliah J, Mohd-Zawawi Z, Kamel KA, Eilan K, Kalyanasundram J, Mohd-Zain R, Thayan R
EPI_ISL_462286, EPI_ISL_462428, EPI_ISL_469094, EPI_ISL_469095, EPI_ISL_469098, EPI_ISL_469103, EPI_ISL_469104, EPI_ISL_469121, EPI_ISL_469153	National Public Health Laboratory, National Centre for Infectious Diseases	National Public Health Laboratory, National Centre for Infectious Diseases	Mak TM, Octavia S, Chavatte JM, Cui L, Lin RTP
EPI_ISL_479579, EPI_ISL_479580, EPI_ISL_479581, EPI_ISL_479582, EPI_ISL_483621, EPI_ISL_490058, EPI_ISL_493422, EPI_ISL_493423, EPI_ISL_493425 EPI_ISL_525474 EPI_ISL_525479	National Public Health Laboratory, National Centre for Infectious Diseases Centre for Dengue Research Centre for Dengue Research	National Public Health Laboratory, National Centre for Infectious Diseases Centre for Dengue Research, USJ, SL Centre for Dengue Research	Mak TM, Octavia S, Zhou Z, Chavatte JM, Cui L, Lin RTP Chandima Jeewandara, Deshni Jayathilaka, Dinuka Ariyaratne, Laksiri Gomes, Diyanath Ranasinghe, Dinuka Guruge, Ruwan Wijayamuni, Gathsaurie Neelika Malavige Chandima Jeewandara, Deshni Jayathilaka, Dinuka Ariyaratne, Laksiri Gomes, Diyanath Ranasinghe, Ananda Wijewickrama, Eranga Narangoda, Damayanthi Idampitiya, Gathsaurie Neelika Malavige Tze Minn Mak, Sophie Octavia, Zhenyang Zhou, Lin Cui, Raymond Tzer Pin Lin
EPI_ISL_574541, EPI_ISL_574542	National Public Health Laboratory, National Centre for Infectious Diseases	National Public Health Laboratory, National Centre for Infectious Diseases	