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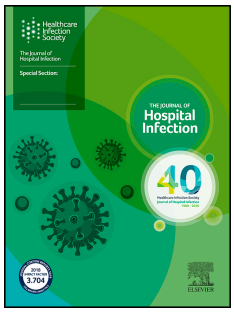

A Two-Ward Acute Care Hospital Outbreak of SARS-CoV-2 Delta Variant Including a Point-Source Outbreak Associated with the Use of a Mobile Vital Signs Cart and Sub-Optimal Doffing of Personal Protective Equipment

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Title: A Two-Ward Acute Care Hospital Outbreak of SARS-CoV-2 Delta Variant Including a Point-Source Outbreak Associated with the Use of a Mobile Vital Signs Cart and Sub-Optimal Doffing of Personal Protective Equipment

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Running Title: SARS-CoV-2 two-ward outbreak

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Summary

Background: We conducted a detailed epidemiological investigation of a linked 2-ward COVID-19 Delta variant outbreak to elucidate its source, risk factors, and control measures.

Methods: Investigations included epidemiologic analysis, detailed case review serial SARS-CoV-2 RT-PCR testing of patients and healthcare workers (HCWs), viral culture, environmental swabbing, HCW-unaware personal protective equipment (PPE) audits, ventilation assessments, and the use of whole genome sequencing (WGS).

Results: This linked 2-ward outbreak resulted in 17 patient and 12 HCW cases, despite an 83% vaccination rate. In this setting suboptimal adherence and compliance to PPE protocols, suboptimal hand hygiene, multi-bedded rooms, and a contaminated vital signs cart (VSC) with potential fomite or spread via the hands of HCWs were identified as significant risk factors for nosocomial COVID-19 infection. Sudden onset of symptoms, within 72h, was observed in 79% of all Ward 2 patients and 93% of all cases (patients and HCWs) on Ward 2 occurred within one incubation period, consistent with a point source outbreak. RT-PCR assays showed low Cycle threshold (Ct) values, indicating high viral load from environmental swabs including the VSC. WGS results with ≤ 3 SNP differences between specimens were observed.

Conclusions: Outbreaks on both wards settled rapidly, within 3 weeks, using a 'back-to-basics' approach without extraordinary measures or changes to standard PPE requirements. Strict adherence to recommended PPE, hand hygiene, education, assistance from infected cases (interviews and testing), and additional measures such as limiting movement of patients and staff temporarily were all deemed to have contributed to prompt resolution of the outbreak.

Introduction

The arrival of the Delta variant of SARS-CoV-2 was associated with increased transmissibility, reported to be as high as 97% compared to the ancestral lineages, and causing illness of greater severity [1–3]. Reports of nosocomial outbreaks of Delta variant COVID-19 in acute care hospitals have been described but control measures varied widely [4–7].

We describe a two-ward acute care hospital outbreak of Delta variant where the probable modes of transmission were elucidated using epidemiologic, laboratory and virologic investigations, environmental investigations and whole genome sequencing (WGS).

Methods

The outbreak investigation and reporting followed the ORION guidelines [8], with the exception of the exact start and finish dates, to protect patient and HCW confidentiality.

Outbreak Setting and Epidemiologic Investigations

Ward 1

Entry of the Delta Variant occurred in an 1100 bed tertiary acute care facility in the spring of 2021 via a designated support person (DSP) with community COVID-19 acquisition and secondary transmission via close contact, to the index patient (Figure 1A). The entry of the virus to Ward 1 and the subsequent outbreak occurred during a time of relatively low community transmission in our jurisdiction (active cases 153 /100,000; https://covid-tracker.chi-csm.ca/) during an interwave period and just before the Delta wave emergence in our jurisdiction. Further to the first case, two additional hospital-acquired (HA) patient cases (Supplemental File S1: Definitions for case definitions; HA cases require the absence of any epidemiologic evidence to support a community or household exposure) in separate rooms on the same ward were identified following respiratory symptom onset 4 and 6 days later, respectively (Figure 1A, 1B). Three HCWs who became infected, all of whom developed respiratory symptoms, had worked directly with at least one of the affected patients. It was noted that all three infected patients had high dependency needs. Nasopharyngeal (NP) swabs were obtained from all patients on the ward and were requested from all HCWs who attended Ward 1 (patient census = 45; Ward staff = 140; physicians = 25; medical ward). Patients were tested serially (q3 days), with SARS-CoV-2 RT-PCR [9] until closure of the outbreak.

Ward 2

An initial patient case was identified on Ward 2 (census = 41; medical ward), in a separate building, after onset of fever and cough 10 days following the last identified case on Ward 1. Symptom onset occurred in eight patients within 24 hours and within 72 hours, eleven patients had symptoms (Figure 1B). NP swabs

were obtained from all patients and were requested from all HCWs who attended Ward 2 (patient census = 41; Ward staff = 109; physicians = 28; medical ward). The patient NP swabs were collected serially (q2-3 days) and tested by RT-PCR [9] until closure of the outbreak .

For both wards HCWs were offered SARS-CoV-2 NP testing and it was strongly encouraged. Neither vaccination nor testing were mandatory. Investigations by the Outbreak Management Team were conducted using classic epidemiologic tools, including interviews of infected individuals, review of medical records, review of patient placement, patient and HCW movement between wards and HCW contact tracing using forward and backward contact tracing [10] and a linkage interview, with the aim of determining the transmission routes to patients (Supplemental File S1) and HCWs and to facilitate outbreak control measures.

Environmental Investigations

Environmental swabs were collected from multiple sites in patient rooms and from shared medical equipment, including a mobile vital signs cart (VSC). One set of swabs was collected the day the outbreak was declared on Ward 2 and a second set the following day. As a negative control, swabs were taken from the main shower room, which was in a section of the unit separate from where the initial positive patients were identified. Environmental specimen PCR assays were performed according to methods previously described [9,11–13]. Typing of strains were confirmed using Variant testing PCR, as previously described [3].

Laboratory and Virologic Investigations

Clinical specimens, primarily NP swabs, but in some cases throat swabs, were collected and tested for SARS-CoV-2 using RT-PCR. Serial NP swab COVID-19 testing was done with 13 patients (Ward 2) by experienced HCWs to observe viral kinetics over time in patients using a validated RT-PCR assay, based

on an E gene target with internal controls [9]. To confirm the presence of infectious virus, clinical samples from consented patients were cultured using Vero cells as described by Lin et al. [12].

In addition, HCWs were offered voluntary prevalence testing on site to increase uptake and convenience of testing. Testing was highly recommended every 5 days for “on unit” and “off unit” staff who attended the ward in the 14 days prior to and since the start of the outbreak. Based upon the numbers of tests completed, it was learned that HCW testing was incomplete and that the number of HCWs tested dramatically reduced after the initial round of prevalence testing.

HCW Symptom Screening

A daily "Fit-for-Work" symptom review was required for all HCWs. A HCW was deemed fit for work if they were asymptomatic, as well as having no discrete COVID-19 exposure risk. HCWs were required to show their fit for work status on arrival at work and mid-way through shift. If a HCW developed COVID-19 symptoms while at work they were directed to leave, isolate and test for COVID-19.

PPE Compliance Based on Covert Observations

Anonymous "HCW unaware" audits of adherence to PPE and hand hygiene had been ongoing in the hospital for several months and stored on an accessible database. Multiple audits were completed just prior to the outbreak on the affected ward and were available for comparison to the designated COVID-19 Wards across the health region. These covert audits were performed by clinical nurse educators from other hospital wards and hence were unknown to the HCWs on the audited ward. A standardized audit tool was utilized and loaded into a RedCap database. The audit tool addressed the individual components for each step of PPE use including the PPE environment (i.e. availability of PPE materials), donning of all components of the PPE and the doffing of all PPE components, including the gloves, gowns, eye protection and masks plus the required hand hygiene for each doffing step. Separate from the audits, any infected HCWs were asked via questionnaire about the individual elements of PPE and to self-describe their doffing procedures and hand hygiene technique as part of the contact tracing interviews.

Whole Genome Sequencing

WGS of patient and HCW samples was done retrospectively. The full genome of SARS-CoV-2 strains obtained from the NP swabs of HCWs and patients between the 2 wards was amplified by multiplex PCR according to the LoCost ARTIC protocol [14] (https://www.protocols.io/view/ncov-2019-sequencing-protocol-v3-locost-bh42j8ye) using the Freed oligos [15] as 1,200-bp amplicons with sequencing done using Oxford Nanopore or Illumina sequencing technology. Consensus sequences were aligned with

mafft [16] and visualized using snipit (https://github.com/aineniamh/snipit). The full protocol was completed as outlined previously [11].

Ventilation Assessments

Ventilation was measured in air exchanges per hour (AEH), by the Facilities, Maintenance, and Engineering department of the hospital, at the end of the outbreak. Values were interpreted relative to the Canadian Safety Association standards for Heating, Ventilation, and Air Conditioning (HVAC) Systems in Health Care Facilities (CSA-Z317.2-15).

Outbreak Control Measures

Multiple measures were employed concomitantly for control of the outbreak including isolation of patients, frequent clinical monitoring using a comprehensive COVID-19 symptom/sign monitoring tool [17], serial testing for SARS-CoV-2, selected transfer of infected patients (to designated COVID-19 wards), implementation of enhanced environmental cleaning and review of all cleaning and disinfection practices for the patient environment and shared medical equipment, staff and visitor restrictions, review of ventilation parameters, and coached adherence to contact and droplet PPE by all HCWs (medical masks, goggles/face shields, gowns, gloves). All break and lunch rooms were reviewed for compliance with the restrictions, occupancy limits and segregated physical distancing limits implemented by Site Administration at the beginning of the pandemic.

Statistical analysis

Statistical analysis was performed using chi square or student's t for categorical and continuous variables as appropriate; a p value <0.05 was considered significant.

Results

Descriptive Epidemiology Wards 1 and 2

Following initial entry of the Delta Variant via a designated support person (DSP) as described above, epidemiologic investigations identified transmission to patients 2 and 3 occurred when patient 1, with known difficulty masking from underlying medical conditions, and having core respiratory symptoms, including frequent coughing, was inadvertently seated directly beside patients 2 and 3 (masking status unknown) in a treatment waiting area elsewhere in the facility on day 2 (Figure 1A). The three HCWs who became positive, despite continuous masking (Figure 1A) were considered as patient-to-HCW transmission based on contact tracing, patient assignments and the high dependency needs of the patients. Prospective serial PCR testing (q3 days) of all patients and of HCWs who were tested revealed no other positive cases on Ward 1.

Symptom screening and serial testing identified a total of 14 SARS-CoV-2 infected patients on Ward 2 (Figure 1B. Figure 1C; designated PTs 4-17). One outlier patient case and one HCW case were identified >7 days from outbreak declaration. All Ward 2 patients (n=14) had core respiratory symptoms +/- low grade fever based on the symptom screening tool employed, regardless of their vaccination status. The frequency of vaccinated and unvaccinated patients and HCWs is presented in Table 1. For patients and HCWs, vaccination rates were 77% and 92%, respectively for an overall rate of 83%. The 14 SARS-CoV-2 infected patients had mobility scores indicating they were at higher risk of falls and had higher dependency needs.

Of the total 17 patient cases, were considered hospital-acquired. The median number of days from admission to symptom onset was 14 days; only 4 patient cases had an interval < 10 days, one of whom was the index patient (PT1, Fig 1C) with a known DSP-patient transmission event and the other 3 patient cases (PT 7, 13, 14, Fig 1C) had a least one negative SARS-CoV-2 NP test on admission and /or in the 3-5 days prior to symptom onset.

There were 140 and 109 primary HCW staff (including registered nurses, licensed practical nurses, healthcare aides, unit clerks and allied health staff including physiotherapists/occupational therapists) who were assigned to Wards 1 and Ward 2, respectively, and there were 25 and 28 physicians who worked at various times on Wards 1 and 2, respectively. There was high uptake of SARS-CoV-2 NP prevalence testing during this outbreak with 91.4% of the HCW staff and physicians undertaking NP prevalence testing at least once between the 2 units, based on Public Health records of individuals tested. A total of 551 NP RT-PCR tests were completed between the two wards over the course of the outbreak. Some HCWs had multiple tests done. Of the 12 PCR positive HCWs detected between the 2 wards, some of whom were identified as exposed contacts of cases, none initially reported "exposure" or PPE breaches on initial contact tracing interview, but post-diagnosis questionnaires and interviews conducted on all 12 cases with a detailed selection of additional interview questions, including backwards contact tracing found 6/12 (50%) reported breaches related to either PPE (eye protection or masking), hand hygiene, or environmental exposure or difficulty accessing wipes for shared computer workstations. All HCWs were asked about COVID-19 within their households and none had a household contact prior to their own onset of COVID-19 symptoms. Three of the HCWs reported suspected onward transmission of infections to their household contacts following their occupationally acquired COVID-19. Although initially only 1 HCW was found to have worked between the two wards, more comprehensive and collaborative investigations between ward managers, WHS, IPC and hospital administration identified at least 6 HCWs who had worked between both wards during the 14 days prior to the Ward 2 outbreak, not all of whom were confirmed to have been tested for SARS-CoV-2. It was also learned that many HCWs frequently and simultaneously aided with at least one of the patients reported to have had frequent forceful coughing and who had very high care and dependency needs, particularly for positioning and toileting.

Multi-bedded rooms with shared bathrooms

All but one Ward 2 case occurred in multi-bedded rooms (2, 3 or 4 beds with a shared bathroom) (Figure 2). A significant association with infection (p=0.04) was seen in patients who were in multi-bedded rooms

with a shared bathroom (9/12) versus those in a private room. No aerosol generating medical procedures (AGMPs) [18] were performed in multi-bedded rooms.

Environmental Investigations

SARS-CoV-2 PCR positivity was found on 10/10 swabs from high-touch surfaces on the VSC (Table 2) with Ct values (N gene) between 17.14-19.70, which is in the range highly predictive of infectious virus [12]. All samples, including those from the VSC, were confirmed to be Delta strain by RT-PCR [11]. COVID-19 positive cases were significantly associated with rooms (10/13 vs 0/5; p=0.007) on Ward 2 where the VSC was used by HCWs as opposed to rooms with wall mounted vital signs equipment. No record or log of cleaning the mobile VSC was found.

Laboratory and Virologic Investigations

Viral kinetics studies were done on 13 patients up to 30 days post symptom onset (Figure 3), (n=6 fully immunized; n=7 not fully immunized, File S1 for definitions). On illness day six, 11/11 patients (3 unvaccinated) had Ct values ≤ 25 (E-gene) and 6/6 patients (1 unvaccinated) continued to have Ct values ≤ 25 up to day 10. Viral cultures [12] for two consented patients (both fully immunized) revealed 1.60 x 10^3 plaque forming wards (pfu)/ml (Ct N gene 18.09) at Day 2 and 1.58 x 10^3 pfu/ml (Ct N gene 17.25) at Day 6 of infection (Figure 3).

Monitoring of PPE Compliance Based on Covert Observations

We found a highly significant association with sub-optimal adherence to doffing, hand hygiene and order of doffing on Ward 2 (55% and 64% of the time, respectively) compared to 4 adult designated COVID-19 wards (78% and 89%, respectively; p=0.007; n=54 HCW-unaware audits) in the 3 month period prior to the outbreak. Regarding specific components of the PPE doffing, which may place HCWs at risk of mucous membrane inoculation of SARS-CoV-2, in the 3 months prior to the outbreak, lack of hand hygiene after glove and gown removal was identified in 27.2% and 36.3% of audits, and improper doffing of eye protection and masks in 27.2 % and 36.3% of audits, respectively. In addition, it is noteworthy that in the 4 weeks following the declaration of the outbreak, the lack of hand hygiene after glove and gown removal was markedly reduced, being found in only 2.7% and 5.4 % of audits, respectively while improper doffing of eye protection and masks was noted in only in 13.5% and 16.2% indicating a marked improvement in overall adherence. There was no difference in the type of PPE used (medical mask, googles or face shields, gowns and gloves) between COVID-19 wards and general wards.

Whole Genome Sequencing

WGS revealed ≤ 3 single nucleotide polymorphism (SNP) differences in the strains found in all HCWs and patients from Wards 1 and 2, including individuals who had worked between both wards. The outbreak strain was markedly different (mean 17.5 SNPs) than community Delta strains, demonstrating a unique strain was responsible for both outbreaks (Figure 4).

Ventilation Parameters

The testing of air exchanges per hour (AEH) immediately following the outbreak for the rooms on Ward 2 revealed that they exceeded Canadian safety standards, with variance between 6.9-9.5 AEH, with 100% outside air. The bathrooms were negative pressure with respect to the patient rooms; the patient rooms were positive with respect to the hallway.

Infection Prevention and Control Measures and Outbreak Closure

Measures initiated concomitantly with declaration of the outbreak included serial SARS-CoV-2 PCR prevalence testing of all patients and >90% of the HCWs enabling rapid detection of cases, moving some positive patients to the designated COVID-19 Ward to allow all remaining patients to be in single-bedded rooms on Ward 2, a temporary suspension of all new admissions, restricting HCW movement on multiple wards or sites, purchasing of additional VSCs, enhanced environmental cleaning of surfaces and mobile medical equipment and strict adherence/compliance to our standard PPE measures. Enhanced cleaning by Environmental Services (twice as opposed to once daily) of the patient environment with a hospital approved cleaning product, in addition to standard cleaning at the time of discharge or transfer of a patient to another ward or whenever any visible soling was present. Cleaning and disinfection of any patient related mobile or shared medical equipment was the responsibility of the Ward staff rather than Environmental Services and was to be done after use on any patient and at discharge or transfer. A review of the medical equipment cleaning and disinfection revealed verbal reports of staff not following the cleaning and disinfection process. No logs of the cleaning and disinfection of the shared medical equipment were kept. Reviews of all breakrooms, lunch rooms and the cafeteria and WHS investigations with the HCWs identified no breaches in compliance but nonetheless these measures were reinforced. Outbreaks on both wards settled rapidly, within 3 weeks, without extraordinary measures or changes to PPE other than improved adherence to all measures for PPE donning, doffing [19] and hand hygiene.

Discussion

Patient-to-patient and patient-to-HCW transmission on Ward 1 followed by transmission from Ward 1 to Ward 2 via HCWs who worked between both wards was considered most likely. The two wards were in separate buildings. For Ward 2, with 84% of symptomatic patients presenting within a 72 hour period, as well as a significant association with the use of a mobile VSC and the presence of environmental SARS-CoV-2 RNA contamination with very low Ct values, a point-source transmission from the VSC was considered a plausible explanation based on the epidemiologic and environmental findings. There is evidence that SARS-CoV-2 from clinical sources (cough droplets, saliva, nasal secretions) can be readily cultured from human hands and may persist on common medical surfaces for many hours, including stethoscope diaphragms, pulse oximeters and plastic surfaces, all of which are basic components of the VSCs [12,13]. The lack of systematic cleaning and disinfection of the VSC and its components would have permitted continued growth of the virus on its high touch surfaces. The suboptimal hand hygiene and improper doffing of eyewear and masks in the immediate pre-outbreak period which we documented through the covert audits on the Ward would have provided opportunities for contact transmission of the virus to the mucous membranes of the HCWs. It is also possible that additional HCWs were infected and at work communicable to others unbeknownst to the outbreak response teams given that testing was not mandatory. Transmission may have occurred in association with close contact between patients who were in multi-bedded rooms with a single shared bathroom but it does not explain how 8 patients became symptomatic and were laboratory confirmed COVID-19 on the same day but were in different rooms and no one HCW had assignments to all these patients. The lack of finding of any transmission events associated with patients in single rooms, with the one exception where the mobile VSC was used, and the ventilation parameters exceeding CSA standards does not support long-range airborne transmission across either of the wards. It is possible transmission occurred via infected HCWs travelling with the cart during their interactions with patients but this possibility is not compatible with the timing.

The prolonged presence of low Ct values in patients (Figure 3), that correlate with cultivatable virus [12], combined with a stronger binding avidity to ACE-2 bearing receptor cells [20] provide a potential explanation as to why the Delta variant strain was so transmissible. This outbreak occurred despite mRNA vaccination in a large number of HCWs and patients (Table 1), which corroborates other study findings [4,5].

This outbreak also occurred in the setting of continuous masking by HCWs but thorough investigations led to discovery of well recognized risk factors for transmission: suboptimal adherence and compliance to PPE protocols, suboptimal hand hygiene, risks associated with multi-bedded rooms, and a contaminated VSC with potential fomite or indirect spread via the attendant HCWs. An underlying impression of a "veil of protection" feeling among vaccinated HCWs, illustrative of the bias of purity risk ritual may have contributed [21].

Despite the rigour of investigation and the strength of our findings, there are limitations to this study including imprecision due to not testing all HCWs, recall bias, non-responder bias, and inability to capture every patient-HCW interaction and care being provided without documented patient assignment. Nonetheless, the findings underscore the importance of "shoe leather" epidemiology supplemented with molecular epidemiology and adherence to fundamental IPC principles and rigourous investigations to ascertain modes of transmission during a COVID -19 outbreak.

Unlike other outbreak reports where N95 respirators were employed as a part of the response strategy [6] and considered a necessary component, this outbreak settled rapidly without any change to PPE recommendations. Rather our approach focused on a back-to-basics approach emphasizing PPE adherence and hygienic practices. This approach is similar to the one utilized by Susky et al. [7] and supports results seen in recent systematic reviews [22, 23] and a large matched case-control study in

France [24] where there was no difference in an multivariate analysis in HCWs who acquired COVID-19 whether they were wearing a surgical mask or a N95 respirator.

Transparency Declaration

Conflicts of interest

All authors have filled out an ICMJE Disclosure form. None of the authors have relevant direct conflicts of interest to declare related to the submitted manuscript. All authors have read the submitted version of the manuscript.

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Ethics approval

This investigation was conducted as part of a formal Epidemiologic Investigation under Public Health in the Province of Alberta. It also was assessed using the ARECCI (A Project Ethics Community Consensus Initiative) tool which scored this project as fitting with a quality improvement project for which ethics approval is not required. The consenting and culturing of virus from the affected patients was approved by the University of Calgary Conjoint Research Ethics Board (REB20-0444).

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Author Contributions:

HMO: conceptualization, data curation, formal analysis, investigation, methodology, writing, original draft and review and editing

RH: conceptualization, data curation, investigation, methodology, writing, original draft and review and editing

KS, LT, PY, LW, AF: data curation, investigation, validation, writing – review and editing

PJ, AW, JC: data curation, validation, resources, writing – review and editing

TL, MC, VL, KP, AW, HYZ, TD, KH, BMB, KF: data curation, validation, writing – review and editing

YCL, DE: Data curation, formal analysis, resources, methodology, writing – review and editing

JMC: conceptualization, data curation, formal analysis, investigation, methodology, resources, writing, funding, original draft and review and editing.

Figure 1. Delta SARS-CoV-2 Introduction and Transmission between 2 Wards

(A) Origin of SARS-CoV-2 Delta variant on Ward 1.

CA indicates community acquired; HA indicates hospital acquired; SOD is the date of core respiratory, core GI or expanded COVID symptom onset or the date the case tested positive for COVID-19, whichever is sooner; PT indicates patient; HCW indicates Healthcare Worker; DSP indicates designated support person. Solid lines indicates strong epidemiological link based on work assignment, detailed interview and/or any reported PPE breaches. Direction of arrow indicates direction of transmission.

(B) Epidemic Curve of Delta SARS-CoV-2 Outbreak on Two Medical Wards

Epidemic curve showing cases (patient and HCW) by symptom onset date (SOD). SOD is the date of core respiratory, core GI or expanded COVID symptom onset or the date the case tested positive for COVID-19, whichever is sooner. OB indicates outbreak. Dates of outbreaks on Ward 1 and 2 are indicated by a green and orange line, respectively. Outbreak on Ward 2 closed on day 59 (indicated by forward facing arrow). Black arrow indicates HCW movement between Wards 1 and 2. Open black arrows indicate key epidemiological events.

(C) Introduction and Transmission of Delta SARS-CoV-2 on Ward 2

SOD is the date of core respiratory, core GI or expanded COVID symptom onset or the date the case tested positive for COVID-19, whichever is sooner; PT indicates patient; HCW indicates Healthcare Worker. Solid lines denote transmission event with strong epidemiological link based upon work assignment, detailed interview and/or any reported PPE or hand hygiene breaches; dashed black lines denotes possible transmission based upon care dates and communicable phase of illness; blue lines

indicate patient to patient transmission event or patient who were roommates; black lines indicate HCW to patient transmission event; orange lines indicate patient to HCW transmission event; black frames around HCW cases denote shift overlap with a co-worker. Absence of any line indicates source of infection is unknown/no specific interaction between patients and/or HCWs identified. In all cases the risk period refers the communicable phase of illness (defined as 48 hours before symptom onset until to 14 days after symptom onset).

Figure 2. Room assignment of positive cases

Room number is indicated for each room (1-14) and shower room is indicated by ‡. Symptom onset date (SOD) is indicated by day in blue text and the number of patients that were positive in each room is indicated in italics (n=x). SOD is the date of core respiratory, core GI or expanded COVID symptom onset or the date the case tested positive for COVID-19, whichever is sooner. Solid red boxes indicate shared rooms where positive cases were found; dotted red box indicate private room where positive case was found; solid green boxes indicate shared rooms where no positive cases were found; dotted green box indicates private rooms where no positive cases were found.

Figure 3. Transmission of Delta SARS-CoV-2 cases on Ward 2

Serial Ct values of patients over time.

PFU indicates plaque forming units (per ml); Ct indicates cycle threshold value for the Envelope (E) gene; PT indicates patients (for Ward 2 patients numbering starts at PT 4, as per numbering in Figure 1C). Data represent 13 of 14 patients; PT 17 was not tested for serial CT. Median, minimum and maximum number of serial Ct values per patient is 6, 2 and 11, respectively.

Figure 4. Whole Genome Sequencing of HCWs and patient cases from Ward 1 and Ward 2

PT indicates patient; HCW indicates Healthcare Worker. NC_045512.2 is the genome reference sequence number for SARS-CoV-2 (Wuhan genome). Please refer to Figure 1, which indicates which HCWs and patients are linked to either Ward 1 (Figure 1A) and Ward 2 (Figure 1C).

References

[1] Cherian S, Potdar V, Jadhav S, Yadav P, Gupta N, Das M, et al. SARS-CoV-2 Spike Mutations, L452R, T478K, E484Q and P681R, in the Second Wave of COVID-19 in Maharashtra, India. Microorganisms 2021;9. https://doi.org/10.3390/microorganisms9071542.

[2] Arora P, Sidarovich A, Krüger N, Kempf A, Nehlmeier I, Graichen L, et al. B.1.617.2 enters and fuses lung cells with increased efficiency and evades antibodies induced by infection and vaccination. Cell Rep 2021;37:109825. https://doi.org/10.1016/j.celrep.2021.109825.

[3] Tian D, Sun Y, Zhou J, Ye Q. The Global Epidemic of the SARS-CoV-2 Delta Variant, Key Spike Mutations and Immune Escape. Front Immunol 2021;12:751778. https://doi.org/10.3389/fimmu.2021.751778.

[4] Lim W-Y, Tan GSE, Htun HL, Phua HP, Kyaw WM, Guo H, et al. First nosocomial cluster of COVID-19 due to the Delta variant in a major acute care hospital in Singapore: investigations and outbreak response. J Hosp Infect 2021;122:27–34. https://doi.org/10.1016/j.jhin.2021.12.011.

[5] Shitrit P, Zuckerman NS, Mor O, Gottesman B-S, Chowers M. Nosocomial outbreak caused by the SARS-CoV-2 Delta variant in a highly vaccinated population, Israel, July 2021. Euro Surveill Bull Eur Sur Les Mal Transm = Eur Commun Dis Bull 2021;26. https://doi.org/10.2807/1560-7917.ES.2021.26.39.2100822.

[6] Hetemäki I, Kääriäinen S, Alho P, Mikkola J, Savolainen-Kopra C, Ikonen N, et al. An outbreak caused by the SARS-CoV-2 Delta variant (B.1.617.2) in a secondary care hospital in Finland, May 2021. Euro Surveill Bull Eur Sur Les Mal Transm = Eur Commun Dis Bull 2021;26. https://doi.org/10.2807/1560-7917.ES.2021.26.30.2100636.

[7] Susky EK, Hota S, Armstrong IE, Mazzulli T, Kestenberg S, Casaubon LK, et al. Hospital outbreak of the severe acute respiratory coronavirus virus 2 (SARS-CoV-2) delta variant in partially and fully vaccinated patients and healthcare workers in Toronto, Canada. Infect Control Hosp Epidemiol 2021:1–4. https://doi.org/10.1017/ice.2021.471.

[8] Stone SP, Cooper BS, Kibbler CC, Cookson BD, Roberts JA, Medley GF, et al. The ORION

statement: guidelines for transparent reporting of Outbreak Reports and Intervention studies Of Nosocomial infection. J Antimicrob Chemother 2007;59:833–40. https://doi.org/10.1093/jac/dkm055.

[9] Pabbaraju K, Wong AA, Douesnard M, Ma R, Gill K, Dieu P, et al. Development and validation of RT-PCR assays for testing for SARS-CoV-2. Off J Assoc Med Microbiol Infect Dis Canada 2021;6:16–22.

[10] Endo A, Leclerc QJ, Knight GM, Medley GF, Atkins KE, Funk S, et al. Implication of backward contact tracing in the presence of overdispersed transmission in COVID-19 outbreaks. Wellcome Open Res 2020;5:239. https://doi.org/10.12688/wellcomeopenres.16344.3.

[11] Zelyas N, Pabbaraju K, Croxen MA, Lynch T, Buss E, Murphy SA, et al. Precision response to the rise of the SARS-CoV-2 B.1.1.7 variant of concern by combining novel PCR assays and genome sequencing for rapid variant detection and surveillance. Microbiol Spectr 2021;9:e0031521. https://doi.org/10.1128/Spectrum.00315-21.

[12] Lin Y-C, Malott RJ, Ward L, Kiplagat L, Pabbaraju K, Gill K, et al. Detection and quantification of infectious severe acute respiratory coronavirus-2 in diverse clinical and environmental samples. Sci Rep 2022;12:5418. https://doi.org/10.1101/2021.07.08.21259744.

[13] Rajakumar I, Isaac DL, Fine NM, Clarke B, Ward LP, Malott RJ, et al. Extensive environmental contamination and prolonged severe acute respiratory coronavirus-2 (SARS CoV-2) viability in immunosuppressed recent heart transplant recipients with clinical and virologic benefit with remdesivir. Infect Control Hosp Epidemiol 2021:1–3. https://doi.org/10.1017/ice.2021.89.

[14] Tyson JR, James P, Stoddart D, Sparks N, Wickenhagen A, Hall G, et al. Improvements to the ARTIC multiplex PCR method for SARS-CoV-2 genome sequencing using nanopore. BioRxiv Prepr Serv Biol 2020. https://doi.org/10.1101/2020.09.04.283077.

[15] Freed NE, Vlková M, Faisal MB, Silander OK. Rapid and inexpensive whole-genome sequencing of SARS-CoV-2 using 1200 bp tiled amplicons and Oxford Nanopore Rapid Barcoding. Biol Methods Protoc 2020;5:bpaa014. https://doi.org/10.1093/biomethods/bpaa014.

[16] Katoh K, Standley DM. A simple method to control over-alignment in the MAFFT multiple sequence alignment program. Bioinformatics 2016;32:1933–42. https://doi.org/10.1093/bioinformatics/btw108.

[17] O'Grady HM, Dixit D, Khawaja Z, Snedeker K, Ellison J, Erebor J, et al. Asymptomatic severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection in adults is uncommon using rigorous symptom characterization and follow-up in an acute care adult hospital outbreak. Infect Control Hosp Epidemiol 2022:1–25. https://doi.org/10.1017/ice.2022.168.

[18] Alberta Health Services IP and C. Aerosol-Generating Medical Procedure Guidance Tool n.d.:9. https://www.albertahealthservices.ca/topics/Page17091.aspx.

[19] Alberta Health Services IP and C. Personal Protective Equipment n.d. https://www.albertahealthservices.ca/ipc/page6422.aspx.

[20] Augusto G, Mohsen MO, Zinkhan S, Liu X, Vogel M, Bachmann MF. In vitro data suggest that Indian delta variant B.1.617 of SARS-CoV-2 escapes neutralization by both receptor affinity and immune evasion. Allergy 2022;77:111–7. https://doi.org/10.1111/all.15065.

[21] VanSteelandt A, Conly J, Ghali W, Mather C. Implications of design on infection prevention and control practice in a novel hospital unit: the Medical Ward of the 21st Century. Anthropol Med 2015;22:149–61. https://doi.org/10.1080/13648470.2014.1003795.

[22] Bartoszko JJ, Farooqi MAM, Alhazzani W, Loeb M. Medical masks vs N95 respirators for preventing COVID-19 in healthcare workers: A systematic review and meta-analysis of randomized trials. Influenza Other Respi Viruses 2020;14:365–73. https://doi.org/10.1111/irv.12745.

[23] Jefferson T, Del Mar CB, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database Syst Rev 2020;2020. https://doi.org/10.1002/14651858.CD006207.pub5.

[24] Belan M, Charmet T, Schaeffer L, Tubiana S, Duval X, Lucet J-C, et al. SARS-CoV-2 exposures of healthcare workers from primary care, long-term care facilities and hospitals: A nationwide

matched case-control study. 2022 Jun 29:S1198-743X(22)00334-2. doi:
10.1016/j.cmi.2022.05.038.

Table 1. Number of Delta SARS-CoV-2 cases and vaccination status on Wards 1 and 2

Ward	HCW				Patient			
	n=0	***n=1***	***n=2***	**Total**	***n=0***	***n=1***	***n=2***	**Total**
1	*0*	*1*	*2*	***3***	0	3	0	***3***
2	*1*	*3*	*5*	***9***	4	4	6	***14***
Number of cases	**1**	**4**	**7**	***12***	**4**	**7**	**6**	***17***

n refers to the number of vaccine doses

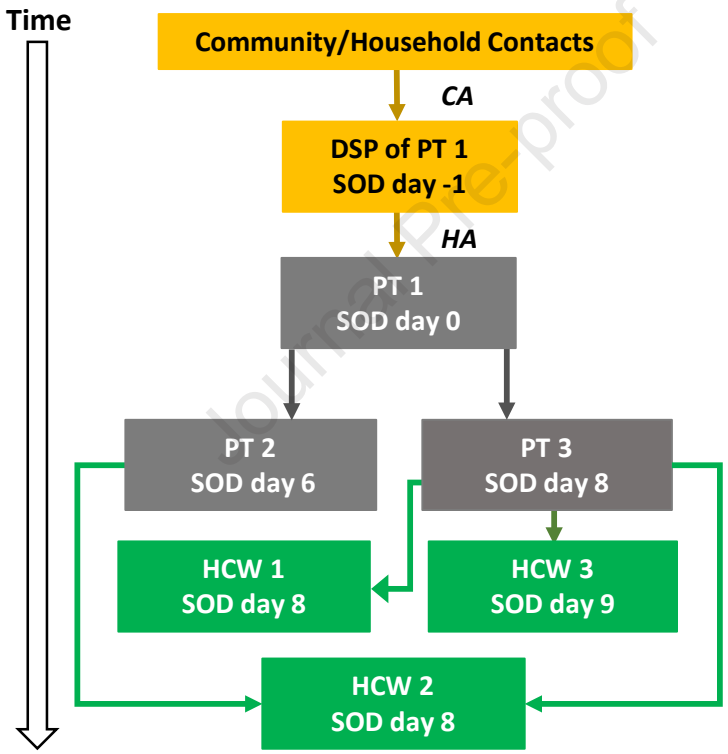
Table 2. Environmental specimens from Ward 2 taken on days 1 and 2[a]

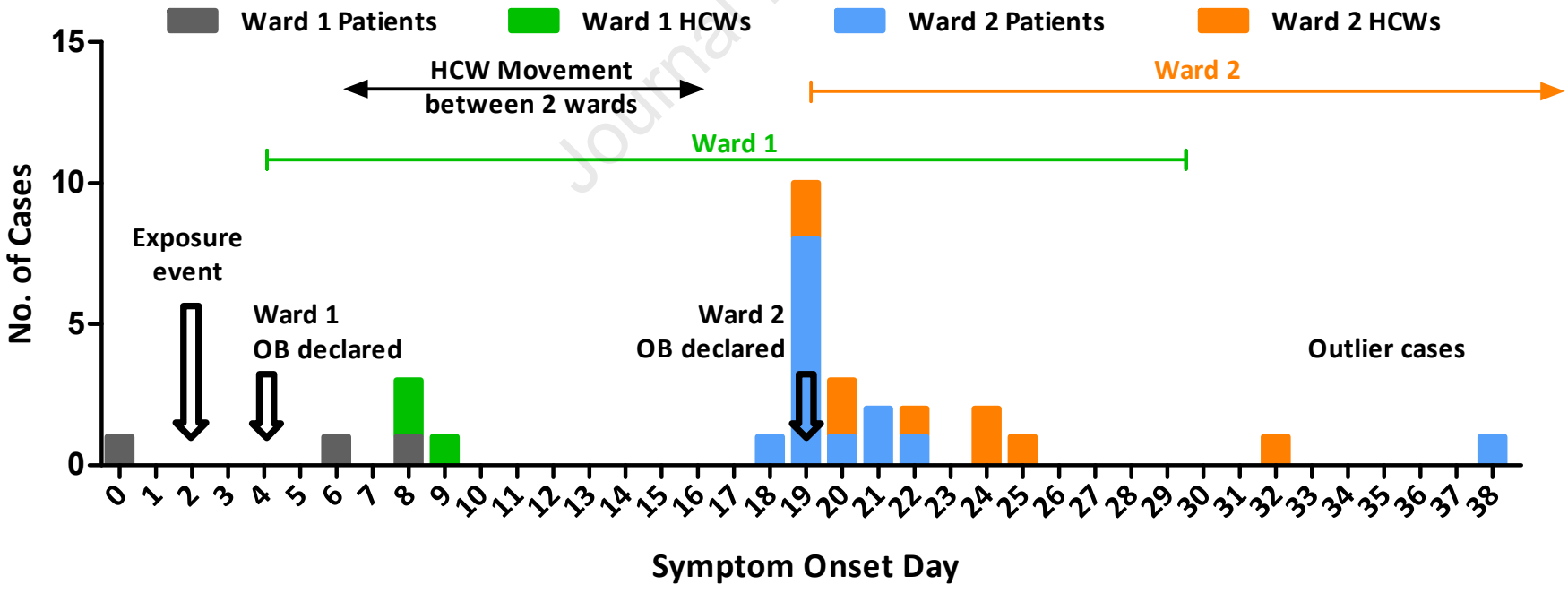
Environmental Specimens	**RT-PCR**
RT-PCR (Ward 2 Day 1) [b]	**CT (E gene)**
Patient room 11 (2-bed)	
Call bell	32.28
Commode	34.82
Bed rail	33.92
Table top	31.98
A random blood pressure monitor, thermometer, bladder scanner and O_2 monitor and shower room (n=5)	negative
Room 13 specimens (call bell, bed rail, light switch, table top (n=4))	negative
RT-PCR (Ward 2 Day 2)	**CT (N gene)**
Room 13 (overcapacity space)	
Vital signs cart 1: Thermometer 1	19.14
Vital signs cart 1: metal temperature probe	18.27
Vitals signs cart 1:pulse oximeter	19.15
Vitals signs cart 1:push handle	17.14
Commode: under seat and armrests	19.26
Patient room 14 (4-bed)	
Vital signs cart 2: Thermometer 2	18.1
Vital signs cart 2: Pulse oximeter 2	18.8
Vital signs cart 2: Push handle and monitor buttons	20.14
Vital signs cart 2: Stethoscope	18.06
Patient room 11 (2-bed)	
Commode: under seat, armrests	16.92
Patient room 9 (2-bed)	
Commode	15.2
Bed rail	19.4
Call bell	20.08
Stethoscope hanging on door	19.7
Patient room 12 (Private)	
Room sink taps and vanity counter	18.48
Call bell (on bedrail only)	18.5
Vitals monitor buttons, thermometer, pulse oximeter	18.53

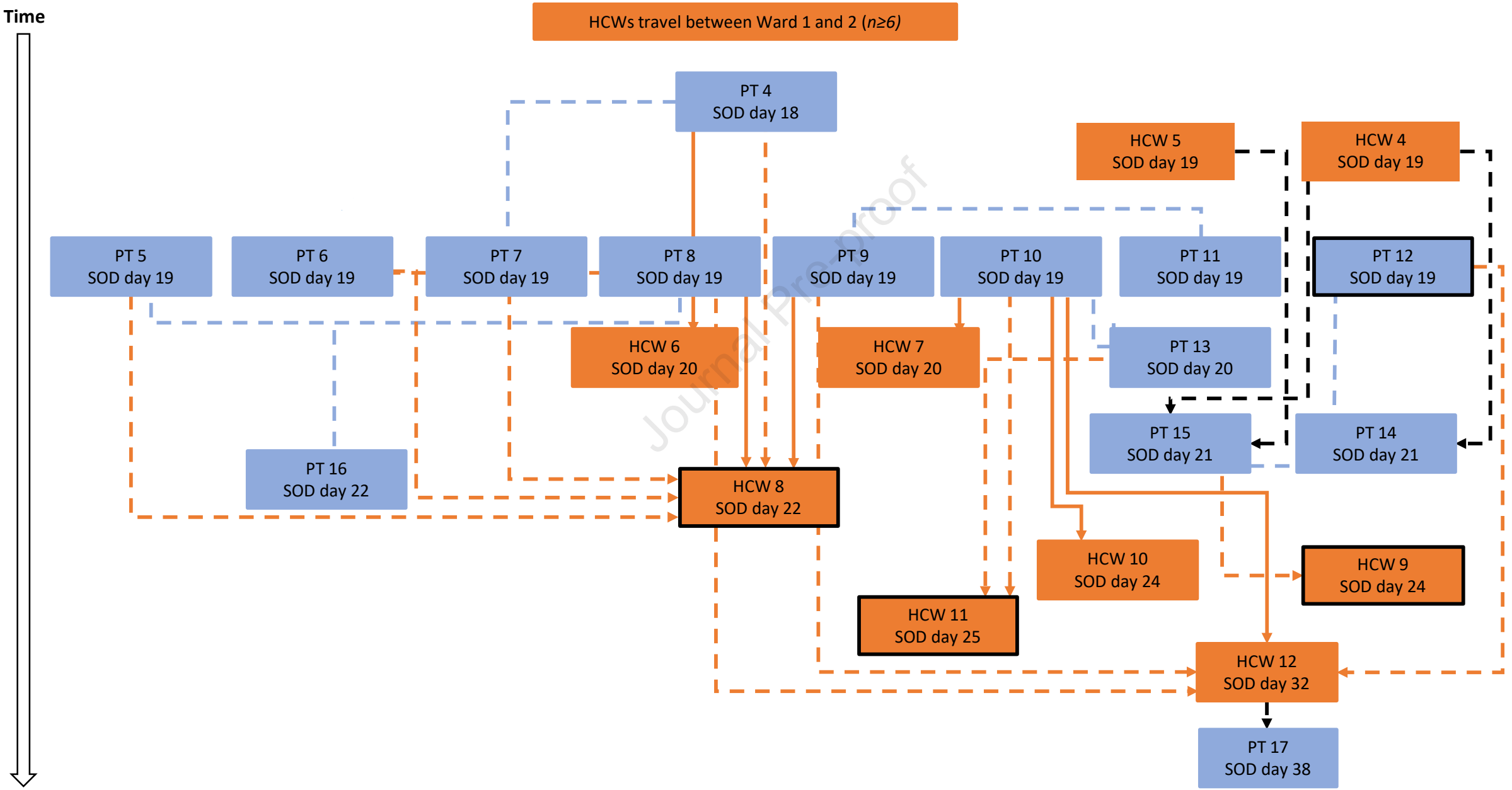
Computer on Wheels (COW) between rooms 10 and 11	
Computer keyboard and mouse	17.23
Shared Equipment stored across from room 5	
Bladder scanner - push handle, wand, monitor buttons, gel bottle	16.96
Masimo vital cart - push handles, temp probe, monitor buttons, pulse oximeter	17.44

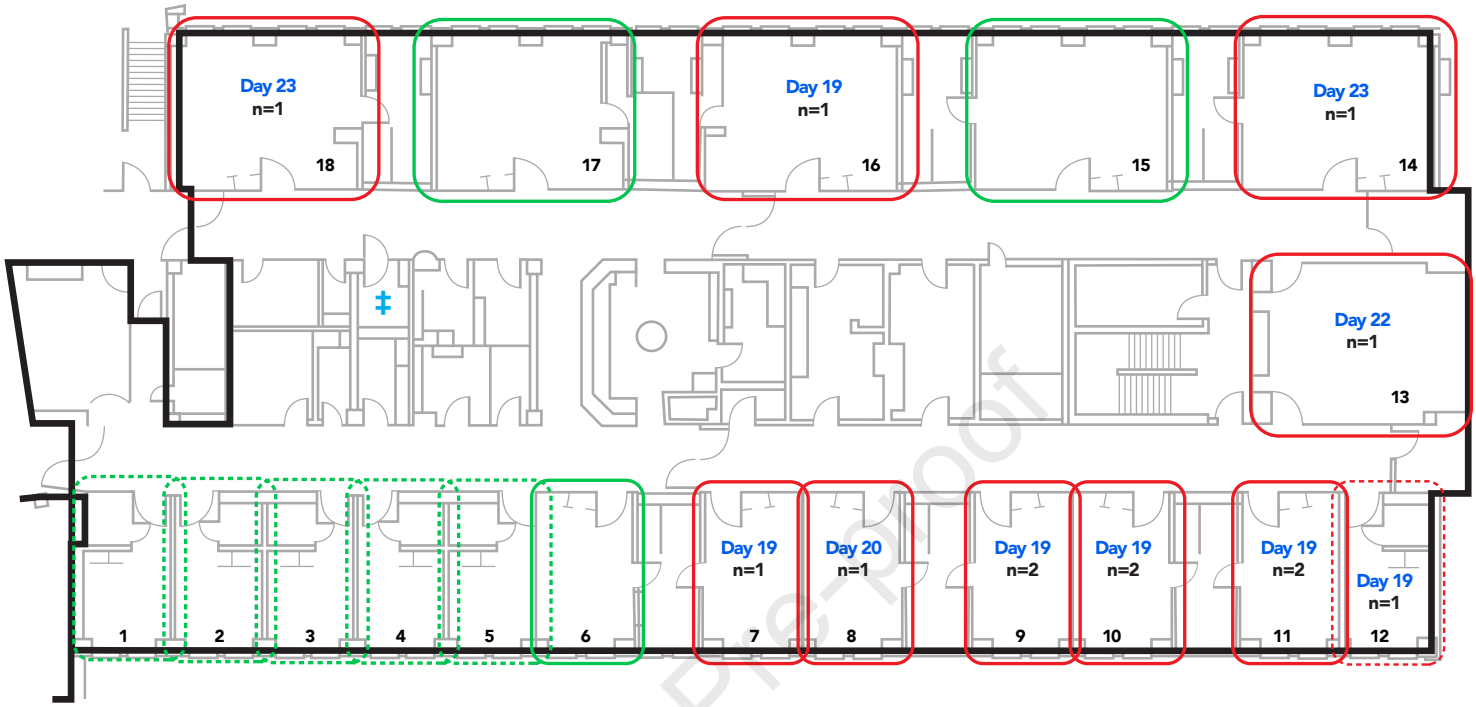
[a]Day 1 and 2 on Ward 2 corresponds to day 19 and 20 (related to Ward 1), as per Figure 2B

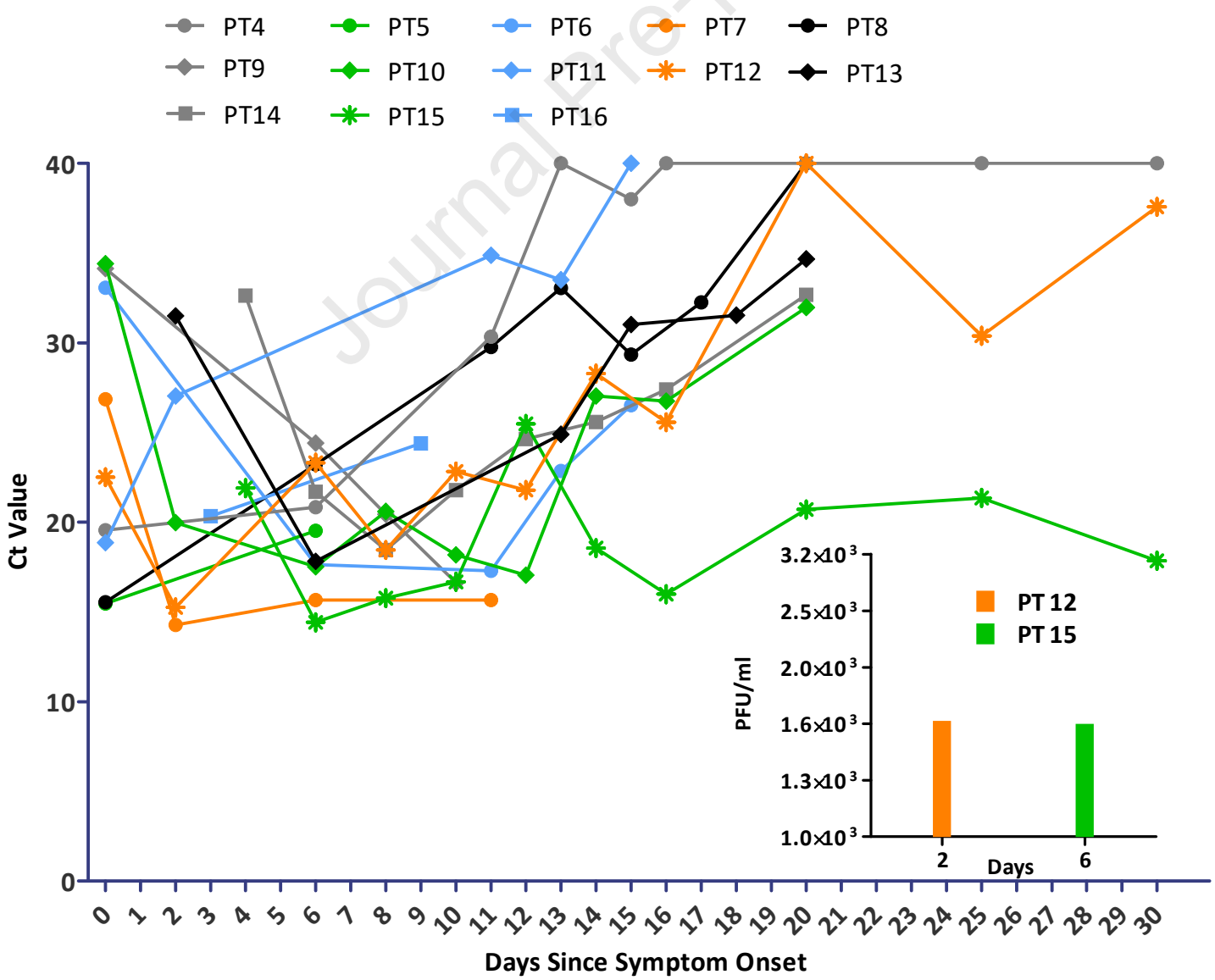
[b]All strains were confirmed Delta by RT-PCR [11]

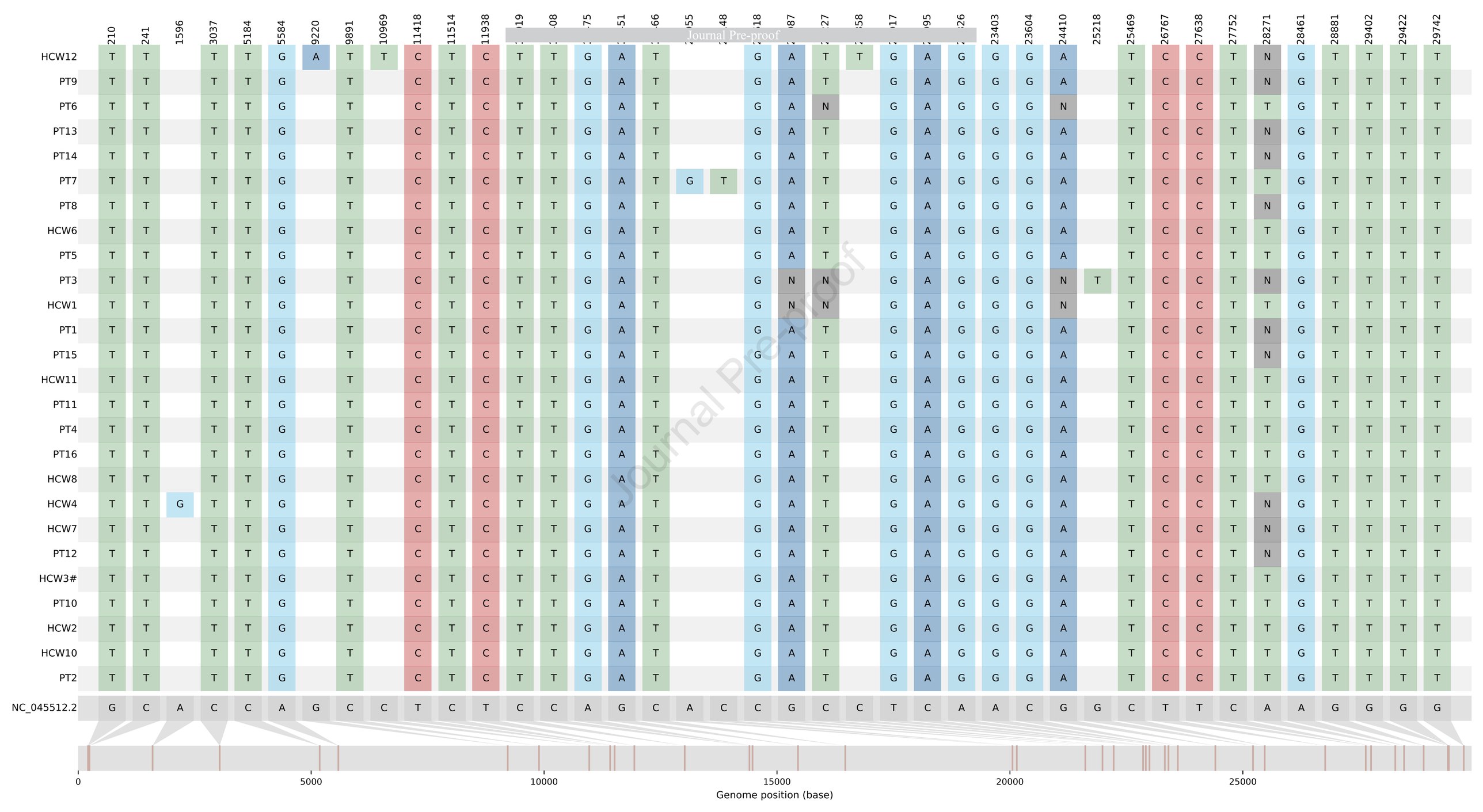








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Genome position (base)