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MAJOR ARTICLE

Integrated Genomic and Social Network Analyses of Severe Acute Respiratory Syndrome Coronavirus 2 Transmission in the Healthcare Setting

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Background. Infection prevention (IP) measures are designed to mitigate the transmission of pathogens in healthcare. Using large-scale viral genomic and social network analyses, we determined if IP measures used during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic were adequate in protecting healthcare workers (HCWs) and patients from acquiring SARS-CoV-2.

Methods. We performed retrospective cross-sectional analyses of viral genomics from all available SARS-CoV-2 viral samples collected at UC San Diego Health and social network analysis using the electronic medical record to derive temporospatial overlap of infections among related viromes and supplemented with contact tracing data. The outcome measure was any instance of healthcare transmission, defined as cases with closely related viral genomes and epidemiological connection within the healthcare setting during the infection window. Between November 2020 through January 2022, 12 933 viral genomes were obtained from 35 666 patients and HCWs.

Results. Among 5112 SARS-CoV-2 viral samples sequenced from the second and third waves of SARS-CoV-2 (pre-Omicron), 291 pairs were derived from persons with a plausible healthcare overlap. Of these, 34 pairs (12%) were phylogenetically linked: 19 attributable to household and 14 to healthcare transmission. During the Omicron wave, 2106 contact pairs among 7821 sequences resulted in 120 (6%) related pairs among 32 clusters, of which 10 were consistent with healthcare transmission. Transmission was more likely to occur in shared spaces in the older hospital compared with the newer hospital (2.54 vs 0.63 transmission events per 1000 admissions, $P < .001$).

Conclusions. IP strategies were effective at identifying and preventing healthcare SARS-CoV-2 transmission.

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Keywords. SARS-CoV-2 pandemic; infection prevention precautions; healthcare transmission of SARS-CoV-2; whole-genome sequencing; social network analyses and contact tracing.

Infection prevention measures and policies designed to prevent transmission of infectious diseases have been standard practice for decades in healthcare. Despite the wide use of these practices, there are limited clinical data supporting their efficacy. In the first few months of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, viral transmission within healthcare settings was pervasive, and personal protective equipment (PPE) was in short supply [1–3]. Additionally, cases that were spatially and temporally associated were assumed to be evidence of transmission. The use of genetic analysis eliminates these spurious associations. Healthcare systems had to adapt in the setting of resource limitations and evolving knowledge about the transmission characteristics of the virus. After the adoption of measures including universal masking, eye protection [4], symptom screening protocols, and routine testing within healthcare settings, SARS-CoV-2 incidence declined among healthcare workers (HCWs) and remained at or below local community rates [5, 6]. However, a lack of dedicated studies to determine the effectiveness of infection prevention practices (including PPE and optimized air exchanges and filtration) in the healthcare setting has resulted in varied approaches and persistent questions as to their effectiveness at preventing transmission, especially during periods of high community prevalence when the rates of transmission in healthcare could be overestimated without genetic validation of transmission [5–7].

Genetic analysis has been widely used to identify linkages between bacterial and viral strains associated with transmission clusters [8–11], including in SARS-CoV-2. Likewise, social network analysis (tracking movements and interactions among HCWs and patients) has been used as an infection prevention tool to identify sources of hospital-onset infections and predict transmission events [12–15]. In this cross-sectional analysis, we established a temporospatial network of contacts among SARS-CoV-2–infected HCWs and patients. We then used viral whole-genome sequencing of cases within this network to identify possible instances of transmission within the health system.

This study was performed to determine whether the institutional infection prevention protocols and contact tracing practices that were in place over 3 distinct waves of the SARS-CoV-2 pandemic (including during the emergence of the highly transmissible Omicron variant [BA.1/B.1.1.526] in late 2021 [6, 16, 17]) were effective at mitigating and identifying transmission events.

METHODS

Electronic Contact Record

We performed a retrospective analysis of all individuals with a positive test for SARS-CoV-2 at the University of California San Diego Health (UCSDH), including the workforce and patient population (both inpatient and outpatient) from 1 November 2020 through 27 January 2022. During this time, all symptomatic HCWs were tested, and routine mandated weekly asymptomatic or post-exposure testing was performed as well. Information on patient and HCW location and movement within UCSDH was obtained from the electronic health record (EHR) to characterize their interactions and is here termed the electronic contact record (ECR). All SARS-CoV-2–positive samples identified at UCSDH during that time period underwent whole-genome sequencing if sufficient high-quality viral material was identified on the specimen swab. To assess plausible epidemiologic links, social network analysis was compared to the results of maximum likelihood phylogenetic and genetic analyses of the viral sequences obtained during the study period.

Detailed methods regarding SARS-CoV-2 whole-genome sequencing, phylogenetic and genetic network, contact tracing, and retrospective tracing analyses are included in the Supplementary Appendix. Statistical analyses using the χ^2 test and *t* test were performed using R-Studio. All SARS-CoV-2 genomes used in this analysis have been uploaded to GISAID as part of the SEARCH Alliance.

Institutional review board review exemption was obtained for this quality improvement initiative, which was approved through UCSDH's Aligning and Coordinating Quality Improvement, Research and Evaluation Committee [18].

RESULTS

We set out to determine if our ECR tool was effective at identifying healthcare-associated SARS-CoV-2 transmission events and if cryptic transmission occurred within UCSDH. From 1 November 2020 through 27 January 2022, there were 35 666 SARS-CoV-2 polymerase chain reaction–positive tests of 1 303 622 total tests performed (2.74%) at UCSDH. We obtained high-quality SARS-CoV-2 whole-genome sequences from 12 933 individuals and identified 2397 pair interactions in the ECR among these individuals. Given the high transmissibility and rapid spread of the Omicron variant, we divided our population into 2 analyses: the second and third SARS-CoV-2 epidemic waves and the Omicron wave.

When comparing the demographic characteristics of the second and third waves of SARS-CoV-2 expanded to the Omicron analysis, the population infected with the Omicron variant tended to be older, was more likely to have been vaccinated at the time of a positive test, and had a higher proportion of HCWs compared with those infected during the prior 2 waves (Table 1).

Table 1. Demographic Characteristics, Healthcare Worker Job Titles, and Vaccination Status of the Study Population

Demographic	Second and Third Waves of SARS-CoV-2 Original (n = 39)	Second and Third Waves of SARS-CoV-2 Expanded (n = 91)	Omicron (n = 126)	*P* Value
Age, y				*P* = .054
Median	39	36	38	
Interquartile range	24.8–49.8	27.5–51.5	33–52	
Range	2–92	2–92	19–95	
Sex				*P* = .21
Male	15	43	48	
Female	24	48	76	
Nonbinary/Unknown			2	
Race				
White	13	33	59	
Black	3	7	4	
Asian	1	5	13	
Native Hawaiian or other Pacific Islander	0	0	1	
More than 1 race	0	0	6	
Other/Unknown	22	46	43	
Ethnicity				
Hispanic/Latino	10	29	41	
Not Hispanic/Latino	28	56	74	
Other/Unknown	1	6	11	
Job title				Patient-to-healthcare worker proportion *P* < .001
Nurse	6	10	36	
Physician (including medical student, resident, and fellow)	0	1	22	
Advanced practice provider (including Nurse Practicioner, Physician Assistant)	0	0	6	
Medical assistant	0	1	7	
Front office/Administrative/Billing	1	3	4	
Technician (electroencephalogram, electrocardiogram, radiology, anesthesia)	0	0	8	
Care coordinator/Navigator	0	0	3	
Respiratory therapy	2	2	4	
Physical therapy, Occupational therapy/Social work	0	1	3	
Environmental services	0	0	1	
Nutrition	0	1	1	
Patient	30	72	31	
Vaccination status at time of positive, doses				Vaccinated to unvaccinated *P* < .001
1	1	4	2	
2	4	14	52	
3	0	1	52	
Unvaccinated	34	72	20/	

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Second and Third Waves of SARS-CoV-2

UCSDH infection prevention protocols during the second and third waves of SARS-CoV-2 (November 2020 through December 2021) included universal masking with surgical masks for both patients and HCWs as well as eye protection for HCWs when a patient was not masked and testing of patients upon admission to the hospital and prior to undergoing any aerosolizing procedures. While providing direct care for coronavirus disease 2019 (COVID-19) patients, HCWs were required to wear N95 respirators, eye protection, gowns, and gloves. Unvaccinated HCWs were tested twice weekly regardless of symptoms, and vaccinated HCWs were tested weekly during times of high community prevalence. Each HCW completed a daily COVID-19 symptom survey, and any positive symptom or known exposure prompted a referral for testing. Given the limited number of negative-pressure rooms, COVID-19 patients were not systematically placed in such rooms, and often the doors of these patients' rooms were kept open for safety to allow for direct observation.

UCSDH obtained high-quality SARS-CoV-2 genomes from 5112 HCWs and patients during the second and third waves of SARS-CoV-2 (Figure 1*A*) among whom the ECR algorithm

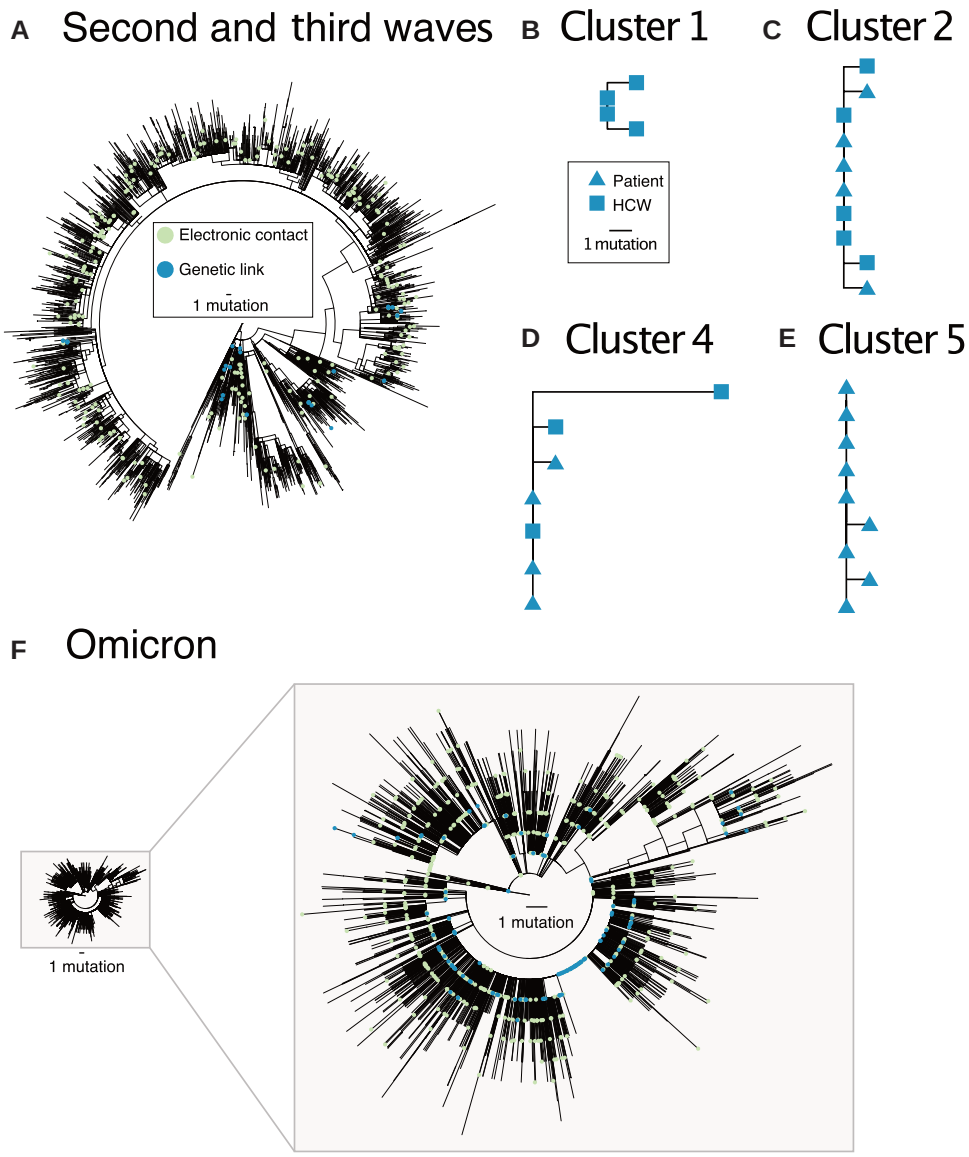

Figure 1. Clusters of people with links in the electronic contact records (ECRs) on the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) phylogeny. *A*, SARS-CoV-2 maximum likelihood phylogeny from the second and third pandemic waves. Tip shapes indicate that the viral genome came from a person with an ECR. Green indicates that these genomes were not linked. Blue indicates that they were genetically linked. *B–E*, Expanded view of clusters 1, 2, 4, and 5 from the second and third pandemic waves. Shape denotes patients (triangles) and HCWs (squares). *F*, SARS-CoV-2 maximum likelihood phylogeny from the BA.1 Omicron wave, shown on the same scale as the second and third waves and expanded for greater resolution (in the gray box). Abbreviation: HCW, healthcare worker.

then identified 291 contact pairs. Of these contacts, 34 pairs (39 unique individuals) had genetically linked viral sequences corresponding to a 12% (34 of 291) positive predictive value of the ECR algorithm at identifying a transmission partner (Figure 2*A*). The remaining 257 pairs were phylogenetically inconsistent with viral transmission, indicating that although these people had contemporaneous infections and had some general overlap in the healthcare system, their viral sequences were more genetically related to SARS-CoV-2 circulating in the wider community.

The 34 genetically linked ECR contacts formed 13 distinct clusters (Table 2). Three of these clusters were consistent with healthcare transmission (clusters 1, 2, and 4; Figure 1*B–D*). Of the remaining 20 pairs, 19 were associated with shared residences, suggesting household transmission. The remaining pair (cluster 3) could not be determined to have any meaningful contact within the healthcare system via their self-report of dates worked and only interacted with each other 24 hours prior to testing positive, suggesting community acquisition prior to this interaction within the healthcare system.

To identify gaps in our ECR framework, we expanded the membership of these 13 clusters to include individuals who had genetically related viral genomes but were not identified by our ECR framework. We identified an additional 52

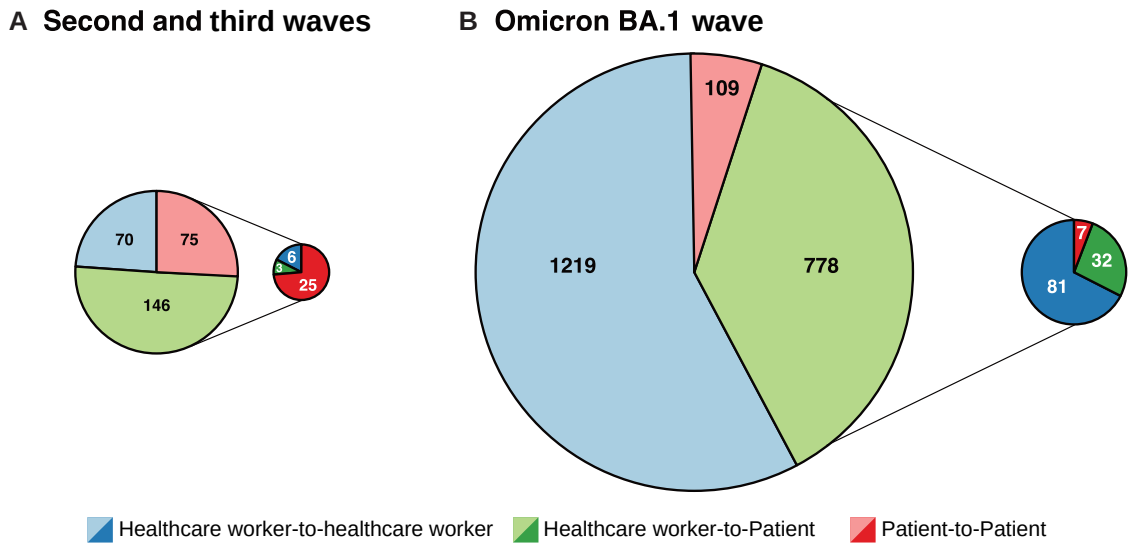

Figure 2. Contacts in the electronic contact records (ECRs) that are consistent with viral transmission based on severe acute respiratory syndrome coronavirus 2 phylogenetic analysis. *A*, Contacts during the second and third waves. *B*, Contacts during the BA.1 Omicron wave. The larger, lighter-colored pie represents links in the ECR. The smaller, darker-colored pie represents phylogenetic links. Color denotes the type of link: healthcare worker-to-healthcare worker in blue, healthcare worker-to-patient in green, and patient-to-patient in red. The area of the pies is proportional to the number of links represented.

individuals who had genomes that were identical or closely related to those of the original 39 cases. The expanded network comprised 91 individuals (from 9 HCWs and 30 patients before to 19 HCWs and 72 patients after; Table 1). By combining the original contact tracing information with retrospective case tracing analysis, we determined that the additional members of these clusters were not related by any healthcare interaction.

Evaluation of Healthcare Transmission During the Second and Third Waves of SARS-CoV-2

Three clusters were identified as healthcare-associated transmission in the second and third waves of SARS-CoV-2.

All 3 of these clusters had been previously identified by the contact tracing team. Several HCWs were able to identify the source of their infection as an unmasked patient with a negative test upon admission but within the incubation period. No instances of previously unrecognized transmissions during the second and third waves of SARS-CoV-2 were identified.

To validate our ECR algorithm, we examined its effectiveness at successfully ruling out unrelated cases through the retrospective case tracing analysis. The ECR algorithm correctly identified 12 of 17 (71%) cases that were genetically linked to others and had evidence of overlap in the healthcare system consistent with healthcare transmission. Of the 46 individuals with no evidence of healthcare transmission, the ECR algorithm correctly excluded 44 of them (96%).

Omicron Analysis

After demonstrating the effectiveness of the ECR tool at identifying potential transmission events in the healthcare system, we sought to identify similar events in a time of widespread community transmission of the Omicron variant. During the months of December 2021 and January 2022, 1376 HCWs were infected, a rise of more than 800% from the previous 2 months. At the peak of the Omicron wave, up to 257 HCWs tested positive per day. As a result of the increased transmissibility [9, 17, 19], UCSDH updated infection prevention measures starting on 18 December 2021. There were increased testing protocols for patients (on admission and day 3 of hospital stay) and HCWs (weekly for vaccinated, twice weekly for unvaccinated). Additionally, use of KN95 (or N95) respirators was strongly recommended for HCWs in all areas of healthcare as well as eye protection when in close contact with patients (in addition to ongoing N95, eye protection, gowns, and gloves for care of confirmed COVID-19 patients).

Between December 2021 and January 2022, high-quality SARS-CoV-2 genomes were obtained from 7821 HCWs and patients infected with the Omicron variant (99.8% BA.1 and 0.2% BA.2; Figure 1*B*). The ECR algorithm identified 2106 contact pairs, all with the BA.1 virus. One hundred and twenty pairs infected with the BA.1 subvariant were genetically closely related (126 individuals: 95 HCWs and 31 patients; Table 1) and formed 32 clusters, corresponding to a positive predictive value of 6% (126 of 2106). Of these pairs, 81 were between HCWs, 32 were between HCWs and patients, and 7 were between patients (Figure 2).

Unlike the prior SARS-CoV-2 waves, Omicron was exceptionally genetically homogeneous (Figure 1*F*), with approximately 10% of genomes having the identical sequence and 25% of

Table 2. Clusters, Transmission Characteristics, Healthcare Worker/Patient Ratio of Genetically Linked Electronic Contact Record (ECR) Contacts during the Second and Third SARS-CoV-2 Waves

Cluster Number	Number of Individuals in Original Cluster (HCW:Patient)	Number of Individuals in Expanded Cluster (HCW:Patient)	Healthcare Transmission	Type of Transmission	Comments
1	3 (3:0)	4 (4:0)	Yes	Workplace	Shared office space
2	4 (3:1)	10 (5:5)	Yes	Shared room, workplace, community	6 cases (4 HCWs, 2 patients) with healthcare transmission
3	2 (2:0)	7 (4:3)	Possible	Community	Two HCWs worked in the same department but only overlapped in the 24 hours prior to testing positive
4	5 (1:4)	7 (3:4)	Yes	Shared room, workplace	All 7 were on the same unit, 4 patients in a shared room
5	8 (0:8)	9 (0:9)	No	Household	Extended family, 3 households overlapping emergency contacts
6	2 (0:2)	5 (0:5)	No	Household, community	Original cluster members shared household
7	2 (0:2)	2 (0:2)	No	Household	
8	2 (0:2)	7 (2:5)	No	Household, community	Two pairs with shared household
9	3 (0:3)	25 (1:24)	No	Household, community	Original cluster members shared household; expanded cluster with cases spaced from April 2020– February 2021
10	2 (0:2)	8 (0:8)	No	Household, community	Original cluster members shared household
11	2 (0:2)	3 (0:3)	No	Household, community	Original cluster members shared household
12	2 (0:2)	2 (0:2)	No	Household	
13	2 (0:2)	2 (0:2)	No	Household	

Abbreviation: HCW, healthcare worker.

genomes within 1 mutation of this cluster of identical genomes. Based on the genetic homogeneity in Omicron, we would expect between 34 and 108 pairs (95% range) of HCW pairs, 21 and 63 HCW–patient pairs, and 1 and 11 patient–patient pairs to be genetically closely related by chance alone (Figure 3). For all contact types, the observed number of genetically linked contact pairs did not exceed these expected ranges, indicating that there was not a significant excess of Omicron transmission events between ECR contacts within our hospital system.

We performed a retrospective case tracing analysis of the 32 clusters. Cluster 1 was the largest cluster, with 81 pairs between 56 individuals. Of note, cluster 1 included the genotype shared by 10% of all sequenced Omicron cases. Therefore, we considered only cluster 1 members where contact tracing analysis supported healthcare overlap between the pairs: termed subclusters 1a, 1b, 1c, 1d, and 1e (Table 3).

Of the 120 genetically linked pairs (Figure 2*B*), we identified 24 instances of transmission in the healthcare setting and 2 of household transmission. We were unable to determine if there was any healthcare overlap in 7 pairs, and 87 pairs had no overlap in the healthcare system or at home (Supplementary Figure 2*B*).

Transmissions by Healthcare Campus

UCSDH consists of 2 campuses: the older Hillcrest campus, established in 1966, consists of a 381-bed hospital that contains multiple shared patient rooms and the newer 418-bed La Jolla campus, built between 1993 and 2016, that has a majority of single-occupancy rooms. During the study period (November 2020 through January 2022), there were 15 333 adult admissions at the Hillcrest campus and 20 765 at the La Jolla campus.

Most healthcare pair transmission events occurred at the older Hillcrest campus; 79% (11 pairs) during the second and third waves and 75% (18 pairs) during Omicron, in contrast to 21% (3 pairs) and 21% (5 pairs) at the La Jolla campus, respectively. Thirty-nine individuals (both HCWs and patients) were part of likely transmission events at Hillcrest compared with only 13 at the La Jolla campus. The rate of SARS-CoV-2 transmissions per 1000 admissions was 2.54 at Hillcrest compared with 0.63 at the La Jolla campus (χ^2 test; $P < .001$). Additionally, most patients who either acquired or transmitted SARS-CoV-2 in the hospital were in a shared room during part of their stay (6 of 6 patients during the second and third waves of SARS-CoV-2, 4 of 6 patients during Omicron). We did not identify a single transmission event from exposures via open doors of COVID-19 patients or from patients being placed in nonnegative-pressure rooms, except for exposure to roommates or their direct healthcare providers. Further, no instance of transmission from COVID-19 patients in the intensive care unit to HCWs was identified.

DISCUSSION

Infection prevention protocols had to be adapted to the increasing demands of a health system dealing with a novel, evolving, and highly transmissible respiratory pathogen. Most health systems lacked sufficient negative-pressure rooms to house all patients with acute SARS-CoV-2 infection. Masking and standard ventilation requirements for hospitals were the primary

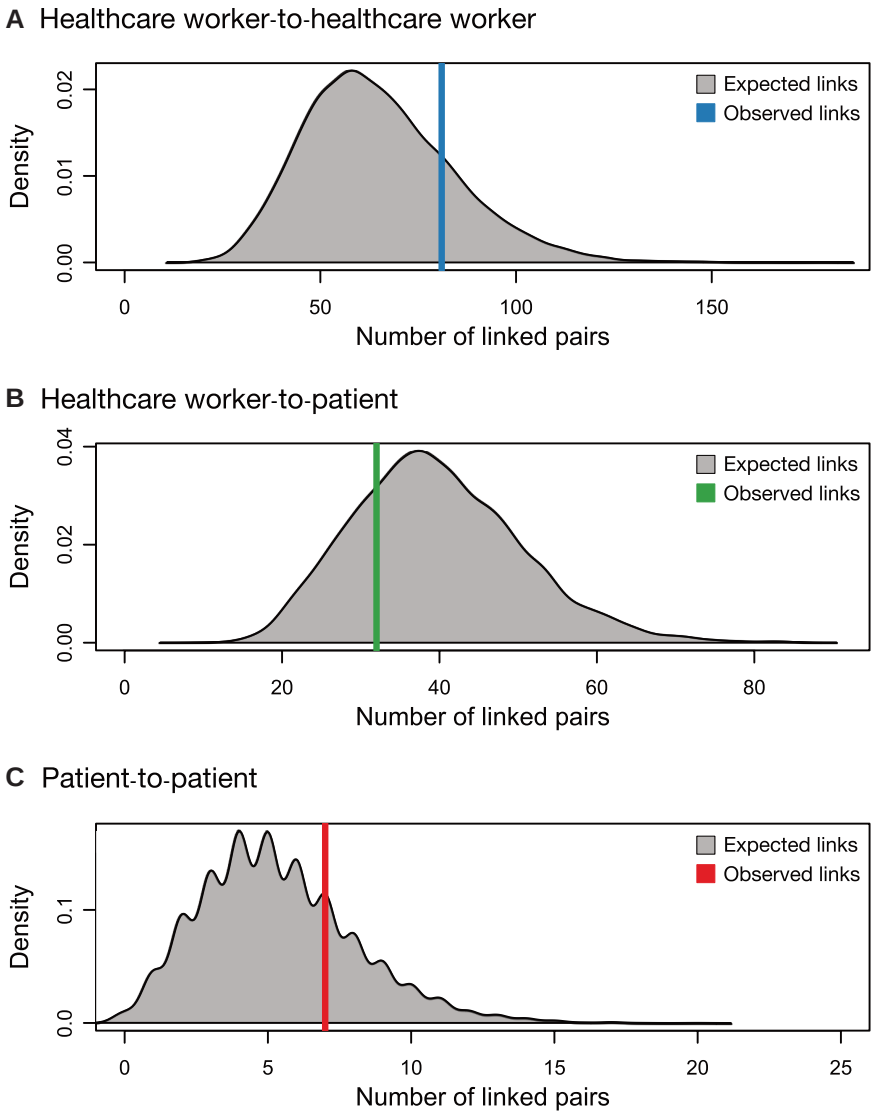

Figure 3. Expected and observed linked pairs during the BA.1 Omicron wave. *A*, Healthcare worker-to-healthcare worker genetically linked pairs. *B*, Healthcare worker-to-patient genetically linked pairs. *C*, Patient-to-patient genetically linked pairs. Number of observed linked pairs is indicated by the colored bars. Number of expected linked pairs based on 10 000 permutations is shown in gray.

physical measures used consistently to prevent transmission in the general work environment [20–22]. Combined with symptom screening, an aggressive testing regimen, and use of COVID-19 vaccination requirements, these measures protected HCWs and patients during the pandemic.

During the second and third SARS-CoV-2 epidemic waves, we determined that there were no instances of cryptic transmission evidenced in the ECR among the cases with a sequenced viral genome. The identified transmissions were previously known to our contact tracing team and occurred either in the setting of shared workspaces where HCWs were often observed not wearing masks or in shared patient rooms with unmasked patients. We did not identify any transmission occurring from known COVID-19 patients to HCWs, suggesting that the infection control measures in place for prevention of SARS-CoV-2 transmission from known cases were protective. Further, we were able to identify lapses in infection prevention practices (eg, shared spaces with limited masking) among the identified instances of healthcare transmission, suggesting that our infection control practices were successful when implemented properly.

We validated that our ECR tool accurately identified healthcare-related transmission events with a positive predictive value of 12%. Most contacts were not consistent with transmission events; in line with prior literature [17], this suggests that most SARS-CoV-2 cases among HCWs were due to community transmission rather than nosocomial spread.

During the Omicron wave, we identified instances of cryptic transmission that were consistent with the increased

Table 3. Clusters, Transmission Characteristics, Healthcare Worker/Patient Ratio of Genetically Linked Electronic Contact Record (ECR) Contacts during the Omicron SARS-CoV-2 Wave

Cluster Number	Number of Individuals in Each Cluster (HCW:Patient)	Healthcare Transmission	Type of Transmission	Comments
1	56 (46:10)	Y	Workplace, shared room, community	5 subclusters of transmission: A: 10 HCWs, same unit or exposure to same unit B: 1 patient, 1 HCW C: shared room, 1 patient, 3 HCWs D: Shared office, 3 HCWs E: 1 patient, 1 HCW
2	2 (2:0)	Y	Workplace	Likely overlap in commonly serviced unit
3	2 (2:0)	Y	Workplace	Same unit
4	2 (2:0)	N	Community	
5	3 (3:0)	N	Community	
6	2 (2:0)	Y	Workplace	Same unit
7	3 (3:0)	N	Community	
8	2 (2:0)	Y	Workplace	Same unit
9	2 (2:0)	Y	Workplace	Same site
10	2 (2:0)	Y	Workplace	Same unit
11	3 (3:0)	Y	Workplace, Community	Two worked on same unit, 1 unassociated
12	3 (3:0)	Possible	Workplace, Community	Two members, both worked nights at the same hospital
13	4 (4:0)	Possible	Community, Workplace	Two members, both worked at the same hospital
14	2 (2:0)	N	Community	
15	2 (2:0)	N	Community	
16	2 (1:1)	N	Community	
17	2 (2:0)	N	Community	
18	3 (1:2)	Y	Workplace, Community	The 2 patients were on the same unit; the HCW is unconnected
19	2 (1:1)	N	Community	
20	2 (1:1)	N	Community	
21	3 (1:2)	N	Community	
22	2 (1:1)	Y	Workplace	HCW cared for patient
23	2 (1:1)	N	Community	
24	1 (1:1)	N	Community	
25	2 (2:0)	N	Community	
26	2 (1:1)	N	Community	
27	2 (0:2)	N	Community	
28	2 (0:2)	N	Community	
29	2 (2:0)	N	Community	
30	2 (0:2)	N	Community	
31	2 (0:2)	N	Household	
32	2 (0:2)	N	Household	

Abbreviation: HCW, healthcare worker.

transmissibility of this variant. However, we were only able to identify 3 previously unidentified likely transmission events in the healthcare setting involving patients who had not been accounted for by contact tracing. The other instances of healthcare transmission with Omicron were known by our contact tracing team through self-report of healthcare employees and were associated with known outbreaks, social events outside of the hospital, or presumably occurred during breakroom interactions among HCWs. Mask compliance of HCWs when caring for patients was consistent, whereas mask use was less consistent in nonclinical settings such as breakrooms and workrooms. Again, we did not identify any transmission occurring between known positive cases and HCWs, suggesting that existing infection control practices were effective in preventing nosocomial transmission from confirmed COVID-19 patients.

We observed significantly more SARS-CoV-2 cases with probable healthcare acquisition at the older Hillcrest campus compared with the newer La Jolla campus, most likely due to the higher proportion of shared rooms at Hillcrest. Patients were not routinely housed in airborne isolation rooms at either campus, nor were doors closed in patients' rooms who had SARS-CoV-2 if those patients were a fall risk. No cases of transmission among staff performing "high-risk" procedures or aerosol generating procedures were identified.

Patients were expected to mask while in proximity to another person, but compliance was inconsistent. Each HCW with

confirmed SARS-CoV-2 was asked during contact tracing whether they removed their mask for more than 15 minutes and within 6 feet of another person; however, shorter exposures could not be accounted for. Additionally, we know that there were lapses in compliance with eye protection. Thus, we are unable to determine if the HCW–HCW transmissions were due to deficiencies in infection prevention protocols, gaps in following the protocols, or other reasons.

Several outbreaks during the Omicron surge were not fully characterized by our ECR tool. Transmission events on shared inpatient units with communal patient areas were largely unaccounted for as the ECR only included information on room assignments and transportation events. Further, any HCW movements outside of scheduled staffing and patient assignments could not be accounted for. For example, laboratory technicians, phlebotomists, and food delivery staff, who may have also interacted with a patient, could not be included in the ECR framework. In the analysis of the second and third SARS-CoV-2 epidemic waves, we were able to adjust for the ECR gaps by including all related sequences in the original clusters. However, given the homogeneity of Omicron sequences, we were unable to expand this analysis to include additional related sequences.

Finally, all positive viral samples were evaluated for whole-genome sequencing. However, viral samples had to have sufficient quantity and quality of viral genetic material for viral sequencing, and thus not all SARS-CoV-2 samples were captured in this dataset. Nevertheless, we were able to analyze more than a third of all positive tests, and the 12 933 genomes sequenced were a substantial representation that did not reveal concerning patterns of lapses in infection prevention measures.

CONCLUSIONS

The majority of healthcare-associated transmission events happened either between HCWs when there were breaks in masking protocol or in the setting of shared patient rooms in a hospital with older infrastructure. There were no healthcare-associated SARS-CoV-2 transmissions among individuals identified with this infection. Our findings of limited transmissions in the healthcare setting support multipronged, scalable infection control protocols and suggest that airborne infectious isolation rooms with negative-pressure differential are not indispensable to safely managing patients infected with SARS-CoV-2. We highlight that masking for source control is effective. However, given that there are inevitable lapses in adherence to infection prevention protocols, healthcare facilities could further benefit by expanding mitigation measures, including enhancing ventilation and air exchanges in all spaces during a future respiratory virus pandemic and supporting single occupancy rooms. Last, we believe that this innovative analysis from our learning health system [18] could also inform a data-driven framework for infection prevention protocols in all healthcare [21, 22], congregate, and educational settings.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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