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Original Article

Viral whole-genome sequencing to assess impact of universal masking on SARS-CoV-2 transmission among pediatric healthcare workers

Larry K. Kociolek MD MSCI[1,2], Ami B. Patel MD, MPH[1,2], Judd F. Hultquist PhD[1], Egon A. Ozer MD, PhD[1], Lacy M. Simons BS[1], Matthew McHugh MS[2], William J. Muller MD, PhD[1,2] and Ramon Lorenzo-Redondo PhD[1]

[1]Northwestern University Feinberg School of Medicine, Chicago, Illinois and [2]Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois

Abstract

Objective: To identify the impact of universal masking on COVID-19 incidence and putative SARS-CoV-2 transmissions events among children's hospital healthcare workers (HCWs).

Design: Quasi-experimental study.

Setting: Single academic free-standing children's hospital.

Methods: We performed whole-genome sequencing of SARS-CoV-2- PCR-positive samples collected from HCWs 3 weeks before and 6 weeks after implementing a universal masking policy. Phylogenetic analyses were performed to identify clusters of clonally related SARS-CoV-2 indicative of putative transmission events. We measured COVID-19 incidence, SARS-CoV-2 test positivity rates, and frequency of putative transmission events before and after the masking policy was implemented.

Results: HCW COVID-19 incidence and test positivity declined from 14.3 to 4.3 cases per week, and from 18.4% to 9.0%, respectively. Putative transmission events were only identified prior to universal masking.

Conclusions: A universal masking policy was associated with reductions in HCW COVID-19 infections and occupational acquisition of SARS-CoV-2.

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During the coronavirus disease 2019 (COVID-19) pandemic, healthcare facilities implemented multilayered infection control measures to prevent nosocomial transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In addition to personal protective equipment (PPE) for healthcare workers (HCWs) while caring for patients with suspected or confirmed COVID-19, hospitals implemented universal masking that required HCWs, patients, and visitors to wear a face mask while on hospital premises. Universal masking, utilized in conjunction with other policies, such as symptom screening, is associated with lower rates of SARS-CoV-2 positivity among HCWs,[1,2] presumably by providing source control of nasal and oral respiratory droplets.[3] Prior data support effectiveness of universal masking to prevent healthcare-associated transmission of other respiratory viruses.[4,5] With a prolonged 2-week incubation period and widespread community activity, discriminating between occupational and community SARS-CoV-2 transmission can be challenging.

Author for correspondence: Larry K. Kociolek, E-mail: lkociolek@luriechildrens.org
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To identify putative transmission events among HCWs, we used whole-genome sequencing (WGS) of SARS-CoV-2–positive specimens to evaluate genomic relationships between SARS-CoV-2 from HCWs. Secondarily, we compared inpatient and HCW SARS-CoV-2–positive specimens to identify transmission between patients and HCW. By comparing data before and after universal masking, these data provide insight regarding the impact of the universal masking on HCW COVID-19.

Methods

Study setting

This quasi-experimental study at the Ann & Robert H. Lurie Children's Hospital of Chicago, an academic free-standing children's hospital, was approved by the institutional review board. During the study period, SARS-CoV-2 polymerase chain reaction (PCR) testing was performed using the Abbott RealTime SARS-CoV-2 assay (Abbott Molecular, Abbott Park, IL). All SARS-CoV-2 PCR–positive samples collected from inpatients and HCW diagnosed with COVID-19 between March 24, 2020, through May 25, 2020, were eligible for WGS. Thus, this study was performed prior to availability of a COVID-19 vaccine. Nasopharyngeal specimen viral transport media (VTM) underwent RNA extraction, WGS, and bioinformatics

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Table 1. COVID-19 Risk Mitigation Policies in Place During Pre- and Postintervention Periods

COVID-19 Risk Mitigation Policy	Policy Description	Study Period During Which Policy was In Place
Patient isolation precautions	All inpatients with signs and/or symptoms of COVID-19 were placed in a negative pressure room, when available, and care was provided by HCWs wearing gown, gloves, eye protection, and a ASTM level 1 face mask or respirator (if undergoing high-risk aerosol generating procedures). Infection prevention and control personnel rounded daily to educate about appropriate personal protective equipment use.	Same policy in place during both pre- and postintervention periods
Visitor restrictions	Only 1 adult parent or caregiver was allowed at visit. Parents or caregivers were symptom screened daily by bedside nurse and strongly discouraged from visiting if they had symptoms of COVID-19. If they chose to visit, patient and family would be placed on isolation (described above) and symptomatic caregiver was confined to patient room throughout the hospitalization.	Same policy in place during both pre- and postintervention periods
HCW symptom screening	Employees were instructed to self-screen for fever and other signs and symptoms of COVID-19 twice daily and, if present, refrain from working and seek COVID-19 testing from employee health.	HCWs were instructed to symptom screen during both the pre- and postintervention periods. An electronic screening tool was developed during the postintervention period.
HCW testing, isolation, and quarantine	HCWs diagnosed with COVID-19 were excluded from work for at least 10–14 days if symptoms improved and fever was resolved. HCWs were tested at a hospital drive-through or walk-in testing center. HCWs with exposure to COVID-19 were permitted to work as long as they were without symptoms of COVID-19.	Same policy in place during both the pre- and postintervention periods. No change in testing availability or reporting during the study period.
Universal masking of HCW, patients, and parents	ASTM level 1 face mask provided to all employees to wear at all times in the medical center except when eating (while physically distanced from others) and when alone in private office. ASTM level 1 face mask also provided to patients and their parent or caregiver who donned masks whenever outside their private hospital room. Masks remained in abundant supply throughout the study period.	Policy only in place during postintervention period.

Note. ASTM, American Society for Testing Materials.

analyses. Samples were excluded if VTM had not been saved by the laboratory in sufficient quantity for WGS or PCR cycle threshold was greater than that needed for WGS (ie, insufficient abundance of viral nucleic acid in VTM). HCWs included any individual who worked in the hospital or administrative buildings irrespective of patient exposure. Because of the relatively brief nature of outpatient–HCW interaction, and the infrequency of aerosol generating procedures, and because we did not identify any suspected cases of HCW becoming ill after care of children with known COVID-19 in ambulatory settings, we excluded outpatients from this study.

Laboratory techniques and bioinformatics analyses performed for SARS-CoV-2 WGS are described in the Supplementary Materials (online). SARS-CoV-2 clusters were identified based on genomic relatedness and represented putative transmission events. A universal masking policy requiring all staff, patients (excluding inpatients while in their private hospital room) and requiring all visitors to don an ASTM level 1 face mask was implemented on March 30, 2020. The frequency of putative SARS-CoV-2 transmission events and HCW SARS-CoV-2 incidence and test positivity rates were compared before and after universal masking was implemented. To account for the 14-day SARS-CoV-2 incubation period, the pre- and postintervention periods were defined as March 24, 2020, through April 13, 2020 (3 weeks) and April 14, 2020, through May 25, 2020 (6 weeks), respectively.

Throughout the study, HCWs with SARS-CoV-2 household, community, or occupational exposure were permitted to work if asymptomatic. Care of children with suspected or confirmed COVID-19 required gown, gloves, and eye protection for all encounters. N95 respirators were used for children undergoing high-risk aerosol-generating procedures, which included procedures with manipulation below the vocal cords, nebulized medications, and respiratory support requiring high flow of oxygen delivery or positive pressure noninvasive or mechanical ventilation. Otherwise, American Society for Testing Materials (ASTM) level 1 face masks were worn for other encounter types with children with suspected or diagnosed COVID-19. Table 1 describes in more detail all COVID-19 risk mitigation strategies in place during the study period.

Results

During the study period, 69 HCWs tested positive for SARS-CoV-2, 43 and 26 in the pre- and postintervention periods, respectively. Of the 69 HCWs with COVID-19, symptoms of COVID-19 were documented for 64 of them; presence of symptoms at time of test was not documented in records of 5 HCW, although they were presumed to be symptomatic because local testing policies during the study period required COVID-19 symptoms to be eligible for testing. In terms of known COVID-19 exposures, 30 (43%) reported a known COVID-19 exposure within 2 weeks of symptom onset: HCWs only (n = 15, 22%); household contact only (n = 10, 14%), both an HCW and a household contact (n = 1, 1%), inpatient (n = 1, 1%), both an HCW and an inpatient (n = 1, 1%), or patient parent (n = 2, 3%). Of the 16 HCWs who reported exposure to another positive HCW, 15 (94%) occurred prior to universal HCW masking. Two HCWs who were diagnosed with COVID-19 after exposure to the same parent (who failed to initially disclose their illness) were exposed prior to universal masking of HCWs and visitors; only 1 of the 2 HCW

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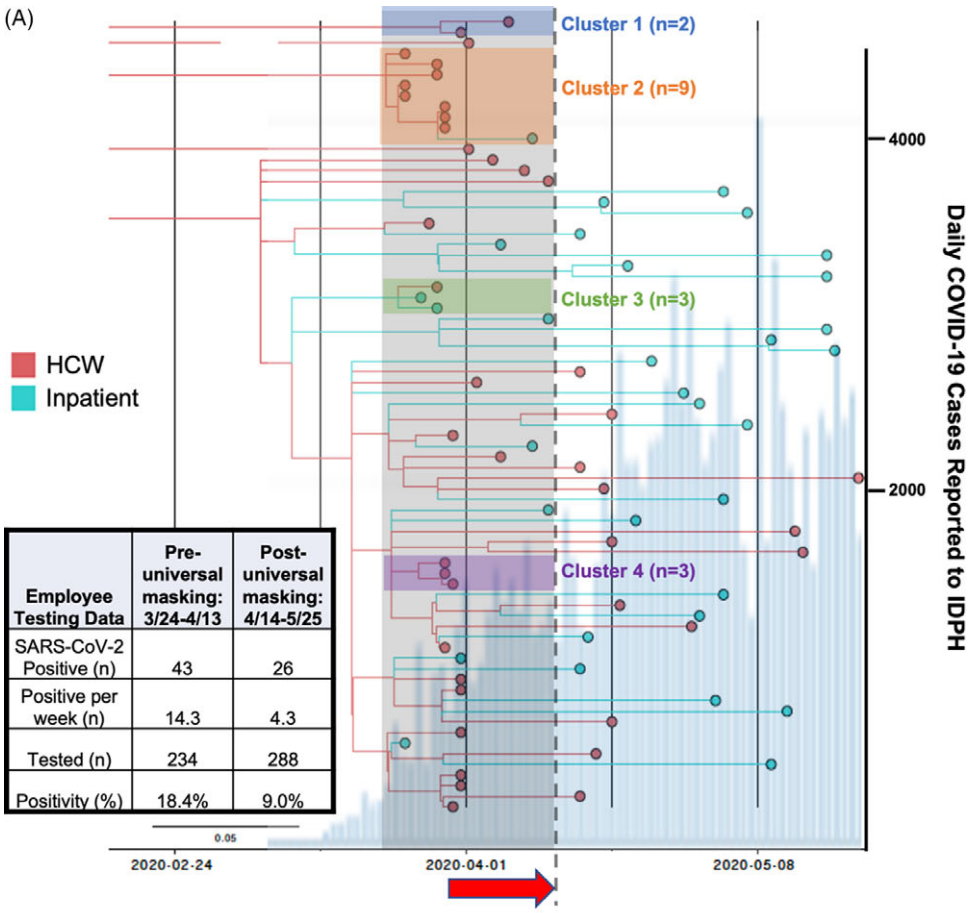

Employee Testing Data	Pre-universal masking: 3/24-4/13	Post-universal masking: 4/14-5/25
SARS-CoV-2 Positive (n)	43	26
Positive per week (n)	14.3	4.3
Tested (n)	234	288
Positivity (%)	18.4%	9.0%

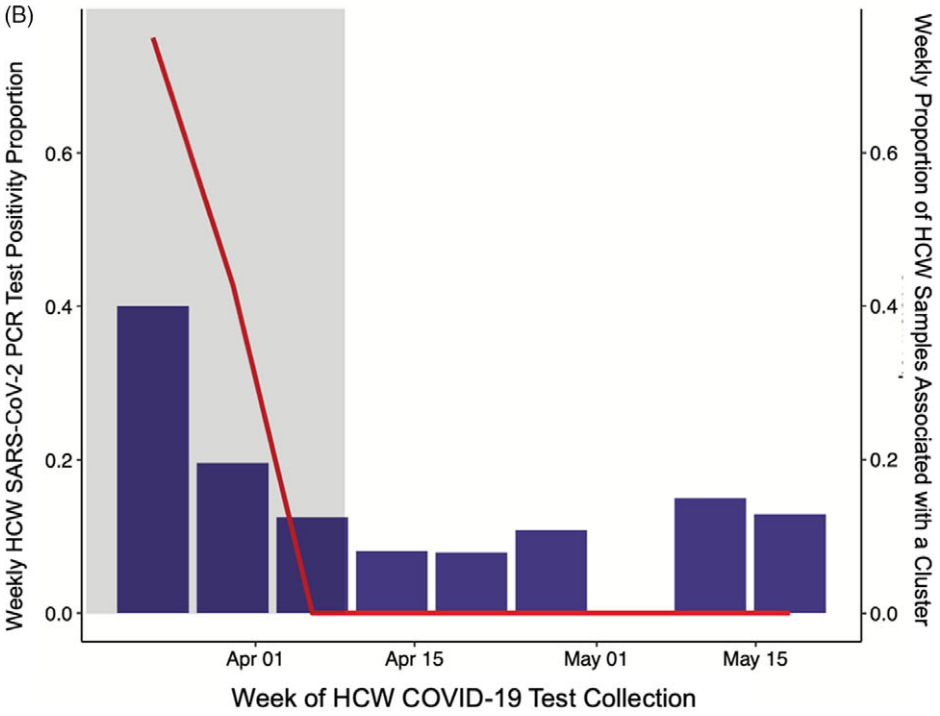

Fig. 1. (A) Phylogeny of SARS-CoV-2 from pediatric healthcare workers (HCWs, red) and pediatric inpatients (blue). Samples are displayed along x-axis based on sample collection date. The shaded region identifies the 3-week preintervention period prior to universal masking of patients, families, and HCWs. The red arrow spans the 14-day period from the start of universal masking until the end of the SARS-CoV-2 incubation period relative to the universal masking start date. The beginning of the 6-week postintervention period begins after the 14-day incubation period and is delineated by the vertical dashed line. In total, 4 distinct SARS-CoV-2 clusters were identified; all occurred during the preintervention period. Community COVID-19 activity during the study period is represented by the vertical bars overlying the phylogenetic tree. Daily cases of COVID-19 reported to the Illinois Department of Public Health (IDPH) are quantified on the secondary y-axis. Community activity continued to rise and peaked ~6 weeks after universal masking was implemented. HCW COVID-19 incidence and test positivity rate declined after universal masking implemented despite the rise in community activity. (B) Weekly HCW SARS-CoV-2 test positivity proportion (vertical bars) and weekly proportion of HCW associated with a SARS-CoV-2 cluster (red line). The shaded region identifies the preintervention period prior to universal masking of patients, families, and HCWs.

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Table 2. Epidemiologic Investigation of Patients and Healthcare Workers Identified in Distinct SARS-CoV-2 Clusters

Distinct Cluster	HCWs in Cluster, No.	Patients in Cluster, No.	Epidemiologic Findings
Cluster 1	2	0	HCWs work together in the same nonclinical department and had presumed direct contact.
Cluster 2	8	1	HCWs all work together with clinical and/or administrative responsibilities in the same division and had presumed direct contact with each other. Patient receives subspecialty care from same this division. We were unable to determine the directionality of transmission between HCW and patient.
Cluster 3	1	2	No epidemiologic links identified. One patient had no prior exposure to healthcare facility prior to illness onset, and HCW had household COVID-19 exposure and no contact with either patient.
Cluster 4	3	0	Two of three HCW work in same hospital department, providing care to patients in many different hospital units throughout the day, and had presumed direct contact. The third HCW provides patient care in one hospital unit and may have had contact with the other HCWs. Common exposure to a patient or caregiver with undiagnosed COVID-19 cannot be ruled out.

Note. HCW, healthcare worker.

samples was sequenced successfully. Of the 2 HCWs who reported exposure to a patient with COVID-19 in the prior 2 weeks, one had very brief (<5 minutes) interaction in a patient room but without direct patient contact. The other HCW had extensive patient interaction, including exposure during aerosol generating procedures, and the HCW reported no breaches in use of their fit-tested N95 mask and other recommended PPE. Because of high SARS-CoV-2 PCR cycle thresholds in some samples, we were not able to successfully sequence both samples from these 2 patient–HCW dyads.

Of the 69 HCWs with COVID-19, samples from 43 (62%) were successfully sequenced: 30 (70%) of 43 and 13 (50%) of 26 samples from the pre- and postintervention periods, respectively. Also, 26 samples (38%) were excluded because the PCR cycle threshold was too high or the remaining sample volume was insufficient for WGS. To supplement our assessment of transmission, we also included 32 (9 and 23 during the pre- and postintervention periods, respectively) sequenced SARS-CoV-2–positive samples from pediatric inpatients during the study period; these data represented 42% of the 77 inpatients during that period. Figure 1A demonstrates genomic relationships between SARS-CoV-2 samples among HCWs and pediatric inpatients. During the 3- and 6-week pre- and postintervention periods, respectively, 14.3 and 4.3 HCWs per week tested positive for SARS-CoV-2, and the test positivity rates were 18.4% and 9.0%, respectively. These declines in HCW COVID-19 incidence and test positivity rate were observed concomitant with rising community COVID-19 activity during the postintervention period (Fig. 1A); COVID-19 activity in Illinois peaked ~6 weeks after universal masking was implemented. During the same pre- and postintervention periods, the overall SARS-CoV-2 positivity rates in our clinical microbiology laboratory were 10.7% and 12.8%, respectively. In addition to the decline in COVID-19 diagnoses among HCWs after universal masking was implemented, clusters of closely related SARS-CoV-2 (ie, putative transmission events) were only identified during the preintervention period (Fig. 1A and 1B). Potential epidemiologic links of direct contact in the medical center were identified in 3 of the 4 clusters (Table 2).

Discussion

Our clinical and molecular epidemiologic investigation of COVID-19 in HCWs at a children's hospital demonstrate that universal masking was associated with a reduction in HCW COVID-19 incidence, SARS-CoV-2 test positivity frequency, and WGS-confirmed putative occupational transmission events among HCWs. These data, strengthened by the addition of genome-based investigation to clinical epidemiologic surveillance, provide additional evidence[6] of the benefits of universal masking for SARS-CoV-2 prevention in occupational settings.

Although reduction in putative transmission events among HCWs likely resulted from universal masking in the healthcare setting and is consistent with prior clinical epidemiological data where molecular epidemiologic data were not available,[2] universal masking at work in addition to behaviors outside of the hospital particularly during periods of rising community activity likely also contributed to the overall decline in HCW COVID-19 diagnoses. Although a shelter-in-place order was advised in Chicago on March 18, 2020, prior to hospital universal masking, other changes did not start until after hospital universal masking was implemented, including Centers for Disease Control and Prevention guidance for masking in public (early April 2020) and an Illinois public mask mandate (May 1, 2020).

Our study has several limitations. HCWs may not have reported COVID-19 diagnoses made elsewhere to the employee health department. Furthermore, of the positive tests in HCWs processed at our hospital, only two-thirds of samples underwent WGS because many had SARS-CoV-2 PCR cycle thresholds above that required for WGS; thus, some putative transmission events may have been undetected. Furthermore, COVID-19 testing in HCWs was primarily limited to symptomatic individuals, so we may have missed transmission events resulting in asymptomatic infections, which may more commonly occur from exposures while masked.[7,8] We were unable to discern the impact of or compliance with masking specifically because of several other concomitant risk mitigation strategies (Table 1), such as symptom screening and omission of those with symptoms from work, a policy that was present throughout the study period but continually reinforced over time. Finally, the role of patients and visitors in transmitting to an HCW, and vice versa, is incompletely assessed by this study because of lack of clinical and genome-based surveillance of COVID-19 in visitors and lack of WGS data from more than half of inpatient and all of our outpatient SARS-CoV-2 positive samples, including from some inpatients who received care from an HCW prior to the HCW developing COVID-19.

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This study had several limitations. Our findings may not be generalizable to all settings. First, while the vast majority of samples in our study belonged to the viral lineage with the spike gene D614G mutation, our study was completed prior to emergence of other more transmissible variants. The D614G mutation may have led to increased SARS-CoV-2 transmissibility, but that hypothesis is controversial.[8–10] Importantly, while most of the samples in this study had the D614G mutation, SARS-CoV-2 from clusters 1 and 2, the latter being the largest cluster, were both viral lineages without the D614G mutation. This finding underscores the importance of risk mitigation irrespective of viral lineage. Finally, the study was performed prior to COVID-19 vaccination; it is unclear whether the benefits of universal masking persist with high rates of HCW COVID-19 vaccination.

In summary, universal masking of a population of HCWs shortly after the onset of the COVID-19 pandemic was associated with a significant decline in COVID-19 incidence, SARS-CoV-2 test positivity rate, and evidence of transmission among HCWs. The utility of universal masking in a population of HCWs vaccinated against SARS-CoV-2 remains unknown.

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Conflicts of interest. All authors report no conflicts of interest relevant to this article.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2021.415

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