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Original Article

Hospital-acquired coronavirus disease 2019 (COVID-19) among patients of two acute-care hospitals: Implications for surveillance

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Abstract

Objectives: We quantified hospital-acquired coronavirus disease 2019 (COVID-19) during the early phases of the pandemic, and we evaluated solely temporal determinations of hospital acquisition.

Design: Retrospective observational study during early phases of the COVID-19 pandemic, March 1–November 30, 2020. We identified laboratory-detected severe acute respiratory coronavirus virus 2 (SARS-CoV-2) from 30 days before admission through discharge. All cases detected after hospital day 5 were categorized by chart review as community or unlikely hospital-acquired cases, or possible or probable hospital-acquired cases.

Setting: The study was conducted in 2 acute-care hospitals in Chicago, Illinois.

Patients: The study included all hospitalized patients including an inpatient rehabilitation unit.

Interventions: Each hospital implemented infection-control precautions soon after identifying COVID-19 cases, including patient and staff cohort protocols, universal masking, and restricted visitation policies.

Results: Among 2,667 patients with SARS-CoV-2, detection before hospital day 6 was most common (n = 2,612; 98%); detection during hospital days 6–14 was uncommon (n = 43; 1.6%); and detection after hospital day 14 was rare (n = 16; 0.6%). By chart review, most cases after day 5 were categorized as community acquired, usually because SARS-CoV-2 had been detected at a prior healthcare facility (68% of cases on days 6–14 and 53% of cases after day 14). The incidence rates of possible and probable hospital-acquired cases per 10,000 patient days were similar for ICU- and non-ICU patients at hospital A (1.2 vs 1.3 difference, 0.1; 95% CI, −2.8 to 3.0) and hospital B (2.8 vs 1.2 difference, 1.6; 95% CI, −0.1 to 4.0).

Conclusions: Most patients were protected by early and sustained application of infection-control precautions modified to reduce SARS-CoV-2 transmission. Using solely temporal criteria to discriminate hospital versus community acquisition would have misclassified many "late onset" SARS-CoV-2–positive cases.

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The coronavirus disease 2019 (COVID-19) pandemic has posed unprecedented challenges to infection control and public health professionals. These challenges have necessitated rapid development and implementation of interventions using reports from worldwide sentinel locations,[1] recognized best practices for control of respiratory virus transmission,[2,3] and professional websites.[4] With sparse evidence and personal protective equipment shortages, infection control departments adopted a necessarily agile framework for rapid iterative decision making to control intrafacility transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Decision-making domains have included mask and respirator use, face shields, extended use and reuse of personal protective equipment, protections for aerosol-generating procedures, visitation policies, patient and healthcare personnel (HCP) screening, and patient and HCP cohorting protocols.

Before the COVID-19 surge in the Chicago region, early publications and anecdotal evidence documented a high reproductive rate for SARS-CoV-2, with potential to spread both among and between hospital patients and HCWs.[5,6] The efficiency of SARS-CoV-2 transmission exceeds that of pandemic influenza and MERS,[7] underscoring the high risk of transmission in confined indoor spaces with close interpersonal contact,[8,9] such as hospitals. Fortunately, subsequent evidence from an acute-care institution indicated that stringent infection-control interventions can successfully minimize SARS-CoV-2 spread.[10] However, infection clusters remain possible and likely are driven by patient and ecological factors (eg, opportunities for exposure to SARS-CoV-2).[11]

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To understand whether infection control policies and practices remain effective as COVID-19 evolves, we need standardized, reliable capture of hospital-acquired COVID-19 cases. It is appealing to leverage lessons learned from algorithmic determinations of other healthcare-associated events to COVID-19 and to rely solely on readily available data routinely captured in the electronic medical record such as laboratory-identified event reporting for *Clostridium difficile*.[12] However, detection of COVID-19 solely through electronically available data might be susceptible to misclassification.

We performed a retrospective observational study addressing 2 objectives. First, we evaluated the extent of hospital-acquired SARS-CoV-2 infection among inpatients by performing an electronic query for potential cases followed by chart review. Second, we assessed the possibility of automated detection of hospital-acquired SARS-CoV-2 using solely temporal criteria. We retrieved all SARS-CoV-2 test results and, relying on timing of specimen collection in electronic healthcare record (EHR) data, we identified cases of potential hospital acquisition. We performed chart review to classify potential cases as community or unlikely hospital-acquired cases versus possible or probable hospital-acquired cases.

Methods

Participating sites

We evaluated patients hospitalized between March 1, 2020, and November 30, 2020, in 2 tertiary-care, acute-care hospitals (with 464 and 664 beds, respectively) in Chicago, Illinois. Both hospitals have transformed electronic health data into a normalized database with standardized clinical vocabularies using the PCORnet common data model[13] and have sent these data to the Medical Research Analytics and Informatics Alliance (www.mraia.org). Because no identifiable data left study sites (ie, all centralized data were deidentified), the Chicago Area Institutional Review Board approved the study as minimal risk and provided a waiver of informed consent.

Data acquisition and definitions

To standardize data extraction across sites, we developed and validated the hospital-acquired SARS-CoV-2 phenotype using structured query language queries against the EHR common data model. The resultant list contained inpatients at both hospitals who tested positive for SARS-CoV-2 from 30 days prior to admission until hospital discharge. Using the queries, we electronically captured demographics (eg, age, sex, race, or ethnicity) and categorized SARS-CoV-2 positivity by hospital day of onset as ≤5 days, 6–14 days, or >14 days. The admission date was defined as day 1. We chose a minimum cutoff of 5 days because of literature reporting and a mean incubation period for SARS-CoV-2 of 5 days[14] and a cutoff of 14 days to more easily categorize a case as hospital-acquired based on prior literature[10,15,16] and what is considered to be near the upper bound to clinically manifest COVID-19.[17]

We performed manual chart reviews for all patients whose initial SARS-CoV-2–positive specimen was collected after hospital day 5. During these reviews, we collected the following information: (1) presence of symptoms on presentation to the hospital, (2) SARS-CoV-2 test results from other healthcare facilities as reported by the patient or other facility, (3) chest radiograph and computed tomography results on hospital admission, (4) reason for SARS-CoV-2 test (eg, clinical deterioration or screening), and (5) timing of respiratory deterioration or increased need for supplemental oxygen relative to the date of specimen acquisition. Chart reviews were performed by a single individual at each hospital (W.T. and C.S.). At hospital A, we validated our project's chart reviews through comparison with comprehensive prior reviews by the infection control department.

We categorized all SARS-CoV-2–positive patients as community-acquired (hospital day of onset on or before day 5, or onset during days 6–14 either without COVID-19 symptoms or with symptoms present on admission) or hospital-acquired (onset during hospital days 6–14 with COVID-19 symptoms not present on admission, or onset after day 14). We further classified the likelihood of hospital acquisition based on clinical interpretations: (1) unlikely hospital acquired (days 6–14 with COVID-19 symptoms attributed to a more likely alternative diagnosis), (2) possibly hospital acquired (days 6–14 with no alternative diagnosis or onset after day 14 either without COVID-19 symptoms or with COVID-19 symptoms and a more likely alternative diagnosis), and (3) probably hospital acquired (onset day after 14 with COVID symptoms and no alternative diagnosis). Notably, our definition imposed the condition that any case with an onset during hospital days 6–14 could at most be classified as possibly hospital acquired, due to the uncertainty of timing of SARS-CoV-2 acquisition within the incubation period.

To establish the relationship between clinical symptoms and SARS-CoV-2 infection, we evaluated a 3-day time window: the specimen collection day and 1 day before and 1 day after specimen acquisition. Although we documented a variety of COVID-19 symptoms, for our clinical determinations, we focused on the presence of pulmonary involvement (eg, new or worsening hypoxia accompanied by either pulmonary symptoms or newly detected pulmonary infiltrates) or new or worsening dyspnea accompanied by newly detected pulmonary infiltrates. We did not include patterns of radiographic abnormalities as a criterion.

Analysis

We stratified SARS-CoV-2 infection incidence by ICU versus non-ICU patient care. We aggregated all ICUs because most ICU types cared for patients with COVID-19 during the pandemic. We considered the geographically distinct inpatient rehabilitation unit at one hospital as a separate patient-care area to reflect the different level of care and length of stay in that unit, which is consistent with reporting to the National Health Safety Network (NHSN) as a discrete unit.

We calculated SARS-CoV-2 positivity incidence as the number of possible or probable hospital-acquired cases per 10,000 patient days at risk. At-risk patient days included only patients admitted for at least the minimum number of days to be classified as a possible nosocomial case (ie, hospital day 6). Patients who were SARS-CoV-2 positive in the community-acquired time frame (ie, preadmission or within the first 5 hospital days) were excluded from at-risk patient-day calculations. Patients contributed at-risk time for all days present, such that an individual transferred between the major unit types (ICU, outside ICU, inpatient rehabilitation) could contribute time to each unit on which they were present on a given day. We separately calculated incidence for (1) cases identified as hospital acquired by the electronic phenotype (ie, all cases with hospital day of onset >5), and (2) cases identified by chart review as possibly or probably hospital acquired. We used Stata version 14.2 software (StataCorp, College Station, TX) to compare ICU

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Table 1. Characteristics of Inpatients With Laboratory-Detected SARS-CoV-2, March 1–November 30, 2020, Chicago, Illinois

	Hospital A (N=1,294)		Hospital B (N=1,377)	
Characteristic	Median	IQR	Median	IQR
Age, y	54	44–64	58	46–69
	No.	%	No.	%
Sex, male	807	62	737	54
Race or ethnicity				
Hispanic	731	56	602	44
NH black	435	34	528	38
NH white	79	6	152	11
NH Asian	21	1.6	24	1.7
Other/missing	28	2.2	71	5.2
Hospital onset day[a]				
≤5 d	1,285	99	1,327	96
6–14 d	7	0.5	36	2.6
>14 d	2	0.2	14	1.0

Note. IQR, interquartile range; NH, non-Hispanic; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
[a]All initial positive SARS-CoV-2 specimens acquired after hospital day 5 underwent chart review to categorize cases as community acquired (CA), unlikely hospital acquired (HA), possibly HA, or probably HA. Specimens acquired on or before hospital day 5 were considered CA without chart review.

and non-ICU incidence rates using incidence rate differences and 95% confidence intervals.

Infection control precautions

During the study period, each hospital implemented similar infection-control precautions as guided dynamically by US Centers for Disease Control and Prevention (CDC) guidelines. HCP interventions included universal use of medical-grade face masks and provision of N95 respirators, not working if ill, and cohort protocols for physicians and nurses on COVID-19 units. Patient-directed interventions included COVID-19 cohort units. Universal patient face masking was required at hospital A; hospital B only has single-occupancy rooms and required patient face-mask use for transportation outside their room. SARS-CoV-2 testing prior to procedures or at clinician discretion—universal SARS-CoV-2 testing on admission was not implemented. Visitors were restricted but were allowed for end-of-life care. We did not collect data on adherence to recommended precautions.

Results

The 2,671 hospital patients identified as laboratory-confirmed SARS-CoV-2 positive cases were approximately evenly divided between the 2 hospitals. Most were male, of Hispanic ethnicity, and aged >50 years (Table 1). Almost all SARS-CoV-2–positive specimens were collected before admission or on or before hospital day 5 (n = 2,612, 98%). As shown in Table 1, SARS-CoV-2 detection during hospital days 6–14 was uncommon (n = 43, 1.6%) and was rare after day 14 (n = 16, 0.6%).

We reviewed the charts of 59 cases with hospital onset after hospital day 5; we excluded 4 cases due to false positivity based on the initial positive result being from a point-of-care test (nucleic amplification test) immediately followed by negative RT-PCR in the laboratory and absence of COVID-19 clinical symptoms. Among the chart-reviewed cases, most were categorized as community acquired regardless of onset during days 6–14 or after day14, most commonly due to clinical notes documenting a prior positive SARS-CoV-2 laboratory result from an outside facility (Fig. 1). Of the 20 cases judged to be possibly or probably hospital acquired, 13 occurred during hospital days 6–14 and thus were classified as possibly hospital acquired. Of the 7 possible or probable hospital-acquired cases that occurred after hospital day 14, 2 cases were classified as possibly hospital acquired due to the absence of symptoms, 1 case was classified as possibly hospital acquired due to the presence of an alternate diagnosis, and the remaining 5 cases were classified as probably hospital acquired. Notably, 94% of the patients who developed symptoms within 1 day of the SARS-CoV-2–positive specimen collection had symptoms attributable to COVID-19 rather than an equally likely alternative diagnosis. No possible or probable hospital-acquired cases were exposed to SARS-CoV-2–positive roommates at hospital A; hospital B only has single-occupancy rooms.

As shown in Table 2, the incidence of hospital-acquired COVID-19 was ~3-fold higher when cases were identified solely by the temporal laboratory criteria compared to incidence based on chart review. When calculated after manual chart review, the hospital-acquired COVID-19 incidences within and outside ICU patient-care areas were similar. At hospital B, the incidence was much higher among patients in the inpatient rehabilitation unit, which was the location of a known epidemiologic cluster of positive SARS-CoV-2 test results among healthcare personnel and some patients.

Discussion

Early implementation of a multidimensional, sustained infection-control intervention program informed by prevailing Centers for Disease Control and Prevention (CDC) and public health guidance were associated with a relatively low number of late-onset COVID-19 among patients in 2 large hospitals that provided inpatient care for a high volume of COVID-19 patients (ie, an average of ~150 COVID-19 patient admissions per hospital each month). Although electronic determinations for monitoring hospital acquisition of SARS-CoV-2 would be relatively easy to operationalize, we found that using temporal laboratory criteria alone to determine hospital acquisition would have been overly sensitive, misclassifying many community-acquired cases as hospital acquired.

Although healthcare institutions undoubtedly strive for zero SARS-CoV-2 acquisitions, this goal has been challenged by several important factors: the nearly universally susceptible population during the initial phases of the pandemic; the high risk of exposures due to the large number of COVID-19 inpatients; high transmissibility, including during the presymptomatic phase of infection; and the high prevalence of asymptomatic infections.[18,19] Hospitals are not closed systems, the constant influx of staff, visitors, and new patients, all of whom have community exposures and often require close interpersonal contact. These exposures present opportunities for ongoing reintroduction and spread of SARS-CoV-2. Restricting visitation presents a particularly vexing challenge given the potentially therapeutic benefit and emotional need for companionship to comfort critically ill hospital patients.[20] Although a benchmark for rates of SARS-CoV-2 hospital acquisition has not yet been established, our assertion that infection control measures in our 2 hospitals minimized transmission is

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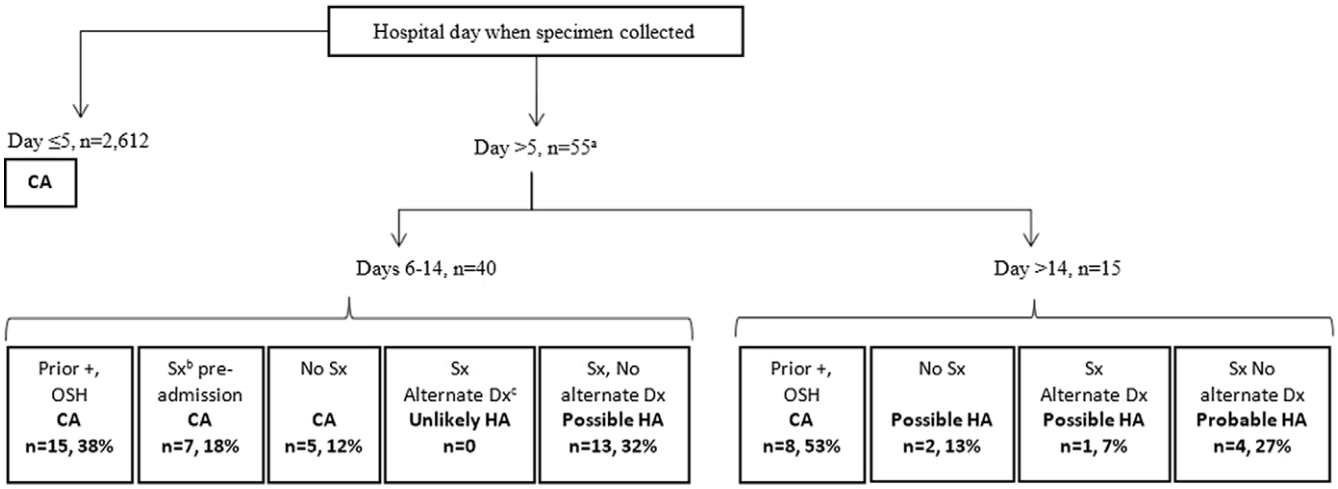

Fig. 1. Flowchart for categorization of SARS-CoV-2–positive specimens acquired during an acute-care hospital stay at 2 hospitals in Chicago, Illinois. Note. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; CA, community acquired; OSH, other hospital; Sx, signs or symptoms; Dx, diagnosis; HA, hospital acquired. [a]From Table 1, 4 patients were excluded as false positives because SARS-CoV-2 was detected by a point-of-care test, and all 4 had at least a subsequent negative RT-PCR assay and no COVID-19 symptoms. [b]Evaluated for COVID-19 symptoms or signs and chest radiographs within 1 day before or after specimen collection date for initial SARS-CoV-2 positive result, as follows: (1) new or worsening hypoxia and new symptoms or (2) new or progressive radiographically identified pulmonary infiltrates and new symptoms. [c]Alternate Dx, a diagnosis deemed as likely or more likely than COVID-19.

supported indirectly by several observations. The overall incidence of COVID-19 was similar to that reported for hospital-acquired influenza,[21] which has a lower reproductive number and a less susceptible population due to influenza vaccination (ie, SARS-CoV-2 vaccine was not available during our study period). Also, the burden of infected hospital patients was much lower.[22] A dramatically lower proportion of our SARS-CoV-2 cases was categorized as hospital-acquired SARS-CoV-2 compared to regions that had less preparation time and were likely less aware of the capacity for SARS-CoV-2 transmission.[15,23–25] In contrast to these early reports, another hospital reported that hospital-acquisition was uncommon after implementation of a bundle of infection control interventions.[10]

Establishing a benchmark for hospital-acquired COVID-19 will be complicated by the highly dynamic nature of the COVID-19 pandemic, including development of mutations that promote transmission, the geographic and temporal variability in the burden of disease, and the penetration of vaccination among patients and HCP. Despite these challenges, a standardized method for identifying hospital-acquired COVID-19 is essential to better understanding whether interventions are protecting patients. Electronic determinations that rely solely on the temporality of SARS-CoV-2 positivity to identify hospital acquisition would be efficient, but as we have shown, they are prone to misclassification. We chose to evaluate by chart review all cases of SARS-CoV-2 positivity after hospital day 5 because it was the reported median incubation period. We were concerned about exposures in the emergency department and during potentially high-exposure risks, which could occur during the first hospital day when patient movement is necessary for diagnostic tests and transfer to inpatient locations. We expected that duration of time to positive SARS-CoV-2 test result would be associated with hospital acquisition; thus, we constructed separate criteria for SARS-CoV-2 positivity on hospital days 6–14 compared to after day 14. More than two-thirds of the cases occurring after hospital day 5 occurred during hospital days 6–14, but most of these patients had COVID-19 symptoms on admission but either tested negative (ie, a false-negative initial test) or were not tested prior to the electronically identified positive specimen. After chart review, most cases were classified as community acquired, leading to a 3-fold lower incidence of hospital acquisition compared to the incidence based solely on temporal criteria. A more stringent temporal criterion (eg, SARS-CoV-2 detection after hospital day 14) would likely be more specific for hospital acquisition. However, among late-onset cases, the medical record often revealed a prior infection detected at an outside facility. Because SARS-CoV-2 can be detected in nucleic acid amplification test specimens for several months after initial infection,[26] we believe that many late-onset cases are "false-positive" hospital acquisitions due to persistent shedding of noninfectious SARS-CoV-2. Comprehensive, regional capture of SARS-CoV-2–positive results with data sharing between public health and healthcare institutions would minimize misclassification of events, though determinations would still be complicated by regional variability in testing practices across communities and healthcare systems.

Despite having a higher intensity of care and in an environment in which aerosol-generating procedures are performed routinely, ICU patients were at no higher risk than patients admitted to non-ICU locations. We noted a higher incidence of possible or probable hospital-acquired SARS-CoV-2 infection in the inpatient rehabilitation unit. The higher incidence in this unit was driven by a cluster of SARS-CoV-2 infections among healthcare personnel. This finding highlights the risk of SARS-CoV-2 transmission, particularly in units that involve long lengths of hospital stay and close interactions between staff and patients, such as during rehabilitative care. The cluster was controlled after unit-wide point-prevalence surveys among patients and staff for asymptomatic SARS-CoV-2 infection and re-emphasis of COVID-19 infection control precautions. Such clusters indicate that healthcare facility acquisition remains possible[27,28] and that adherence to infection control measures needs to be maintained.

Our evaluation had several limitations. First, across the 2 hospitals, most isolates were not available at the time of this study for application of advanced molecular methods to identify transmission events. Second, we did not perform postdischarge surveillance; it is possible that some hospital-acquired infections did

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Table 2. Incidence Rates for ICU Patients Compared to Non-ICU Patients[a] for SARS-CoV-2–Positive Specimens Collected >5 Days After Hospital Admission

		Recovery after Hospital Day 5		Possibly or Probably HA by Chart Review	
	Patient Days	No.	Incidence (95% CI)[b]	No.	Incidence[b] (95% CI)
Hospital A					
Overall	23,288	9	3.9 (2.0–7.4)	3	1.3 (0.4–4.0)
Outside ICU	15,457	6	3.9 (1.7–8.6)	2	1.3 (0.3–5.2)[c]
ICU	8,582	3	3.5 (1.1–10.8)	1	1.2 (0.2–8.3)[c]
Hospital B					
Overall	51,354	46	9.0 (6.7–12)	17	3.3 (2.1–5.3)
Outside ICU	36,110	21	5.8 (3.8–8.9)	10	2.8 (1.5–5.1)[d]
ICU	16,778	20	11.9 (7.7–18)	2	1.2 (0.3–4.8)[d]
Rehabilitation[e]	3,428	5	14.6 (6.1–35)	5	14.6 (6.1–35)[e]

Note. ICU, intensive care unit; CI, confidence interval; HA, hospital acquired; NHSN, National Healthcare Safety Network.
[a]Patients in multiple units on the day of COVID-19 positivity were assigned to the first unit for that hospital day.
[b]Expressed per 10,000 patient days.
[c]Hospital A: Rate difference between ICU and non-ICU patients = 0.13; 95% CI, −2.78 to 3.03 per 10,000 patient days, $P = .97$.
[d]Hospital B: Rate difference between ICU and non-ICU patients = 1.58; 95% CI, −0.08 to 3.96 per 10,000 patient days, $P = .28$.
[e]Inpatient rehabilitation categorized as a discrete patient care area because it is reported to the NHSN as a separate patient-care unit. The incidence was higher for inpatient rehabilitation compared to ICU ($P = .002$) or non-ICU units ($P = .008$).

not manifest until after discharge. Furthermore, we did not have measures for adherence to infection-control recommendations; however, this study was not designed to assess the effect of specific infection control measures on SARS-CoV-2 prevention. Lastly, we found that SARS-CoV-2 testing during hospitalization often was triggered by new, unexplained dyspnea or hypoxia, rather than mild symptoms such as rhinorrhea. Testing in response to dyspnea or hypoxia could result in missing mildly symptomatic cases, and conversely, may overestimate hospital acquisition under time-based surveillance rules designed to only account for the probable incubation period, since the median time to dyspnea during COVID-19 illness course is 5–8 days after illness onset.[6,29]

Our findings suggest that hospital-acquired SARS-CoV-2 infection among inpatients was uncommon. Nevertheless, the COVID-19 pandemic has highlighted a need for hospitals to monitor and protect patients from respiratory virus transmission. To improve validity in categorizing 'late-onset' SARS-CoV-2 cases, an algorithmic surveillance rule based on SARS-CoV-2 PCR test results would ideally include prior results from external facilities. With reliable surveillance of hospital-acquired SARS-CoV-2 infection, the impact of patient safety interventions, such as COVID-19 vaccination campaigns, could be better evaluated.

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

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