Infection Control & Hospital Epidemiology (2023), **44**, 1458–1466
doi:10.1017/ice.2022.300

SHEA

Original Article

Impact of changing case definitions for coronavirus disease 2019 (COVID-19) hospitalization on pandemic metrics

Claire N. Shappell MD[1,2], Michael Klompas MD, MPH[1,3], Christina Chan MPH[1], Tom Chen PhD[1] and Chanu Rhee MD, MPH[1,3]

[1]Department of Population Medicine, Harvard Medical School/Harvard Pilgrim Health Care Institute, Boston, Massachusetts, [2]Division of Pulmonary and Critical Care Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts and [3]Division of Infectious Diseases, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts

Abstract

Objective: To examine the impact of commonly used case definitions for coronavirus disease 2019 (COVID-19) hospitalizations on case counts and outcomes.

Design, patients, and setting: Retrospective analysis of all adults hospitalized between March 1, 2020, and March 1, 2022, at 5 Massachusetts acute-care hospitals.

Interventions: We applied 6 commonly used definitions of COVID-19 hospitalization: positive severe acute respiratory coronavirus virus 2 (SARS-CoV-2) polymerase chain reaction (PCR) assay within 14 days of admission, PCR plus dexamethasone administration, PCR plus remdesivir, PCR plus hypoxemia, institutional COVID-19 flag, or COVID-19 *International Classification of Disease, Tenth Revision* (ICD-10) codes. Outcomes included case counts and in-hospital mortality. Overall, 100 PCR-positive cases were reviewed to determine each definition's accuracy for distinguishing primary or contributing versus incidental COVID-19 hospitalizations.

Results: Of 306,387 hospital encounters, 15,436 (5.0%) met the PCR-based definition. COVID-19 hospitalization counts varied substantially between definitions: 4,628 (1.5% of all encounters) for PCR plus dexamethasone, 5,757 (1.9%) for PCR plus remdesivir, 11,801 (3.9%) for PCR plus hypoxemia, 15,673 (5.1%) for institutional flags, and 15,868 (5.2%) for ICD-10 codes. Definitions requiring dexamethasone, hypoxemia, or remdesivir selected sicker patients compared to PCR alone (mortality rates 12.2%, 10.7%, and 8.8% vs 8.3%, respectively). Definitions requiring PCR plus remdesivir or dexamethasone did not detect a reduction in in-hospital mortality associated with the SARS-CoV-2 Omicron variant. ICD-10 codes had the highest sensitivity (98.4%) but low specificity (39.5%) for distinguishing primary or contributing versus incidental COVID-19 hospitalizations. PCR plus dexamethasone had the highest specificity (92.1%) but low sensitivity (35.5%).

Conclusions: Commonly used definitions for COVID-19 hospitalizations generate variable case counts and outcomes and differentiate poorly between primary or contributing versus incidental COVID-19 hospitalizations. Surveillance definitions that better capture and delineate COVID-19–associated hospitalizations are needed.

(Received 10 August 2022; accepted 10 November 2022; electronically published 13 March 2023)

The coronavirus disease 2019 (COVID-19) hospitalization rate is a key surveillance metric used by public health officials to estimate the population burden of severe acute respiratory coronavirus virus 2 (SARS-CoV-2) infections that are severe. COVID-19 hospitalization rates are also used by the US Centers for Disease Control and Prevention (CDC), in conjunction with case counts and percentage of inpatient beds occupied by COVID-19 patients, to estimate community COVID-19 risk levels that in turn inform recommendations such as indoor masking.[1]

The CDC initially defined "COVID-19 hospitalizations" as any person hospitalized within 14 days of a positive PCR result for SARS-CoV-2, regardless of the patient's presenting syndrome or reason for admission.[2] This definition initially served well for estimating the burden of severe illness, but widespread vaccination, universal testing, prolonged PCR positivity after infection, increasing rates of prior infection, and new and potentially milder SARS-CoV-2 variants such as Omicron have challenged the validity of this measure as a severity indicator. High community infection rates will lead to some patients hospitalized for reasons other than COVID-19 testing positive for SARS-CoV-2, including patients with mild, asymptomatic, or resolving infections. These so-called "incidental" SARS-CoV-2–positive patients are still counted by the traditional CDC definition as COVID-19 hospitalizations without differentiating them from patients hospitalized specifically for COVID-19.

Public health agencies and hospital officials have therefore proposed, and in many cases implemented, alternative definitions to identify hospitalizations specifically due to COVID-19 illness.

Author for correspondence: Claire N. Shappell, E-mail: cshappell@bwh.harvard.edu
Cite this article: Shappell CN, Klompas M, Chan C, Chen T, Rhee C. Impact of changing case definitions for coronavirus disease 2019 (COVID-19) hospitalization on pandemic metrics. *Infect Control Hosp Epidemiol* 2023. 44: 1458–1466, doi: 10.1017/ice.2022.300

These typically require receipt of SARS-CoV-2 therapeutics (eg, dexamethasone or remdesivir) or need for supplemental oxygen in addition to a positive PCR.[3–5] Large cohort studies have also used different approaches for defining COVID-19 hospitalizations, including a positive PCR alone,[6–9] *International Classification of Disease, Tenth Revision, Clinical Modification* (ICD-10-CM) codes for COVID-19,[10–18] institutional definitions, or combinations of these.[19–25] Notwithstanding the panoply of definitions being used, few data are available that compare estimates of COVID-19 hospitalizations, severity of illness, mortality, and trends between definitions, nor their accuracy in identifying primary or contributing versus incidental infections.

In this study, we assessed the impact of different commonly used definitions for COVID-19 hospitalization in a regional health system on case counts, disease severity, and in-hospital mortality in the period when the Omicron variant was predominant versus the period preceding the Omicron variant. In addition, we evaluated how each definition performed at identifying hospitalizations due to COVID-19 versus hospitalizations with incidental COVID-19 using detailed medical record reviews.

Study design and methods

We performed a retrospective cohort study using electronic health record (EHR) and administrative data from 2 large academic hospitals and 3 community hospitals within the Mass General Brigham healthcare system: Massachusetts General Hospital, Brigham and Women's Hospital, Salem Hospital/Northshore Medical Center, Newton Wellesley Hospital, and Brigham and Women's Faulkner Hospital. The study included all hospitalizations of adults aged ≥18 years, including inpatient admissions and observation stays, as well as emergency department (ED) visits ending in death, with admission dates between March 1, 2020, and March 1, 2022. ED visits ending in death were included to ensure capture of all potential cases of severe disease. Transfers between study hospitals and readmissions on the same date as discharge were treated as continuous encounters. The study was approved with a waiver of informed consent by the institutional review board at Mass General Brigham (protocol no. 2020P001631).

COVID-19 hospitalization definitions

We assessed 6 definitions for COVID-19 hospitalizations modeled after existing strategies currently being used for public health surveillance, clinical monitoring, and/or research[1,3,4,26,27]:

1. PCR only: positive PCR for SARS-CoV-2 between 14 days prior to admission and discharge.
2. PCR plus hypoxemia: positive PCR (using the same timeframe of 14 days preadmission through discharge) and the patient either required supplemental oxygen for any amount of time or had at least 1 oxygen saturation <94% recorded in vital signs during hospitalization.
3. PCR plus dexamethasone: positive PCR and received at least 1 dose of dexamethasone during hospitalization.
4. PCR plus remdesivir: positive PCR and received at least 1 dose of remdesivir during hospitalization.
5. COVID-19 flag: presence of an institutional EHR-based COVID-19 flag maintained for ≥5 days with start and end dates overlapping with the hospitalization. Institutional COVID-19 flags were triggered by a positive PCR result but could be removed by local infection control officials if review of patients' clinical syndrome, initial and repeat PCR tests, cycle thresholds, prior history of known infections, and SARS-CoV-2 anti-nucleocapsid antibody status suggested that the positive PCR was more indicative of a remote infection or a false-positive result.[28]
6. ICD-10: an ICD-10 discharge diagnosis code for COVID-19 (U07.1 or J12.82).

Outcomes

Each definition was applied across all encounters to calculate crude hospitalization counts, percentage of hospitalizations related to COVID-19, and in-hospital mortality rates by month. We also assessed how outcomes estimates varied by their definition in the period preceding the Omicron variant (March 1, 2020–December 16, 2021) versus the period when the Omicron variant was predominant (December 17, 2021–March 1, 2022). We determined these periods in accordance with the emergence and predominance of the Omicron variant in Massachusetts.[29]

Assessing accuracy of definitions for primary, contributing, or incidental COVID-19

From 15,436 PCR-positive encounters, 100 cases were randomly selected for structured medical record reviews using a standardized data abstraction tool in REDCap version 12.0.19 software (Vanderbilt University, 2022) (Supplementary Material online). In total, 50 cases were selected at random from the periods before and after the emergence of the Omicron variant. All available notes, medication records, laboratory and microbiology results, radiology reports and images, and pathology reports were reviewed.

Each case was adjudicated into 1 of 3 categories: (1) primary COVID-19 admission, (2) contributing COVID-19 admission, and (3) incidental COVID-19 admission. A primary COVID-19 admission was defined as an encounter in which the patient presented with a syndrome definitely or probably due to SARS-CoV-2 infection (eg, COVID-19 pneumonia or COVID-related myocarditis). A contributing COVID-19 admission was defined as any encounter not meeting primary COVID-19 criteria but likely triggered by or related to SARS-CoV-2 infection (eg, exacerbation of underlying disease such as congestive heart failure, chronic lung disease, or arrhythmia) or an encounter during which the patient presented for non–COVID-19 reasons, developed COVID-19 after admission, and the infection led to complications such as medically prolonged stay, ICU transfer, or death. Notably, receipt of a COVID-19 therapeutic in of itself was not considered evidence of primary or contributing COVID-19 hospitalization. Incidental COVID-19 hospitalizations were those in which SARS-CoV-2 was not relevant to the syndrome causing admission and did not cause complications. Positive tests deemed to be false positives or residual RNA from previous infection were categorized as "incidental."[28] Please see Supplementary Table 1 (online) for complete descriptions of these categories and representative examples.

The first 15 cases were reviewed independently by 2 physician reviewers (C.S. and C.R.); interrater reliability for classifying COVID-19–relevance categories was moderate to strong (agreement on 13 of 15 cases; Krippendorff α, 0.77). All 15 cases were discussed between the 2 reviewers to make final adjudications for the 2 discrepant classifications and to ensure a standardized process moving forward. The remaining 85 cases were reviewed by 1 physician (C.S); the 12 cases in which classifications were

https://doi.org/10.1017/ice.2022.300 Published online by Cambridge University Press

unclear were subsequently discussed with 2 additional reviewers (C.R. and M.K.) to achieve consensus.

Statistical analysis

Patient characteristics and outcomes were compared across groups using χ^2 tests for categorical variables and ANOVA tests for continuous variables. Comparisons between the periods before and after the emergence of the Omicron variant were performed for each definition by calculating incidence of COVID-19 cases per 100 admissions and incidence of ICU admissions, need for mechanical ventilation, and in-hospital deaths per 100 COVID-19 cases. We then calculated incidence rate ratios (IRRs) for the periods before and after the emergence of the Omicron variant.

The proportions of COVID-19 hospitalizations due to primary or contributing COVID-19 versus incidental COVID-19 per medical record review were compared across definitions and area under the receiver operating curves (AUROCs), sensitivity, specificity, and positive and negative predictive values were calculated.

Analyses were conducted using Stata version 17 software (StataCorp, 2021, College Station, TX: StataCorp LLC). For all analyses, $P < .05$ was considered statistically significant.

Results

Study cohort

The study cohort included 306,387 hospital encounters associated with 197,434 unique individuals. Overall, 15,436 (5.0%) of 306,387 encounters met the primary PCR-based definition (positive PCR between 14 days prior to admission and discharge). Compared to hospital encounters without a positive PCR test, those meeting the PCR definition were slightly older (median age 62 vs 60 years), more likely to be male (51.8% vs 43.9%), and less likely to be of white race (59.8% vs 75.2%) (Table 1).

COVID-19 hospitalizations, clinical characteristics, and outcomes across definitions

Clinical characteristics and outcomes for all 6 definitions are shown in Table 2. The proportions of encounters meeting criteria for COVID-19 hospitalization were 1.5% for PCR plus dexamethasone, 1.9% PCR plus remdesivir, 3.9% for PCR plus hypoxemia, 5.0% for PCR only, 5.1% for institutional COVID-19 flag, and 5.2% for COVID-19 ICD-10 codes. These proportions varied substantially over time (Fig. 1). In-hospital mortality rates ranged from 8.3% for PCR only to 12.2% for PCR plus dexamethasone versus 2.2% for all non–COVID-19 encounters.

Before and after the predominance of the Omicron variant

Overall, 30,273 (9.9%) of 306,387 encounters occurred during the Omicron variant period versus 276,114 (90.1%) during the period preceding the Omicron variant. However, among PCR-positive encounters, 3,424 of 15,436 (22.2%) occurred during the Omicron period. Median duration of mechanical ventilation was substantially shorter for COVID-19 encounters during the Omicron period across all 6 definitions: 4 versus 11 days for PCR only and 6 versus 13 days for PCR plus dexamethasone. Incidence rate ratios and their respective confidence intervals for ICU admission and the need for mechanical ventilation were <1 across all definitions during the Omicron period indicating lower risk of these outcomes during the period after the emergence of the Omicron variant compared to before. In-hospital mortality was lower during the Omicron period for PCR only, PCR plus hypoxemia, institutional flag, and ICD-10 definitions. However, mortality was similar during the periods before and after the emergence of the Omicron variant for PCR plus dexamethasone and PCR plus remdesivir definitions (Table 3). A sensitivity analysis limiting the period before the emergence of the Omicron variant to November 1, 2020, to December 16, 2021 (ie, when the use of dexamethasone and remdesivir to treat SARS-CoV-2 were well established) yielded similar results (Supplementary Table 4 online).

Distinguishing primary or contributing versus incidental infections

Among 100 cases reviewed, 45 met criteria for primary COVID-19 hospitalizations: 17 were COVID-19 contributing, and 38 were COVID-19 incidental. Among the incidental COVID-19 hospitalizations, 19 cases had PCR results deemed to be a false positive or residual RNA from a previous recovered infection based upon the patient's clinical syndrome, PCR cycle threshold values, repeat test results, and/or timing of recent infections. Proportions of primary, contributing, and incidental cases differed significantly ($P < .001$) between subgroups in the periods before and after the emergence of the Omicron variant: 30 (60%) of 50 primary cases before the Omicron variant versus 15 (33.3%) of 50 cases after the Omicron variant; 8 (16%) of 50 contributing cases before the Omicron variant versus 9 (18%) of 50 cases after the Omicron variant; and 12 (24%) of 50 incidental cases before the Omicron variant versus 26 (52%) of 50 cases after the Omicron variant.

The performance characteristics for each definition are summarized in Figure 2 and Table 4. PCR plus remdesivir had the highest PPV (90.0%; 95% confidence interval [CI], 76.3–97.2) and AUROC (0.74; 95% CI, 0.66–0.82) for a COVID-19 primary or contributing hospitalization. This definition showed moderate sensitivity at best (58.1%; 95% CI, 44.8–70.5) and negative predictive value (56.7%; 95% CI, 43.2–69.4). The ICD-10–based definition had the highest sensitivity (98.4%; 95% CI, 91.3–100) and negative predictive value (93.8%; 95% CI, 69.8–99.8) but poor specificity (39.5%; 95% CI, 24.0–56.6) and a fair positive predictive value (72.6%; 95% CI, 61.8–81.8). In general, the performances of the other definitions were poor to moderate, with AUROCs for primary or contributing hospitalizations ranging from 0.57 (95% CI, 0.47–0.66) for PCR plus hypoxemia to 0.69 (95% CI, 0.61–0.77) for ICD-10 codes. The performances for each definition stratified by periods before and after the emergence of the Omicron variant can be found in Supplementary Table 2 (online).

Discussion

We found substantial variation in COVID-19 hospitalization counts and outcomes across 6 commonly used definitions for COVID-19 hospitalizations. Crude COVID-19 hospitalization counts varied up to 3-fold between the most inclusive definition (based on ICD-10) versus the most restrictive definition (PCR plus dexamethasone). Definitions based upon receipt of COVID-19 therapeutics identified encounters with significantly higher rates of ICU admission, mechanical ventilation, and death. None of the definitions we examined reliably differentiated between primary or contributing versus incidental COVID-19 hospitalizations compared to detailed chart review. The most accurate definition (PCR plus remdesivir) had a very high positive predictive value but identified fewer than two-thirds of primary or contributing cases.

https://doi.org/10.1017/ice.2022.300 Published online by Cambridge University Press

Table 1. Demographics and Baseline Characteristics for COVID-19 and Non–COVID-19–Related Hospital Encounters

Variable	COVID-19 Encounters	Non–COVID-19 Encounters	All Encounters
	Positive SARS-CoV-2 PCR −14 d to DC	No Positive SARS-CoV-2 PCR −14 d to DC	
Overall, no. (%)	15,436 (5)	290,951 (95)	306,387
Age, median (IQR), y	62 (46–75)	60 (40–73)	60 (40–73)
Sex, no. (%)			
Women	7,437 (48.2)	163,236 (56.1)	170,673 (55.7)
Race, no. (%)			
White	9,226 (59.8)	218,923 (75.2)	228,149 (74.5)
Black	2,256 (14.6)	26,602 (9.1)	28,858 (9.4)
Other	3,096 (20.1)	34,052 (11.7)	37,148 (12.1)
Missing	858 (5.6)	11,374 (3.9)	12,232 (4)
BMI, median (IQR)	27.9 (24–32.8)	27.3 (23.6–31.9)	27.3 (23.6–32)
Comorbidities, no. (%)[a]			
Cancer	1,555 (10.1)	46,645 (16)	48,200 (15.7)
Congestive heart failure	2,615 (16.9)	41,770 (14.4)	44,385 (14.5)
Chronic lung disease	3,483 (22.6)	55,302 (19)	58,785 (19.2)
Diabetes	4,967 (32.2)	62,534 (21.5)	67,501 (22)
Neurologic disease	2,187 (14.2)	33,060 (11.4)	35,247 (11.5)
Kidney disease	3,200 (20.7)	43,008 (14.8)	46,208 (15.1)
Elixhauser mortality score, median (IQR)	0 (−3 to 15)	0 (−2 to 13)	0 (−2 to 13)
ICD-10 code for COVID-19	13,451 (87.1)	2,417 (0.8)	15,868 (5.2)
Period			
Before the Omicron variant	12,012 (77.8)	264,102 (90.8)	276,114 (90.1)
During the Omicron variant	3,424 (22.2)	26,849 (9.2)	30,273 (9.9)

Note. DC, discharge; IQR, interquartile range; ICD-10, *International Classification of Disease, Tenth Revision*.
[a]Comorbidities were derived using the Elixhauser index.[38,39] Cancer includes solid tumor with and without metastases and lymphoma. Diabetes includes diabetes with and without complications. Neurologic disease includes movement disorders, seizures, and other neurologic conditions. Kidney disease includes moderate and severe renal failure.

Table 2. Clinical Characteristics and Outcomes of Encounters Meeting Each Definition for COVID-19 Hospitalization

Category	PCR Only	PCR + Hypox	PCR + Dex	PCR + RDV	EHR Flag	ICD-10	Non–COVID-19 (No +PCR)	All Encounters
Total encounters, no. (%)	15,436 (5)	11,801 (3.9)	4,628 (1.5)	5,757 (1.9)	15,673 (5.1)	15,868 (5.2)	290,951	306,387
Omicron period, no. (%)	3,424 (22.2)	2,323 (19.7)	1,066 (23)	1,496 (26)	3,585 (22.9)	3,310 (20.9)	26,849 (9.2)	30,273 (9.9)
Hospital LOS, median d (IQR)	5 (3–10)	6 (4–12)	7 (4–15)	7 (4–13)	5 (2–10)	5 (3–10)	3 (2–6)	3 (2–6)
Required ICU admission, no. (%)	3,088 (20)	3,020 (25.6)	1,462 (31.6)	1,474 (25.6)	3,003 (19.2)	3,168 (20)	28,616 (9.8)	31,704 (10.4)
Any supplemental oxygen, no. (%)	9,379 (60.8)	9,379 (79.5)	4,251 (91.9)	4,686 (81.4)	9,496 (60.6)	9,997 (63)	127,896 (44)	137,275 (44.8)
Any MV, no. (%)	2,140 (13.9)	2,140 (18.1)	1,079 (23.3)	1,029 (17.9)	2,057 (13.1)	2,186 (13.8)	17,294 (5.9)	19,434 (6.3)
Duration of MV, median d (IQR)	10 (3–20)	10 (3–20)	11 (4–21)	11 (4–21)	10 (3–20)	10 (3–20)	2 (1–5)	2 (1–6)
Discharge disposition, no. (%)								
Home	10,771 (69.8)	7,506 (63.6)	3,067 (66.3)	4,071 (70.7)	11,208 (71.5)	11,142 (70.2)	244,140 (83.9)	254,911 (83.2)
Facility or transfer	3,151 (20.4)	2,810 (23.8)	920 (19.9)	1,100 (19.1)	2,838 (18.1)	3,092 (19.5)	36,236 (12.5)	39,387 (12.9)
Hospice	236 (1.5)	218 (1.9)	75 (1.6)	78 (1.4)	221 (1.4)	225 (1.4)	4,212 (1.5)	4,448 (1.5)
Died	1,278 (8.3)	1,267 (10.7)	566 (12.2)	508 (8.8)	1,406 (9.0)	1,409 (8.9)	6,362 (2.2)	7,640 (2.5)

Note. PCR, polymerase chain reaction assay; Hypox, hypoxemia; Dex, dexamethasone; RDV, remdesivir; EHR, electronic health record; ICD-10, *International Classification of Disease, Tenth Revision*; ICU, intensive care unit; LOS, length of stay; MV, mechanical ventilation.

https://doi.org/10.1017/ice.2022.300 Published online by Cambridge University Press

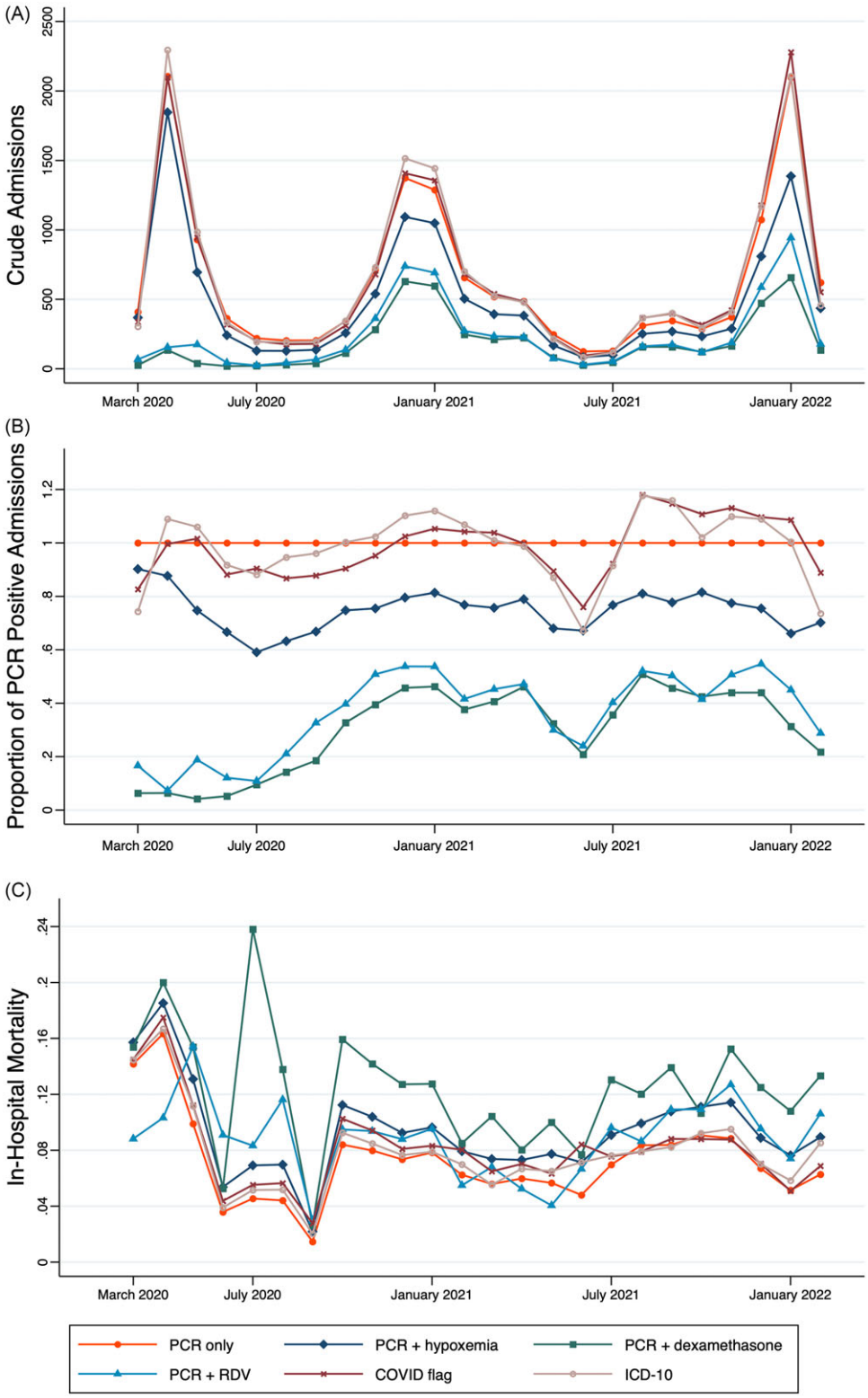

Fig. 1. (A) Crude number of hospitalizations, (B) proportion of COVID-19 hospitalizations divided by PCR–positive hospitalizations, and (C) in-hospital mortality for COVID-19 hospitalization by month for 6 candidate definitions of COVID-19 hospitalization.

Our findings demonstrate the challenge of conducting surveillance for severe SARS-CoV-2 infections in the contemporary context. Hospitalization with a positive PCR assay alone is a poor proxy for severe SARS-CoV-2 infections at this stage of the pandemic. None of the alternative definitions we assessed, however, were both sensitive and specific for severe SARS-CoV-2 infection.

Some of the definitions we evaluated may nonetheless still be useful depending on the purpose of the analysis. The original PCR-based CDC definition, ICD-10–based definition, and institutional COVID-19 flag-based definition were sensitive and produced large cohorts, albeit with lower severity of illness overall and low specificity for primary or contributing COVID-19 infections. These metrics mirror trends in the prevalence of COVID-19 in the

https://doi.org/10.1017/ice.2022.300 Published online by Cambridge University Press

Table 3. Incidence of COVID-19 Hospitalization, ICU Admission, Mechanical Ventilation, and In-Hospital Mortality in the Periods Before and After the Emergence of the SARS-CoV-2 Omicron Variant for Six Definitions of COVID-19 Hospitalization

	Preceding the Omicron Variant		During the Omicron Period		Comparison
Outcome	No.	Incidence[a]	No.	Incidence[a]	IRR (95% CI)
COVID-19 hospitalization					
PCR only	12,012	4.35	3,424	11.31	2.60 (2.50–2.7)
PCR + hypoxemia	9,478	3.43	2,323	7.67	2.24 (2.14–2.34)
PCR + dexamethasone	3,562	1.29	1,066	3.52	2.73 (2.54–2.92)
PCR + remdesivir	4,261	1.54	1,496	4.94	3.20 (3.02–3.4)
COVID-19 flag	12,088	4.38	3,585	11.84	2.71 (2.61–2.81)
ICD-10 code for COVID	12,558	4.55	3,310	10.93	2.40 (2.31–2.5)
ICU admission					
PCR only	2,621	21.82	467	13.64	0.63 (0.57–0.69)
PCR + hypoxemia	2,572	27.14	448	19.29	0.71 (0.64–0.79)
PCR + dexamethasone	1,194	33.52	268	25.14	0.75 (0.66–0.86)
PCR + remdesivir	1,180	27.69	294	19.65	0.71 (0.62–0.81)
COVID-19 flag	2,569	21.25	434	12.11	0.57 (0.51–0.63)
ICD-10 code for COVID	2,718	21.64	450	13.60	0.63 (0.57–0.69)
Mechanical ventilation					
PCR only	1,820	15.15	320	9.35	0.62 (0.55–0.69)
PCR + hypoxemia	1,820	19.20	320	13.78	0.72 (0.63–0.81)
PCR + dexamethasone	885	24.85	194	18.20	0.73 (0.63–0.86)
PCR + remdesivir	824	19.34	205	13.70	0.71 (0.61–0.83)
COVID-19 flag	1,754	14.51	303	8.45	0.58 (0.52–0.66)
ICD-10 code for COVID	1,876	14.94	210	6.34	0.63 (0.56–0.71)
In-hospital mortality					
PCR only	1,085	9.03	193	5.64	0.62 (0.54–0.73)
PCR + hypoxemia	1,076	11.35	191	8.22	0.72 (0.62–0.84)
PCR + dexamethasone	439	12.32	127	11.91	0.97 (0.79–1.18)
PCR + remdesivir	383	8.99	125	8.36	0.93 (0.76–1.14)
COVID-19 flag	1,204	9.96	202	5.63	0.57 (0.49–0.66)
ICD-10 code for COVID	1,199	9.55	210	6.34	0.66 (0.57–0.77)

Note. IRR, incidence rate ratio; CI, confidence interval; PCR, polymerase chain reaction assay.
[a]For COVID-19 hospitalization, incidence is the number of COVID-19 cases per 100 encounters; for ICU admission, mechanical ventilation, and in-hospital mortality, incidence is the number of outcome cases per 100 COVID-19 encounters based on given definition.

local community and accurately reflect the absolute count of cases being managed by hospitals. They are imperfect measures, however, of the incidence of severe COVID-19, particularly during the Omicron period.

Conversely, definitions that incorporated hypoxemia or receipt of anti–COVID-19 therapeutics identified smaller cohorts with higher severity of illness, had greater specificity for primary or contributing infections, and yielded more stable mortality estimates in the periods before and after the emergence of the Omicron variant. The low sensitivity of these definitions renders them poor proxies for estimating the total burden of severe disease, but their high specificity may make them useful candidates for tracking relative changes in the burden of severe disease over time. These characteristics may also make these definitions useful as inclusion criteria for observational studies of inpatient COVID-19 cohorts. Hospitalizations flagged by these definitions are enriched for COVID-19 primary or contributing hospitalizations and experience higher incidence rates of many common study outcomes such as ICU admission or death. However, we urge caution for 2 reasons: risk of selection bias that can distort the magnitude and direction of measured associations if components of the definition used for inclusion qualify as "collider" variables,[30] and their performance will likely change over time as indications, availability, and alternative therapies evolve. Public health agencies and researchers can also consider using multiple definitions with different sensitivities and specificities to provide both "conservative" and "liberal" estimates of the burden of severe COVID-19.

In this study, ICD-10 codes had high sensitivity and good negative predictive value but poor specificity and moderate positive predictive value. Because our medical record reviews were

https://doi.org/10.1017/ice.2022.300 Published online by Cambridge University Press

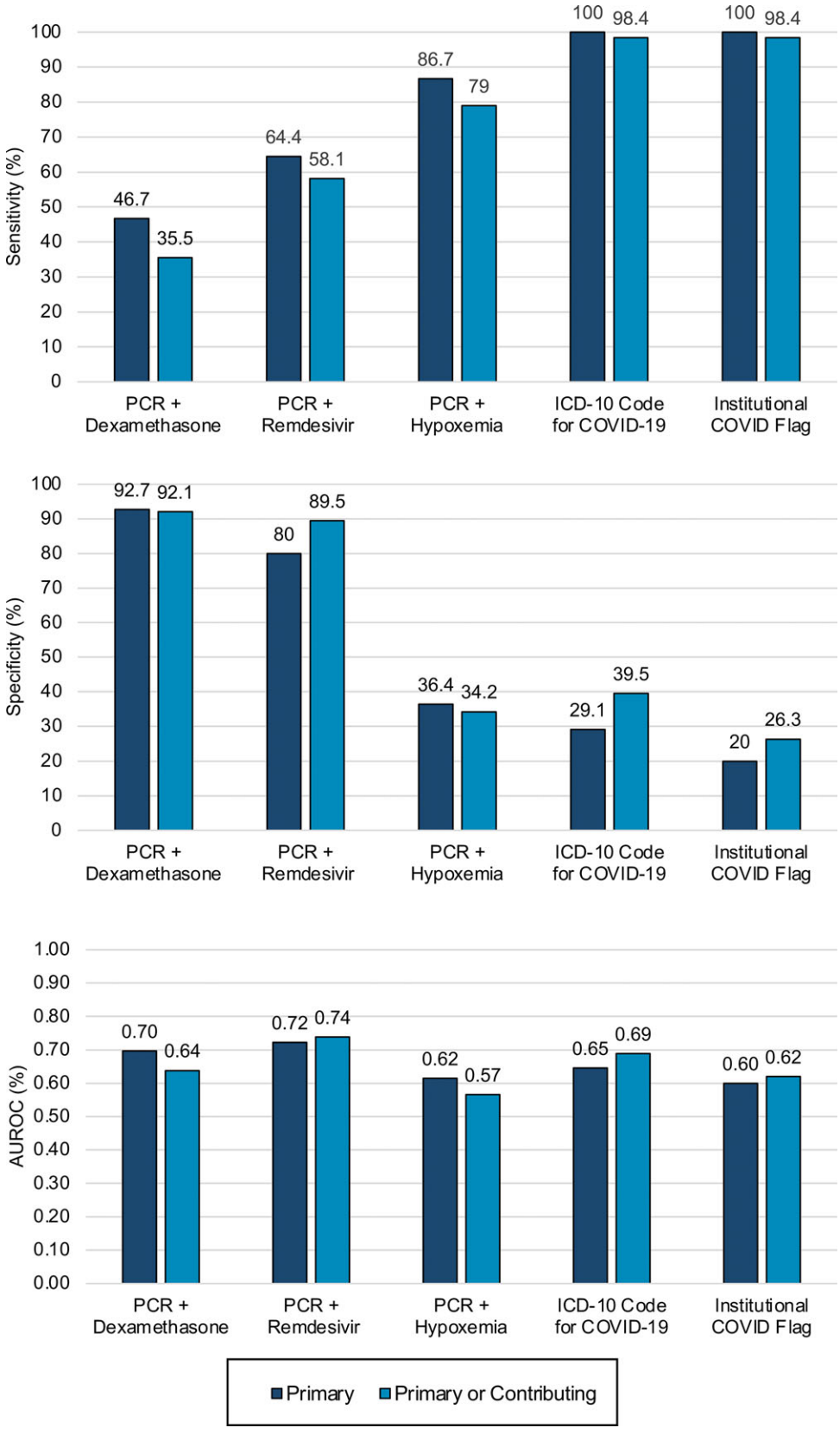

Fig. 2. Performance of 5 definitions of COVID-19 hospitalization versus medical record review for primary and primary or contributing COVID-19 hospitalization.

conducted among PCR-positive hospitalizations, the true positive predictive value of ICD-10 codes might be even lower. This finding contrasts with early assessments of COVID-19 ICD-10 codes which reported excellent positive and negative predictive values for ICD-10 codes compared to PCR data in all patients and critically ill patients, respectively.[8,24,31–34] In retrospect, the excellent performance for ICD-10 codes in these studies was likely due to the use of PCR positivity as the gold standard for COVID-19 hospitalization, as

https://doi.org/10.1017/ice.2022.300 Published online by Cambridge University Press

Table 4. Performance of Candidate Definitions for Identifying Primary or Contributing COVID-19 Hospitalization Versus Manual Chart Review

Definition	Sensitivity (95% CI)	Specificity (95% CI)	AUROC (95% CI)	PPV (95% CI)	NPV (95% CI)
PCR only	. . .[a]	. . .[a]	. . .[a]	62.0 (51.8–71.5)	. . .[a]
PCR + hypoxemia	79.0 (66.8–88.3)	34.2 (19.6–51.4)	0.57 (0.47–0.66)	66.2 (54.3–76.8)	50.0 (29.9–70.1)
PCR + dexamethasone	35.5 (23.7–48.7)	92.1 (78.6–98.3)	0.64 (0.56–0.71)	88.0 (68.8–97.5)	46.7 (35.1–58.6)
PCR + remdesivir	58.1 (44.8–70.5)	89.5 (75.2–97.1)	0.74 (0.66–0.82)	90.0 (76.3–97.2)	56.7 (43.2–69.4)
Institutional COVID–19 flag	98.4 (91.3–100)	26.3 (13.4–43.1)	0.62 (0.55–0.70)	68.5 (57.8–78.0)	90.9 (58.7–99.8)
ICD–10	98.4 (91.3–100)	39.5 (24.0–56.6)	0.69 (0.61–0.77)	72.6 (61.8–81.8)	93.8 (69.8–99.8)

Note. CI, confidence interval; PCR, polymerase chain reaction; ICD-10, *International Classification of Disease, Tenth Revision* (ICD-10); AUROC, area under the receiver operating curve; NPV, negative predictive value; PPV, positive predictive value; PCR, polymerase chain reaction assay.
[a]Sensitivity, specificity, AUROC, and NPV left blank for definition 1 as all reviewed encounters met the PCR-only criteria.

well as the newness of the epidemic, focal use of testing, low healthcare utilization for non–COVID-19 care (hence fewer incidental cases), and fewer false-positive results due to prior infections. We advise caution when interpreting studies which identify COVID-19 hospitalizations using ICD-10 codes during the current era.

The finding that all definitions had poor-to-moderate AUROCs for distinguishing incidental versus primary or contributing COVID-19 underscores the complexity and variability of COVID-19 presentations and the challenge of disentangling the attributable morbidity of SARS-CoV-2 in specific patient encounters. EHR-based approaches using the simple definitions assessed in our study, perhaps unsurprisingly, were ill-equipped to identify such nuance. Our study draws attention to the need to develop better surveillance definitions that more accurately capture and characterize the full spectrum of COVID-19–associated illness in hospitalized patients. Algorithms that incorporate a wider array of EHR data may better distinguish primary versus incidental COVID-19 hospitalizations, but this comes at the cost of generalizability and the broad applicability that is essential for public health surveillance.[35]

Many frequently reported COVID-19 outcomes such as need for ICU admission, use of mechanical ventilation, and in-hospital death were significantly less common during the periods before than after the emergence of the Omicron variant despite much higher case incidence rates during the Omicron period. Prior studies have speculated that this is due to higher rates of population immunity from vaccination and prior infections, a broader armamentarium of therapeutics, and/or lower intrinsic severity for the Omicron variant versus prior variants.[36,37] Our findings also suggest that a fourth contributing factor is the dramatic increase in community incidence during the initial Omicron surge, which led to a large increase in the number of hospitalized patients with incidental COVID-19 and to a consequent decrease in the percentage of COVID-19 hospitalizations with severe disease.

Our study had several limitations. It was conducted using EHR data from a single healthcare system; larger studies with more geographic diversity are needed. Also, it included only adult patients; these results cannot be extended to pediatric populations. Only a small number of cases were manually reviewed to characterize each definition's capacity to distinguish primary or contributing versus incidental infections. Determining the role of COVID-19 in hospitalization can be subjective, but it was mitigated using a standardized data collection tool and discussion of difficult cases with 3 clinicians to reach consensus. Furthermore, the performance of the definitions we evaluated likely fluctuated over the examined period and will continue to change in the future as new variants emerge, therapeutic strategies evolve, and reinfections become more common. Therefore, ongoing periodic reassessment of definitions for COVID-19 hospitalization will be needed to determine their appropriateness to inform public health surveillance, policy recommendations, and research.

In conclusion, estimates of COVID-19 admissions, severity of illness, in-hospital mortality, and trends are significantly affected by how COVID-19 hospitalizations are defined. The traditional PCR-based definition identifies many incidental cases and is associated with less severe illness compared to definitions that incorporate hypoxemia or COVID-19 therapeutics. Most definitions demonstrated improvements in in-hospital mortality rates in the periods before and after the emergence of the Omicron variant, but definitions that required dexamethasone or remdesivir did not. Medical record reviews demonstrated that no definition accurately differentiated between primary or contributing versus incidental hospitalizations, although positive PCR plus remdesivir or dexamethasone had a high positive predictive value for primary or contributing hospitalizations. An ICD-10–based definition had excellent sensitivity but poor positive and negative predictive values. These findings have important implications for public health surveillance and research, including highlighting the need for improved surveillance definitions that better capture and characterize the full spectrum of COVID-19–associated disease in hospitalized patients.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2022.300

Acknowledgments.

Financial support. C.N.S. received grant support from the National Institutes of Health (grant no. 1F32GM143862-01). M.K. and C.R. received grant support from the Centers for Disease Control and Prevention (grant no. 6U54CK000484-04-02).

Conflicts of interest. C.R. reports royalties from UpToDate, Inc., and consulting fees from Cytovale and Pfizer on unrelated topics. M.K. reports royalties from UpToDate, Inc. The other authors report no potential conflict of interest.

References

1. Science brief: indicators for monitoring COVID-19 community levels and making public health recommendations. Centers for Disease Control and Prevention website. https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/indicators-monitoring-community-levels.html#:~:text=CDC%20recommends%20the%20use%20of,per%20100%2C000%20population%20in%20the. Published March 4, 2022. Accessed December 5, 2022.

2. COVID-NET: COVID-19–Associated Hospitalization Surveillance Network. Centers for Disease Control and Prevention website. https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html. Accessed April 25, 2022.
3. Fillmore NR, La J, Zheng C, *et al.* The COVID-19 hospitalization metric in the pre- and postvaccination eras as a measure of pandemic severity: a retrospective, nationwide cohort study. *Infect Control Hosp Epidemiol* 2022. doi: 10.1017/ice.2022.13.
4. Murray S CR, Wachter RM. Is a patient hospitalized "with" COVID-19 or "for" COVID? It can be hard to tell. *The Washington Post* website. https://www.washingtonpost.com/outlook/2022/01/07/hospitalization-covid-statistics-incidental/. Published January 7, 2022. Accessed March 22, 2022.
5. Fatima S. Here's why the state is changing the way it reports COVID-19 hospitalization data. *The Boston Globe* website. https://www.bostonglobe.com/2022/01/07/nation/heres-why-state-is-changing-way-it-reports-covid-hospitalization-data/. Published January 7, 2022. Accessed March 22, 22.
6. Gershengorn HB, Patel S, Shukla B, *et al.* Predictive value of sequential organ failure assessment score across patients with and without COVID-19 infection. *Ann Am Thorac Soc* 2022;19:790–798.
7. Garg S, Patel K, Pham H, *et al.* Clinical trends among US Adults hospitalized with COVID-19, March to December 2020: a cross-sectional study. *Ann Intern Med* 2021;174:1409–1419.
8. Wu G, D'Souza AG, Quan H, *et al.* Validity of ICD-10 codes for COVID-19 patients with hospital admissions or ED visits in Canada: a retrospective cohort study. *BMJ Open* 2022;12:e057838.
9. Myers LC, Mark D, Ley B, *et al.* Validation of respiratory rate-oxygenation index in patients with COVID-19–related respiratory failure. *Crit Care Med* 2022;50:e638–e642.
10. Song Z, Zhang X, Patterson LJ, Barnes CL, Haas DA. Racial and ethnic disparities in hospitalization outcomes among medicare beneficiaries during the COVID-19 pandemic. *JAMA Health Forum* 2021;2:e214223.
11. Montgomery MP, Hong K, Clarke KEN, *et al.* Hospitalizations for COVID-19 among US people experiencing incarceration or homelessness. *JAMA Netw Open* 2022;5:e2143407.
12. Brown HK, Saha S, Chan TCY, *et al.* Outcomes in patients with and without disability admitted to hospital with COVID-19: a retrospective cohort study. *CMAJ* 2022;194:E112–E121.
13. Whitfield GP, Harris AM, Kadri SS, *et al.* Trends in clinical severity of hospitalized patients with coronavirus disease 2019—premier hospital dataset, April 2020–April 2021. *Open Forum Infect Dis* 2022;9:ofab599.
14. Bottle A, Faitna P, Aylin PP. Patient-level and hospital-level variation and related time trends in COVID-19 case fatality rates during the first pandemic wave in England: multilevel modelling analysis of routine data. *BMJ Qual Saf* 2022;31:211–220.
15. Rose AN, Baggs J, Wolford H, *et al.* Trends in antibiotic use in United States hospitals during the coronavirus disease 2019 pandemic. *Open Forum Infect Dis* 2021;8:ofab236.
16. Kadri SS, Sun J, Lawandi A, *et al.* Association between caseload surge and COVID-19 survival in 558 US hospitals, March to August 2020. *Ann Intern Med* 2021;174:1240–1251.
17. Verma AA, Hora T, Jung HY, *et al.* Characteristics and outcomes of hospital admissions for COVID-19 and influenza in the Toronto area. *CMAJ* 2021;193:E410–E418.
18. Musshafen LA, El-Sadek L, Lirette ST, Summers RL, Compretta C, Dobbs TE III. In-hospital mortality disparities among American Indian and Alaska Native, black, and white patients with COVID-19. *JAMA Network Open* 2022;5:e224822–e224822.
19. Bhavani SV, Verhoef PA, Maier CL, *et al.* Coronavirus disease 2019 temperature trajectories correlate with hyperinflammatory and hypercoagulable subphenotypes. *Crit Care Med* 2022;50:212–223.
20. Auld SC, Harrington KRV, Adelman MW, *et al.* Trends in ICU mortality from coronavirus disease 2019: a tale of three surges. *Crit Care Med* 2022;50:245–255.
21. Burnim MS, Wang K, Checkley W, Nolley EP, Xu Y, Garibaldi BT. The effectiveness of high-flow nasal cannula in coronavirus disease 2019 pneumonia: a retrospective cohort study. *Crit Care Med* 2022;50:e253–e262.
22. Wongvibulsin S, Garibaldi BT, Antar AAR, *et al.* Development of severe COVID-19 Adaptive Risk Predictor (SCARP), a calculator to predict severe disease or death in hospitalized patients with COVID-19. *Ann Intern Med* 2021;174:777–785.
23. Pineles BL, Harris AD. In-hospital mortality in a cohort of hospitalized pregnant and nonpregnant patients with COVID-19. *Ann Intern Med* 2021;174:1779–1780.
24. Khera R, Mortazavi BJ, Sangha V, *et al.* A multicenter evaluation of computable phenotyping approaches for SARS-CoV-2 infection and COVID-19 hospitalizations. *NPJ Digit Med* 2022;5:27.
25. Chomistek AK, Liang C, Doherty MC, *et al.* Predictors of critical care, mechanical ventilation, and mortality among hospitalized patients with COVID-19 in an electronic health record database. *BMC Infect Dis* 2022;22:413.
26. COVID-19 interactive data dashboard. Massachusetts Department of Public Health website. https://www.mass.gov/info-details/covid-19-response-reporting#covid-19-interactive-data-dashboard-. Accessed January 15, 2022.
27. Shappell CN, Klompas M, Kanjilal S, Chan C, Rhee C. Prevalence, clinical characteristics, and outcomes of sepsis caused by severe acute respiratory syndrome coronavirus 2 versus other pathogens in hospitalized patients with COVID-19. *Crit Care Explor* 2022;4:e0703.
28. Rhee C, Baker MA, Kanjilal S, *et al.* Prospective clinical assessments of hospitalized patients with positive SARS-CoV-2 PCR tests for necessity of isolation. *Open Forum Infect Dis* 2021;8:ofab194.
29. Tracking the omicron variant in Massachusetts. The Broad Institute website. https://www.broadinstitute.org/news/tracking-omicron-variant-massachusetts. Published 2021. Accessed April 22, 2022.
30. Admon AJ, Bohnert ASB, Cooke CR, Taylor SP. Beyond confounding: identifying selection bias in observational pulmonary and critical care research. *Ann Am Thorac Soc* 2022;19:1084–1089.
31. Kadri SS, Gundrum J, Warner S, *et al.* Uptake and accuracy of the diagnosis code for COVID-19 among US hospitalizations. *JAMA* 2020;324:2553–2554.
32. Lynch KE, Viernes B, Gatsby E, *et al.* Positive predictive value of COVID-19 ICD-10 diagnosis codes across calendar time and clinical setting. *Clin Epidemiol* 2021;13:1011–1018.
33. Bodilsen J, Leth S, Nielsen SL, Holler JG, Benfield T, Omland LH. Positive predictive value of ICD-10 diagnosis codes for COVID-19. *Clin Epidemiol* 2021;13:367–372.
34. Bosch NA, Law AC, Peterson D, Walkey AJ. Validation of the *International Classification of Diseases* code for COVID-19 among critically ill patients. *Ann Am Thorac Soc* 2022;19:861–863.
35. Klann JG, Strasser ZH, Hutch MR, *et al.* Distinguishing admissions specifically for COVID-19 from incidental SARS-CoV-2 admissions: national retrospective electronic health record study. *J Med Internet Res* 2022;24:e37931.
36. Modes ME, Directo MP, Melgar M, *et al.* Clinical characteristics and outcomes among adults hospitalized with laboratory-confirmed SARS-CoV-2 infection during periods of B.1.617.2 (delta) and B.1.1.529 (omicron) variant predominance—One Hospital, California, July 15–September 23, 2021, and December 21, 2021–January 27, 2022. *Morb Mortal Wkly Rep* 2022;71:217–223.
37. Iuliano AD, Brunkard JM, Boehmer TK, *et al.* Trends in disease severity and healthcare utilization during the early omicron variant period compared with previous SARS-CoV-2 high transmission periods—United States, December 2020–January 2022. *Morb Mortal Wkly Rep* 2022;71:146–152.
38. Elixhauser comorbidity software refined for ICD-10-CM healthcare cost and utilization project (HCUP). Healthcare Cost and Utilization Project website. https://www.hcup-us.ahrq.gov/toolssoftware/comorbidityicd10/comorbidity_icd10.jsp. Published 2021. Accessed October 11, 2022.
39. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998;36:8–27.

https://doi.org/10.1017/ice.2022.300 Published online by Cambridge University Press