Open Forum Infectious Diseases

BRIEF REPORT

In-Hospital Mortality Among Hospitalized Coronavirus Disease 2019 Patients in the United States: How Did It Change in 2021?

Rena C. Moon and Ning A. Rosenthal

PINC AI Applied Sciences, Premier Inc., Charlotte, North Carolina, USA

In this retrospective observational study in a US national sample of 501 671 adults hospitalized with coronavirus disease 2019, adjusted in-hospital mortality decreased from 12% in February 2021 to 9% in April 2021. However, adjusted in-hospital mortality increased to 16% in September and October 2021. Adjusted intensive care unit admission fluctuated between 20% and 27% in 2021.

Keywords. COVID-19; in-hospital mortality; trend; 2021.

We previously reported monthly crude and adjusted in-hospital mortality among confirmed coronavirus disease 2019 (COVID-19) inpatients from April 2020 through February 2021 using a geographically diverse all-payer hospital administrative database (Premier PINC AI Healthcare Database [PHD]) that accounts for about 20%–25% of total inpatient encounters in the United States (US) [1]. Our findings showed that adjusted in-hospital mortality was lowest in June 2020 (11.9%); it peaked twice and was significantly higher in most of the months afterward through February 2021. Since December 2020, 3 COVID-19 vaccines were authorized in the US for adults; in-hospital mortality among inpatients was expected to be lower in 2021 than 2020 considering the efficacy of vaccines against severe acute respiratory syndrome coronavirus 2 infection requiring intensive care unit (ICU) admission [2]. However, vaccine hesitancy was prevalent [3] and the Alpha, Delta, and Omicron variants emerged in 2021, complicating the effect of vaccines on mortality [4].

Therefore, we assessed the in-hospital mortality among COVID-19 inpatients from January to December 2021 in this study and reviewed monthly changes in ICU admission.

METHODS

Study Design, Data Source, and Study Population

We performed a retrospective cross-sectional study using the PHD COVID-19 special release (PHD-SR) [5, 6] a standalone version of PHD from 1 January 2019, to the most current data available to accommodate urgent COVID-19 research needs. The PHD-SR is currently used by the National Institutes of Health and the Centers for Disease Control and Prevention for COVID-19–related studies [7–9].

All data were deidentified per US Title 45 Code of Federal Regulations (CFR) 164.502(d), through the "Expert Determination" method and compliant with the Health Insurance Portability and Accountability Act. Based on US Title 45 CFR, Part 46, the study was exempted from institutional review board approval. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines [10].

All adult inpatient discharges between 1 January 2021 and 31 December 2021 with a principal/secondary discharge diagnosis of COVID-19 (*International Classification of Diseases, Tenth Revision, Clinical Modification* [*ICD-10-CM*] code U07.1) were analyzed [11]. We only included visits from hospitals with continuous data submission during the study period.

Outcome Measures and Patient, Hospital, and Visit Characteristics

Because <1% of overall mortality occurred during 30-day follow-up, this analysis focused on in-hospital mortality and ICU admission during the first ("index") COVID-19–related hospitalization. For sensitivity analysis, we also examined (1) "in-hospital mortality + discharged to hospice" during index hospitalization, and (2) in-hospital mortality only among patients with principal discharge diagnosis of COVID-19 during index hospitalization.

Patient demographic and clinical characteristics included age, sex, self-reported race and ethnicity, primary insurance payer, and comorbidities. Hospital characteristics included urbanicity of population served (ie, urban or rural), teaching status, US census region (ie, Midwest, Northeast, South, or West), and bed size. Two separate fields for race and ethnicity were combined into 1 race/ethnicity field and categorized as Hispanic, White, Black, or other/unknown.

Comorbidities, including hypertension, history of smoking, morbid obesity, and individual comorbid conditions included in the Charlson-Deyo Comorbidity Index (CCI) [12] were identified using *ICD-10-CM* discharge diagnosis codes

Received 02 May 2022; editorial decision 27 May 2022; accepted 31 May 2022; published online 7 June 2022

Correspondence: Rena C. Moon, MD, MPH, PINC AI Applied Sciences, Premier Inc, 13034 Ballantyne Corporate Place, Charlotte, NC 28277, USA (rena_moon@premierinc.com).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofac278

Table 1. Baseline Patient and Hospital Characteristics of Adult Coronavirus Disease 2019 Inpatients Discharged Between January and December 2021

Characteristic	Overall (N = 501 671)		1 Jan–30 Jun 2021 (n = 236 736)		1 Jul–31 Dec 2021 (n = 264 935)		*P* Value
Patient characteristic							
Age group, y							
18–44	100 157	(20.0)	39 347	(16.6)	60 810	(23.0)	<.01
45–54	73 502	(14.7)	31 507	(13.3)	41 995	(15.9)	
55–64	103 937	(20.7)	48 800	(20.6)	55 137	(20.8)	
65–74	104 190	(20.8)	52 485	(22.2)	51 705	(19.5)	
75–84	78 691	(15.7)	41 970	(17.7)	36 721	(13.9)	
≥85	41 194	(8.2)	22 627	(9.6)	18 567	(7.0)	
Age, y							
Mean (SD)	60.6	(17.8)	62.6	(17.5)	58.8	(17.9)	<.01
Median (Q1, Q3)	62	(49, 74)	64	(51, 76)	60	(46, 72)	
Sex							
Male	255 859	(51.0)	121 219	(51.2)	134 640	(50.8)	.01
Female	245 793	(49.0)	115 505	(48.8)	130 288	(49.2)	
Unknown	19	(0.0)	12	(0.0)	7	(0.0)	
Race/Ethnicity[a]							
White	305 576	(60.9)	135 987	(57.4)	169 589	(64.0)	<.01
Black	78 757	(15.7)	40 154	(17.0)	38 603	(14.6)	
Hispanic	75 310	(15.0)	38 169	(16.1)	37 141	(14.0)	
Other/Unknown	42 028	(8.4)	22 426	(9.5)	19 602	(7.4)	
Primary payer							
Medicare	236 421	(47.1)	121 781	(51.4)	114 640	(43.3)	<.01
Medicaid	76 384	(15.2)	34 099	(14.4)	42 285	(16.0)	
Private insurance	144 962	(28.9)	63 322	(26.7)	81 640	(30.8)	
Uninsured	17 825	(3.6)	6670	(2.8)	11 155	(4.2)	
Other/Unknown	26 079	(5.2)	10 864	(4.6)	15 215	(5.7)	
Charlson-Deyo comorbidities							
Myocardial infarction	49 014	(9.8)	24 337	(10.3)	24 677	(9.3)	<.01
Congestive heart failure	79 603	(15.9)	42 039	(17.8)	37 564	(14.2)	<.01
Peripheral vascular disease	21 258	(4.2)	10 837	(4.6)	10 421	(3.9)	<.01
Cerebrovascular disease	29 747	(5.9)	15 633	(6.6)	14 114	(5.3)	<.01
Dementia	38 147	(7.6)	21 776	(9.2)	16 371	(6.2)	<.01
Chronic pulmonary disease	117 173	(23.4)	57 476	(24.3)	59 697	(22.5)	<.01
Rheumatic disease	11 840	(2.4)	5811	(2.5)	6029	(2.3)	<.01
Peptic ulcer disease	5257	(1.0)	2797	(1.2)	2460	(0.9)	<.01
Mild liver disease	5678	(1.1)	2875	(1.2)	2803	(1.1)	<.01
Moderate or severe liver disease	5363	(1.1)	2820	(1.2)	2543	(1.0)	<.01
Diabetes mellitus	188 695	(37.6)	96 807	(40.9)	91 888	(34.7)	<.01
Hemiplegia	5290	(1.1)	2726	(1.2)	2564	(1.0)	<.01
Moderate or severe renal disease	62 476	(12.5)	33 805	(14.3)	28 671	(10.8)	<.01
Any malignancy	24 797	(4.9)	12 784	(5.4)	12 013	(4.5)	<.01
Metastatic solid tumor	6610	(1.3)	3480	(1.5)	3130	(1.2)	<.01
HIV disease	1375	(0.3)	715	(0.3)	660	(0.2)	<.01
CCI score, category							
0	169 173	(33.7)	69 791	(29.5)	99 382	(37.5)	<.01
1–3	246 951	(49.2)	120 733	(51.0)	126 218	(47.6)	
≥4	85 547	(17.1)	46 212	(19.5)	39 335	(14.8)	
CCI score							
Mean (SD)	1.8	(2.1)	1.9	(2.1)	1.6	(2.0)	<.01
Median (Q1, Q3)	1	(0, 3)	1	(0, 3)	1	(0, 2)	
Other comorbidities							
Hypertension	319 043	(63.6)	161 127	(68.1)	157 916	(59.6)	<.01
Morbid obesity	123 965	(24.7)	56 608	(23.9)	67 357	(25.4)	<.01
History of smoking	59 349	(11.8)	23 549	(9.9)	35 800	(13.5)	<.01
Hospital characteristics							

Table 1. Continued

Characteristic	Overall (N = 501 671)		1 Jan–30 Jun 2021 (n = 236 736)		1 Jul–31 Dec 2021 (n = 264 935)		*P* Value
Hospital size, No. of beds							
1–299	204 112	(40.7)	91 787	(38.8)	112 325	(42.4)	<.01
300–499	152 869	(30.5)	72 868	(30.8)	80 001	(30.2)	
≥500	143 824	(28.7)	71 662	(30.3)	72 162	(27.2)	
Unknown	866	(0.2)	419	(0.2)	447	(0.2)	
Teaching status							
Teaching	221 465	(44.1)	11 1269	(47.0)	110 196	(41.6)	<.01
Nonteaching	280 206	(55.9)	12 5467	(53.0)	154 739	(58.4)	
Urbanicity of served population							
Urban	433 493	(86.4)	20 9103	(88.3)	224 390	(84.7)	<.01
Rural	68 178	(13.6)	27 633	(11.7)	40 545	(15.3)	
Census region of hospital							
Midwest	106 029	(21.1)	45 051	(19.0)	60 978	(23.0)	<.01
Northeast	66 764	(13.3)	42 378	(17.9)	24 386	(9.2)	
South	244 869	(48.8)	112 225	(47.4)	132 644	(50.1)	
West	84 009	(16.7)	37 082	(15.7)	46 927	(17.7)	

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: CCI, Charlson-Deyo Comorbidity Index; HIV, human immunodeficiency virus; Q1, quartile 1; Q3, quartile 3; SD, standard deviation.

[a]If the patient self-reported Hispanic ethnicity, the patient was categorized as Hispanic. Patients with ethnicity as "not Hispanic" or "unknown" were categorized using race, as White, Black, or other/unknown (ie "White" is White with unknown or non-Hispanic ethnicity).

(Supplementary Table 1) during index hospitalization or any prior visit to the same hospital within 180 days. Weighted CCI score was grouped into 3 categories: 0, 1–3, and ≥4.

Statistical Analysis

Unadjusted in-hospital mortality and ICU admission were calculated as the proportion of hospitalized patients who died or were admitted to the ICU, respectively, during index hospitalization for each month. Adjusted odds of in-hospital mortality and ICU admission by month were assessed using multivariable logistic regression models with mortality/ICU admission as outcome and discharge month as predictor (the lowest points of mortality [July] and ICU admission [August] were used as reference month for each model). A priori covariates included patient and hospital characteristics. Final model covariates were selected using a backward selection method, with a significance level of $P < .10$ for covariates to stay in the model and robust standard errors to adjust for clustering of patients within hospitals. Based on the variance inflation factor, covariate multicollinearity was not present in the final models. Last, covariate-adjusted in-hospital mortality and ICU admission were estimated using recycled prediction method to calculate predicted margins [1, 13].

All analyses were performed using R version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Among a total of 501 671 patients from 579 hospitals (representing 42 states and the District of Columbia), mean age was 60.6 years, 51.0% were male, and 60.9% were White (Table 1). Common comorbidities were hypertension (63.6%), diabetes mellitus (37.6%), morbid obesity (24.7%), and chronic pulmonary disease (23.4%). Most patients (48.8%) were hospitalized in the South (reflective of hospitals included in PHD) and in urban hospitals (86.4%). Patients hospitalized in later months (1 July–31 December) were more likely than those hospitalized in earlier months (1 January–30 June) to be younger (mean age, 58.8 vs 62.6 years, respectively), to be White (64.0% vs 57.4%), and to have morbid obesity (25.4% vs 23.9%) and history of smoking (13.5% vs 9.9%) (all $P < .001$). However, patients hospitalized during later months were healthier and less likely to have any of the CCI comorbidities than those in earlier months (all $P < .01$).

In-Hospital Mortality Over Time

Trends in mortality were similar before and after adjusting for significant patient, hospital, and clinical characteristics (Figure 1*A*, Supplementary Table 2). From the initial high of 12.2% in January 2021, adjusted in-hospital mortality declined to 9.1% in April 2021. It inclined to 11.0% in May and stayed at 9.5%–9.9% in June and July 2021. However, adjusted mortality was >12% throughout the latter 5 months of 2021, peaking at 15.7% and 16.1% in September and October, respectively. Relative to July 2021 (the month with the lowest unadjusted mortality), the odds of mortality were significantly higher in January, February, May, and all months from August through December of 2021 (all $P < 0.01$). Trends in adjusted in-hospital mortality + discharged to hospice followed a similar pattern (Supplementary Table 3). When we limited our observation

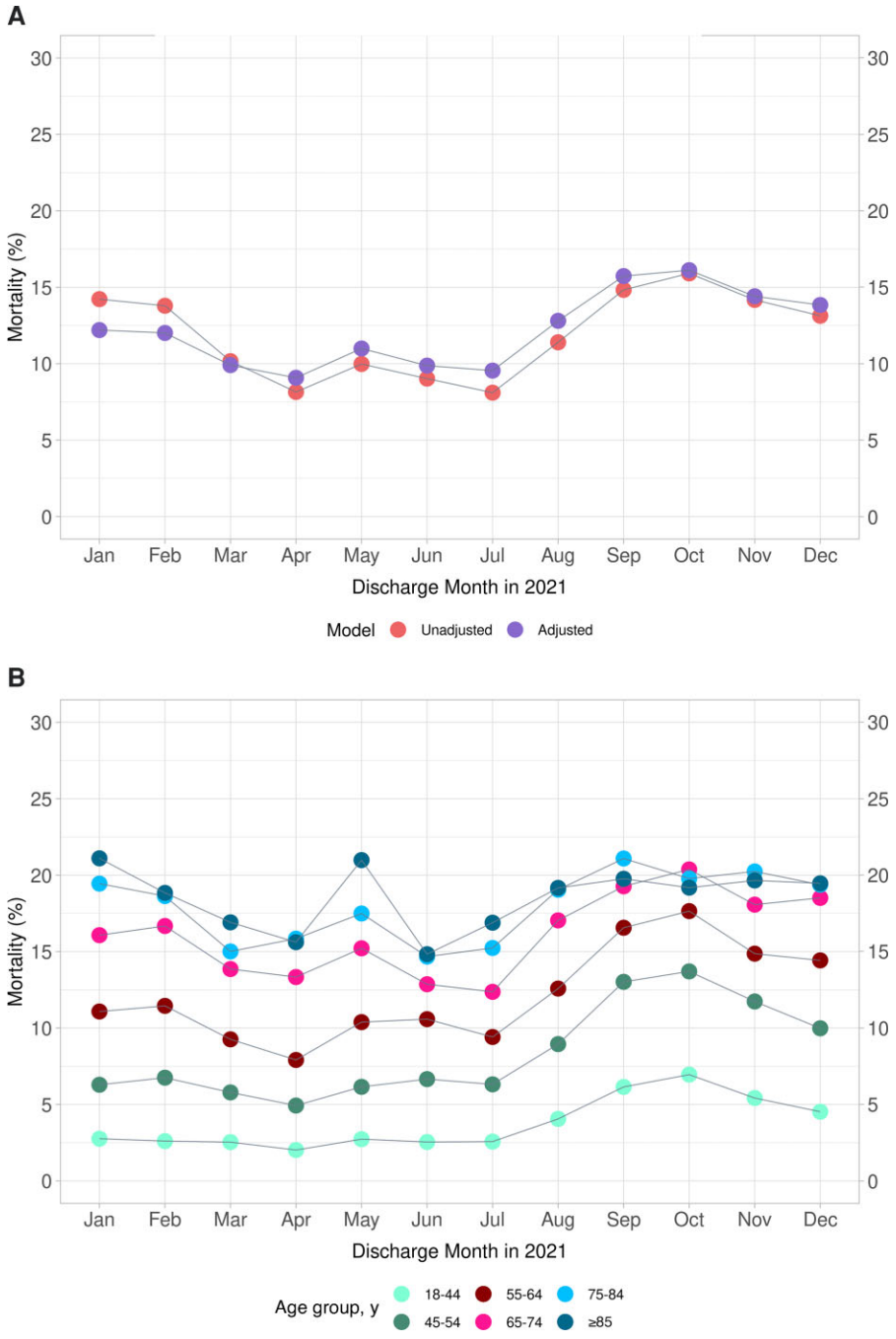

Figure 1. Monthly trends of in-hospital mortality during index hospitalization among hospitalized adult coronavirus disease 2019 patients discharged between January and December 2021. *A*, Adjusted (for month, sex, age group, race/ethnicity, hospital size, hospital teaching status, hospital region, Charlson-Deyo Comorbidity Index score category, morbid obesity, hypertension, moderate or severe renal disease, and diabetes mellitus) and unadjusted in-hospital mortality for overall patients. *B*, Adjusted age group–specific in-hospital mortality (adjusted for month, sex, race/ethnicity, hospital size, hospital teaching status, hospital region, Charlson-Deyo Comorbidity Index score category, morbid obesity, hypertension, moderate or severe renal disease, and diabetes mellitus).

to patients with principal diagnosis of COVID-19 (n = 324 821), adjusted in-hospital mortality decreased slightly for each month (1%–2%), but a similar trend was observed (Supplementary Table 4). Adjusted age group–specific monthly in-hospital mortality trends followed a similar pattern with the overall in-hospital mortality trend - with smaller gaps observed in older (65–74, 75–84, and ≥85 years) age groups (Figure 1*B*, Supplementary Table 5).

ICU Admission Over Time

Trends in ICU admission were very similar before and after adjusting for significant patient and hospital characteristics

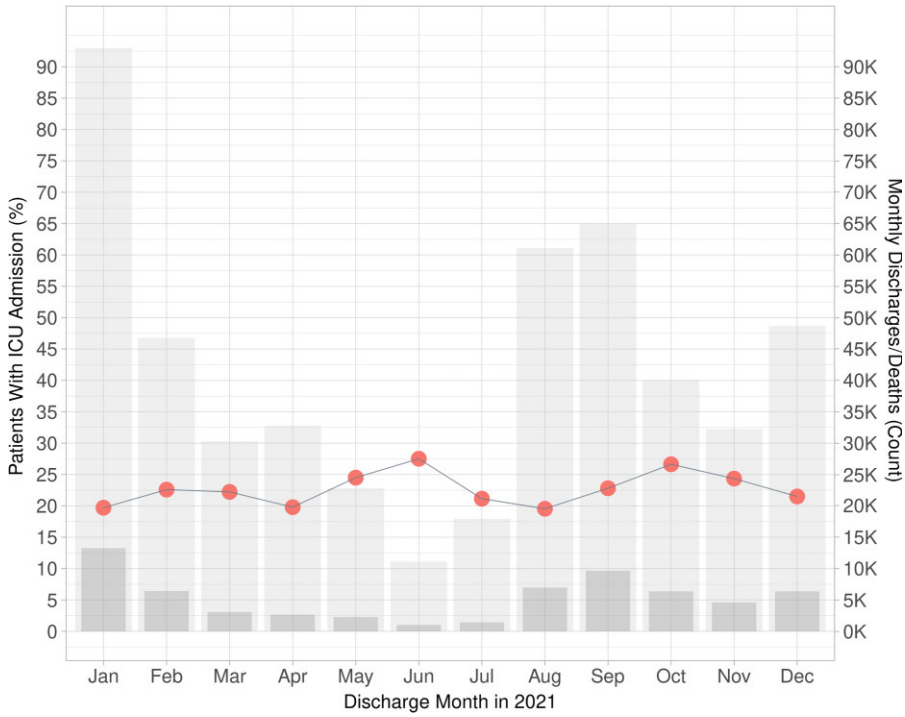

Figure 2. Monthly trends of adjusted intensive care unit (ICU) admission and total number of inpatient discharges and deaths among hospitalized adult coronavirus disease 2019 (COVID-19) inpatients between January and December 2021. Lighter gray bar indicates total number of hospital adult inpatient discharges with primary or secondary discharge diagnosis of COVID-19 each month. Darker gray bar indicates number of deaths occurring during index hospitalization each month. Adjusted for month, sex, age group, race/ethnicity, hospital size, hospital teaching status, hospital region, Charlson-Deyo Comorbidity Index score category, morbid obesity, hypertension, moderate or severe renal disease, and diabetes mellitus.

(Figure 2, Supplementary Table 6). Relative to August 2021 (the month with the lowest unadjusted ICU admission), the adjusted odds of ICU admission were 11% to 60% higher in all months of 2021 except January and April (all $P < .01$). After the initial decline in April (to 19.8%), adjusted probability of ICU admission peaked twice in June (27.5%) and October (27.1%).

DISCUSSION

Using a national database, this study provides covariate-adjusted monthly trends of in-hospital mortality and ICU admission of COVID-19 adult inpatients during January–December 2021. The lowest adjusted mortality in 2021 (9.1%) was lower than that of 2020 (11.9%), possibly due to the introduction of vaccines and improvement in disease management. This is consistent with the analytic model by Vilches et al [14] suggesting that the US COVID-19 vaccination program was associated with decreased hospitalizations and deaths by the more transmissible and lethal Alpha variant during the first 6 months of 2021. However, during the latter 5 months of 2021, adjusted mortality remained high and well above 12%. Even with the wide availability of vaccines, the majority of hospitalized COVID-19 patients were unvaccinated and mortality among them was high, especially when the more lethal Delta variant became prevalent [15]. In addition, the clear parallel trend between different age groups in 2020 was attenuated in 2021 for the older age groups (≥65 years), especially during the last 4 months. However, in these age groups, the positive relationship between age and mortality was less prominent than that in younger age groups in 2020 as well.

We would like to note that during the month with lowest hospitalization (June), the adjusted probability of ICU admission was the highest at 27.5%. We do not think this means that a higher proportion of patients needed an ICU admission compared to other months—on the contrary, this may be due to increased ICU availability and more patients being able to receive an appropriate level of treatment. Both adjusted mortality and ICU admission were high between September and November (14%–16% and 22%–25%, respectively).

This study has several limitations. We were not able to identify the exact variant and vaccination status for each patient, and we defined COVID-19 and other clinical conditions using *ICD-10-CM* diagnosis/procedure codes. Baseline severity of illness is challenging to infer from administrative data, and such differences among patients may have impacted the results.

In 2021, we showed no further decline in mortality despite more time and experience in treating COVID-19. It remains unclear whether the greater mortality risk in later months was the effect of the more lethal Delta variant, a greater proportion of unvaccinated patients being hospitalized, the detrimental effects of caseload surges [9], or a combination of these and other unmeasured factors. With the emergence of Omicron variants, continued monitoring of COVID-19 mortality is warranted.

Supplementary Data

Supplementary materials are available at *Open Forum 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

Acknowledgments. The authors thank Denise Juliano and Myla Maloney for their support of the study, and the PHD-SR data team for making the data available for analysis.

Disclaimer. The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, and approval of the manuscript; or decision to submit the manuscript for publication.

Financial support. This study was funded by Premier, Inc.

Potential conflicts of interest. The authors worked on the study as full-time employees of Premier Inc.

Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Moon RC, Mackey RH, Cao Z, et al. Is COVID-19 less deadly now? Trends of in-hospital mortality among hospitalized COVID-19 patients in the United States [manuscript published online ahead of print 17 September 2021]. Clin Infect Dis **2021**. doi:10.1093/cid/ciab830.
2. Thompson MG, Stenehjem E, Grannis S, et al. Effectiveness of Covid-19 vaccines in ambulatory and inpatient care settings. N Engl J Med **2021**; 385:1355–71.
3. Khubchandani J, Sharma S, Price JH, Wiblishauser MJ, Sharma M, Webb FJ. COVID-19 vaccination hesitancy in the United States: a rapid national assessment. J Community Health **2021**; 46:270–7.
4. Dyer O. Covid-19: Delta infections threaten herd immunity vaccine strategy. BMJ **2021**; 374:n1933.
5. Premier, Inc. Premier Healthcare Database (COVID-19): data that informs and performs. https://offers.premierinc.com/WCFY20PASCOVIDWhitepaper_LandingPage.html. Accessed 20 August 2021.
6. Rosenthal N, Cao Z, Gundrum J, Sianis J, Safo S. Risk factors associated with in-hospital mortality in a US national sample of patients with COVID-19. JAMA Netw Open **2020**; 3:e2029058.
7. Lavery AM, Preston LE, Ko JY, et al. Characteristics of hospitalized COVID-19 patients discharged and experiencing same-hospital readmission—United States. MMWR Morb Mortal Wkly Rep **2020**; 69:1695–99.
8. Kompaniyets L, Goodman AB, Belay B, et al. Body mass index and risk for COVID-19-related hospitalization, intensive care unit admission, invasive mechanical ventilation, and death—United States, March–December 2020. MMWR Morb Mortal Wkly Rep **2021**; 70:355–61.
9. Kadri SS, Sun J, Lawandi A, et al. Association between caseload surge and COVID-19 survival in 558 U.S. hospitals, March to August 2020. Ann Intern Med **2021**; 174:1240–51.
10. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet **2007**; 370:1453–7.
11. Centers for Disease Control and Prevention. *ICD-10-CM* official coding and reporting guidelines, April 1, 2020 through September 30, 2020. https://www.cdc.gov/nchs/data/icd/COVID-19-guidelines-final.pdf. Accessed 26 March 2021.
12. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with *ICD-9-CM* administrative databases. J Clin Epidemiol **1992**; 45:613–9.
13. Basu A, Rathouz PJ. Estimating marginal and incremental effects on health outcomes using flexible link and variance function models. Biostatistics **2005**; 6: 93–109.
14. Vilches TN, Moghadas SM, Sah P, et al. Estimating COVID-19 infections, hospitalizations, and deaths following the US vaccination campaigns during the pandemic. JAMA Netw Open **2022**; 5:e2142725.
15. Tenforde MW, Self WH, Adams K, et al. Association between mRNA vaccination and COVID-19 hospitalization and disease severity. JAMA **2021**; 326:2043–54.