Is COVID-19 Less Deadly Now? -- Trends of In-Hospital Mortality Among Hospitalized COVID-19 Patients in the United States

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Abstract

After an initial decline from April through June 2020 (from 22.2% to 11.9%), adjusted in-hospital mortality in COVID-19 inpatients peaked twice and was significantly higher than June 2020 for subsequent months except in July and October 2020. Adjusted mortality trends differed across age groups between November 2020 and February 2021.

Key Words: In-hospital mortality, COVID-19, trend

Introduction

As of August, 2021, coronavirus disease 2019 (COVID-19) has contributed to over 624,000 deaths in the United States (U.S.).[1] During the early months of the pandemic (April to June of 2020), a sharp decrease in in-hospital mortality was widely reported.[2,3] Monthly crude in-hospital mortality among confirmed COVID-19 inpatients has been estimated using a geographically diverse all-payer hospital administrative database (Premier Healthcare Database [PHD]) that accounts for about 20-25% of total inpatient encounters in the U.S. at the Centers for Disease Control and Prevention (CDC) COVID Data Tracker site (https://covid.cdc.gov/covid-data-tracker/#hospitalizations-severity). Although such information is helpful to the public, crude mortality may not reflect true changes in mortality associated with shift in patient demographics, clinical and hospital characteristics during the pandemic.[2,4-6]

Since both patient and hospital factors can affect mortality among COVID-19 inpatients, it is important to know whether differences in these factors explain any of the observed changes in mortality over the course of the pandemic.[7-10] This study aimed to describe covariate-adjusted monthly trends in overall, age-, and sex-specific in-hospital mortality among U.S. COVID-19 inpatients from April 2020 through February 2021 during both initial encounter and 30-day follow-up.

Methods

Study Design, Data Source, and Study Population

We performed a retrospective cohort study using the Premier Healthcare Database COVID-19 special release (PHD-SR),[9,11] a standalone version of PHD from January 1, 2019 to the most current data available to accommodate urgent COVID-19 research needs. The PHD-SR contains data from approximately 800+ hospitals and is currently used by the National Institute of Health (NIH) and CDC for COVID-19-related studies.[5,12,13]

All data were statistically deidentified and compliant with the Health Insurance Portability and Accountability Act. Based on US Title 45 Code of Federal Regulations, Part 46, the study was exempted from institutional review board approval. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)[14] reporting guideline.

All COVID-19-related inpatient discharges between April 1, 2020 and February 28, 2021 with a principal/secondary discharge diagnosis of COVID-19 (International Classification of Diseases, 10th revision, Clinical Modification [ICD-10-CM] diagnosis code U07.1) were analyzed.[15] To avoid variation over time in hospitals submitting data to PHD-SR, we only included visits from hospitals that continuously submitted data during the study period.

Outcome Measures and Patient, Hospital, and Visit Characteristics

The primary outcome was 'in-hospital mortality' (discharge status equal to "expired") during the "index hospitalization" (first COVID-19-related inpatient admission during the study period) or subsequent COVID-19-related inpatient or outpatient visits to the same hospital within 30 days of discharge.

Patient demographic and clinical characteristics assessed at the index hospitalization included age, sex, self-reported race and ethnicity, primary insurance payer, and comorbidities. Hospital characteristics included urbanicity of population served (i.e., urban or rural), teaching status, U.S. census region (i.e., Midwest, Northeast, South, or West), and bed size (i.e., 1-299, 300-499, 500+ beds). Two separate fields for race and ethnicity were combined into one race/ethnicity field and categorized as Hispanic, white, black, or other/unknown.

Comorbidities, including hypertension, history of smoking, morbid obesity, and comorbidities included in the Charlson-Deyo Comorbidity Index (CCI)[16] were identified using ICD-10-CM discharge diagnosis codes (Supplement eTable 1) during index hospitalization or any prior visit to the same hospital within 180 days. Weighted CCI score was grouped into three categories: 0, 1-4, and 5+.

Statistical Analysis

Unadjusted in-hospital mortality was calculated as the proportion of hospitalized patients who died either during index hospitalization or within 30 days of discharge for each month. Adjusted odds of in-hospital mortality by month were assessed using multivariable logistic regression models with mortality as outcome and discharge month as predictor (the lowest point of mortality during study period, June 2020, was used as reference month). A priori covariates included patient characteristics (sex, age group, race/ethnicity, comorbidities) and hospital characteristics (urban/rural population served, teaching status, geographical region, size). 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 model. Lastly, covariate-adjusted in-hospital mortality was estimated using the recycled prediction method to calculate predicted margins.[17-20] Age- and sex-specific results were calculated using the same methods and covariates, except excluding age (for age-specific), or sex (for sex-specific).

All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, North Carolina), and the figures were generated using R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 528,620 adult patients with one or more COVID-19-related inpatient discharges from 876 hospitals between April 2020 and February 2021 were identified in the PHD-SR. Of these patients, 58,527 were excluded due to non-continuous hospital data submission, leaving 470,093 patients from 508 hospitals in the final study cohort. Excluded patients were more likely to be hospitalized in small (1-299 beds, 66.9% vs. 35.5%), non-teaching (67.9% vs. 51.7%), and rural hospitals (33.3% vs. 9.8%).

The average age of the study population was 63.9 years, 51.7% were male; 53.4% were white, 18% were black, and 18% were Hispanic (Table 1). Common comorbidities were hypertension (69.9%), diabetes mellitus (42.3%), chronic pulmonary disease (23.6%), and morbid obesity (21.5%) (Table 1, Supplement eFigure 1). Most patients (46.1%) were hospitalized in the South (reflective of hospitals included in PHD) and in urban hospitals (90.2%), but patients were evenly distributed across small, medium, and large hospitals.

In-Hospital Mortality Over Time

Trends in mortality were very similar before and after adjusting for significant patient and hospital characteristics (sex, age group, race/ethnicity, CCI score category, morbid obesity, hypertension, chronic kidney disease, diabetes mellitus, hospital urban/rural population served, teaching status, geographical region, bed size) (Figure 1a, Supplement eFigure 2 and eTable 2). From the initial high of 22.2% in April 2020, in-hospital mortality declined to 11.9% by June 2020 but showed no further decline through February 2021. Instead, in-hospital mortality showed two peaks between July 2020 and February 2021 – increasing to 14.0% in August 2020 ($p<.01$ vs. June 2020) and decreasing to 12.2% in October 2020 (12.2%, $p = .36$), and then increasing again to 14.1% in January 2021 ($p<.01$). Relative to June 2020, the month with the lowest mortality, the odds of in-hospital mortality were significantly higher (by about 20%) in August, September, and December of 2020, and January and February of 2021 (adjusted odds ratio [$_a$OR]: 1.23, 1.17, 1.21, 1.24, 1.21, respectively).

We also evaluated age-specific and sex-specific monthly trends in in-hospital mortality. In 85+ years old patients, adjusted mortality significantly increased from June to July 2020 (19.2% to 23.6%, $p<.01$) and decreased from December 2020 to February 2021 (from 24.4% to 21.0%, $p<.01$) (Figure 1b, Supplement eTable 3). The adjusted in-hospital mortality in the 75-84 years old group was stable between November 2020 and February 2021 (between 20.1-21.1%). Between November 2020 and February 2021, increase in in-hospital mortality was observed in both 55-64 and 65-74 years old groups (from 9.3% to 12.0% and 15.1% to 17.7%, respectively, all $p<.05$). Age-specific trends showed

that for all age groups, the lowest mortality was seen in June or July 2020, without additional improvement through February of 2021. Sex-specific trends (Figure 1c, Supplement eTable 4) showed that for both men and women, in-hospital mortality was higher in August and September 2020, and again in November 2020 through February 2021 than in June 2020.

Discussion

Using a national database, this study provides covariate-adjusted monthly trends in in-hospital mortality of COVID-19 inpatients from April 2020 through February 2021. Like prior reports,[2,3] our study demonstrated that overall in-hospital mortality decreased approximately by half from 22.2% to 11.9% between April and June of 2020. We extended the observation period and showed that from July 2020 through February 2021, there was no further decline, and instead, adjusted in-hospital mortality peaked twice and was significantly higher in all months except July and October 2020 compared to June 2020. Our results are congruent with but extend the analytics posted by the CDC COVID tracker using the same database by including 30-day follow-up, requiring continuous data submission by hospitals, and adjusting for differences in important hospital and patient characteristics across time.

The explanation for persistently high in-hospital mortality among COVID-19 inpatients is not clear. However, the peaks may be due at least in part to overcrowding in hospitals when cases surge. Kadri et al.[5] found that between March and August 2020, surges in hospital COVID-19 caseload possibly eroded benefits gained from better treatments. Our study supports these findings by showing that both the total number of deaths and adjusted in-hospital mortality peaked again between December 2020 and February 2021, when cases were surging.

These results are sobering, showing that despite more time and experience in treating COVID-19, there has been no further decline in mortality among inpatients. The current study also adds to the literature by showing the differences in adjusted in-hospital mortality trend in different age groups and by sex, especially between November 2020 and February 2021. Continuous monitoring of COVID-19 mortality and exploration of effective ways to reduce mortality are warranted.

NOTES

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Conflict of Interest Disclosures

All authors worked on the study as full-time employees of Premier Inc. No other conflict of interest exists. ZC, NAG and JAG report owning stock in Premier Inc.

References

1. JohnsHopkinsUniversity. COVID-19 Dashboard by the Center for Systems Science and Engineering at Johns Hopkins University. https://coronavirus.jhu.edu/map.html. Accessed Aug 20, 2021.
2. Asch DA, Sheils NE, Islam MN, et al. Variation in US Hospital Mortality Rates for Patients Admitted With COVID-19 During the First 6 Months of the Pandemic. *JAMA Intern Med.* 2020.
3. Horwitz LI, Jones SA, Cerfolio RJ, et al. Trends in COVID-19 Risk-Adjusted Mortality Rates. *J Hosp Med.* 2020.
4. Madahar P, Wunsch H, Jha P, Slutsky AS, Brodie D. Trends in COVID-19-related in-hospital mortality: lessons learned from nationwide samples. *Lancet Respir Med.* 2021.
5. 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.
6. Moon R, Rosenthal, N., Brown, H. Treatment journey of COVID-19 patients in hospital settings. ISPOR 2021 Annual International Meeting; May19, 2021, 2021; Virtual.
7. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ.* 2020;369:m1966.
8. Team CC-R. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 - United States, February 12-March 28, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(13):382-386.
9. 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(12):e2029058.
10. Bravata DM, Perkins AJ, Myers LJ, et al. Association of Intensive Care Unit Patient Load and Demand With Mortality Rates in US Department of Veterans Affairs Hospitals During the COVID-19 Pandemic. *JAMA Netw Open.* 2021;4(1):e2034266.
11. Premier. Premier Healthcare Database (COVID-19): Data that informs and performs. https://offers.premierinc.com/WCFY20PASCOVIDWhitepaper_LandingPage.html. Published 2020. Accessed Aug 20, 2021.
12. Lavery AM, Preston LE, Ko JY, et al. Characteristics of Hospitalized COVID-19 Patients Discharged and Experiencing Same-Hospital Readmission - United States, March-August 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(45):1695-1699.
13. 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(10):355-361.
14. 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(9596):1453-1457.
15. CDC. 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. Published 2020. Accessed Mar 26, 2021.
16. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol.* 1992;45(6):613-619.
17. Li Z. MG. *Using "Recycled Predictions" for Computing Marginal Effects.* SAS Global Forum 20102010.

18. Basu A, Rathouz PJ. Estimating marginal and incremental effects on health outcomes using flexible link and variance function models. *Biostatistics.* 2005;6(1):93-109.
19. Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD, Ogden CL. Trends in Obesity Among Adults in the United States, 2005 to 2014. *JAMA.* 2016;315(21):2284-2291.
20. Romano SD, Blackstock AJ, Taylor EV, et al. Trends in Racial and Ethnic Disparities in COVID-19 Hospitalizations, by Region - United States, March-December 2020. *MMWR Morb Mortal Wkly Rep.* 2021;70(15):560-565.

Table 1. Baseline demographics of adult COVID-19 inpatients (total and deceased) discharged between April 2020 and February 2021

	Total **n = 470,093**	**Deceased** **n = 67,975**
Patient Characteristics		
Age Category, years, n (%)		
18-44	70719 (15.0%)	1981 (2.9%)
45-54	58449 (12.4%)	3987 (5.9%)
55-64	91667 (19.5%)	10535 (15.5%)
65-74	106170 (22.6%)	18500 (27.2%)
75-84	90159 (19.2%)	19682 (29.0%)
85+	52929 (11.3%)	13290 (19.6%)
Age, years, continuous		
Mean ± SD	63.9 ± 17.5	72.9 ± 13.1
Median (IQR)	66.0 (53.0, 77.0)	74.0 (65.0, 82.0)
Sex, n (%)		
Female	226306 (48.1%)	27611 (40.6%)
Male	243196 (51.7%)	40313 (59.3%)
Unknown	591 (0.1%)	51 (0.1%)
Race/Ethnicity*, n (%)		
White	250964 (53.4%)	37620 (55.3%)
Black	84447 (18.0%)	10845 (16.0%)
Hispanic	84474 (18.0%)	11418 (16.8%)
Other/Unknown	50208 (10.7%)	8092 (11.9%)
Payer, n (%)		
Medicaid	63381 (13.5%)	5630 (8.3%)
Medicare	254892 (54.2%)	49715 (73.1%)
Private Insurance	114220 (24.3%)	8791 (12.9%)
Other/Uninsured	37604 (8.0%)	3839 (5.6%)
Baseline Comorbidities, n (%)		
Morbid Obesity	101261 (21.5%)	14589 (21.5%)
Hypertension	328543 (69.9%)	56051 (82.5%)
History of Smoking	39382 (8.4%)	4745 (7.0%)
Myocardial Infarction	47923 (10.2%)	13009 (19.1%)
Congestive Heart Failure	84334 (17.9%)	20303 (29.9%)
Peripheral Vascular Disease	21286 (4.5%)	4841 (7.1%)
Cerebrovascular Disease	21232 (4.5%)	5195 (7.6%)
Dementia	58646 (12.5%)	13678 (20.1%)
Chronic Pulmonary Disease	110893 (23.6%)	19311 (28.4%)
Rheumatic Disease	11492 (2.4%)	2083 (3.1%)
Peptic Ulcer Disease	5486 (1.2%)	1153 (1.7%)
Diabetes Mellitus	198763 (42.3%)	35287 (51.9%)
Hemiplegia or Paraplegia	6425 (1.4%)	1316 (1.9%)
Chronic Kidney Disease	85718 (18.2%)	20898 (30.7%)
Mild Liver Disease	5201 (1.1%)	1123 (1.7%)
Moderate or Severe Liver Disease	5326 (1.1%)	1708 (2.5%)
Any Malignancy	23632 (5.0%)	5315 (7.8%)

Metastatic Solid Tumor	6174 (1.3%)	1456 (2.1%)
HIV Disease	1400 (0.3%)	194 (0.3%)
Charlson Comorbidity Index Category, n (%)		
0	132574 (28.2%)	8043 (11.8%)
1-4	274253 (58.3%)	43064 (63.4%)
5+	63266 (13.5%)	16868 (24.8%)
Hospital Characteristics		
Hospital Size, n (%)		
1-299 beds	166829 (35.5%)	22429 (33.0%)
300-499 beds	149490 (31.8%)	22878 (33.7%)
500+ beds	153030 (32.6%)	22545 (33.2%)
Other/Unknown	744 (0.2%)	123 (0.2%)
Teaching Status, n (%)		
Non-Teaching Hospital	242993 (51.7%)	33078 (48.7%)
Teaching Hospital	227100 (48.3%)	34897 (51.3%)
Urbanicity of Population Served, n (%)		
Rural	46021 (9.8%)	6591 (9.7%)
Urban	424072 (90.2%)	61384 (90.3%)
Geographic Location, n (%)		
Midwest	97588 (20.8%)	13196 (19.4%)
Northeast	88912 (18.9%)	15085 (22.2%)
South	216616 (46.1%)	29476 (43.4%)
West	66977 (14.2%)	10218 (15.0%)

* 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. (i.e., 'white' is 'white with unknown or non-Hispanic ethnicity)

Figure Legend

Figure 1. Monthly adjusted and unadjusted trends of in-hospital mortality during index hospitalization and 30 days post discharge overall, by age groups, and by sex among hospitalized COVID-19 patients

a. Overall

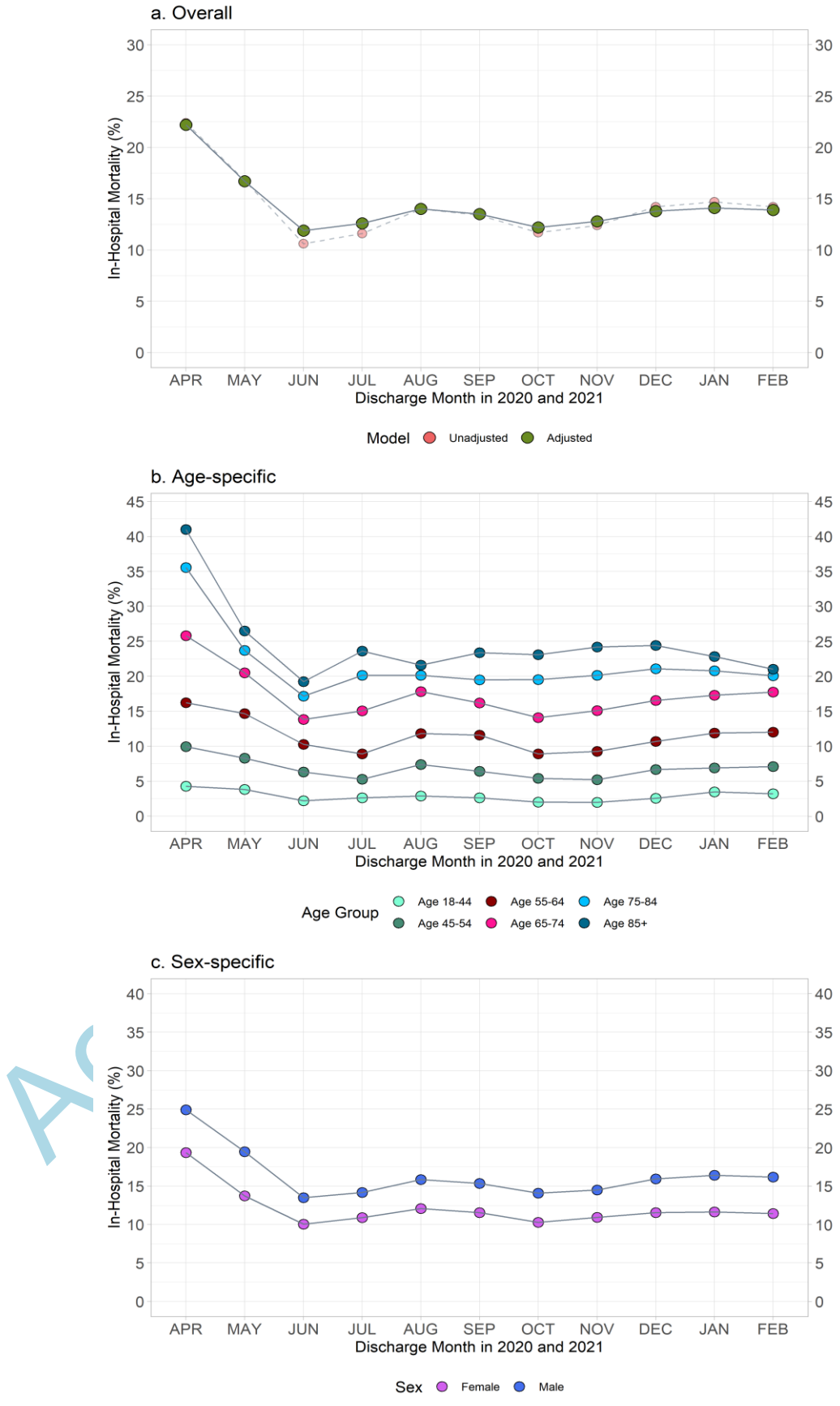
b. Age-specific

c. Sex-specific

footnote:
*Adjusted for month, sex, age group, race/ethnicity, Charlson Comorbidity Index score category, morbid obesity, hypertension, chronic kidney disease, diabetes mellitus, hospital size, hospital teaching status, hospital region, and urbanicity of population served

* Age and sex were not included in the model for age-specific and sex-specific results, respectively.

Figure 1


a. Overall
In-Hospital Mortality (%)
0
5
10
15
20
25
30
APR
MAY
JUN
JUL
AUG
SEP
OCT
NOV
DEC
JAN
FEB
Discharge Month in 2020 and 2021
Model
Unadjusted
Adjusted
b. Age-specific
In-Hospital Mortality (%)
0
5
10
15
20
25
30
35
40
45
APR
MAY
JUN
JUL
AUG
SEP
OCT
NOV
DEC
JAN
FEB
Discharge Month in 2020 and 2021
Age Group
Age 18-44
Age 45-54
Age 55-64
Age 65-74
Age 75-84
Age 85+
c. Sex-specific
In-Hospital Mortality (%)
0
5
10
15
20
25
30
35
40
APR
MAY
JUN
JUL
AUG
SEP
OCT
NOV
DEC
JAN
FEB
Discharge Month in 2020 and 2021
Sex
Female
Male