Factors Associated with Readmission in the US Following Hospitalization with COVID-19

Elizabeth C. Verna, MD, Columbia University Irving Medical Center, New York, NY, USA

Charles Landis, MD, University of Washington, Seattle, WA, USA

Robert S. Brown, Jr, MD, Weill Cornell, New York, NY, USA

Andrea R. Mospan, PhD, Target RWE Health Evidence Solutions, Durham, NC, USA

Julie M. Crawford, MD, Target RWE Health Evidence Solutions, Durham, NC, USA

Janet S. Hildebrand, MPH, Target RWE Health Evidence Solutions, Durham, NC, USA

Heather L. Morris, PhD, Target RWE Health Evidence Solutions, Durham, NC, USA

Breda Munoz, PhD, Target RWE Health Evidence Solutions, Durham, NC, USA

Michael W. Fried, MD, Target RWE Health Evidence Solutions, Durham, NC, USA

K. Rajender Reddy, MD, University of Pennsylvania, Philadelphia, PA, USA

Elizabeth C. Verna, MD [Corresponding Author]

Associate Professor of Medicine

Director of Clinical Research, Transplant Clinical Research Center

Center for Liver Disease and Transplantation

Columbia University Vagelos College of Physicians and Surgeons

Columbia University Irving Medical Center

622 West 168th St

PH 14-105

New York, NY 10032, USA

phone: 212-305-0662

email: ev77@cumc.columbia.edu

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Julie M. Crawford, MD [Alternate Corresponding Author]

Senior Director of Scientific & Medical Affairs

Target RWE Health Evidence Solutions

5001 S Miami Blvd, Ste 100

Durham, NC 27703, USA

phone: 303-905-6896

email: jcrawford@targetrwe.com

Article Summary: This is a retrospective cohort study assessing the rate and risk factors associated with COVID-19 related readmission and inpatient mortality in the United States.

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Abstract

Background: Patients hospitalized for COVID-19 may experience complications following hospitalization and require readmission. This analysis estimates the rate and risk factors associated with COVID-19-related readmission and inpatient mortality.

Methods: This is a retrospective cohort study utilizing deidentified chargemaster data from 297 hospitals across 40 US states on patients hospitalized with COVID-19 February 15-June 09, 2020. Demographics, comorbidities, acute conditions, and clinical characteristics of first hospitalization are summarized. Mulitvariable logistic regression was used to measure risk factor associations with 30-day readmission and in-hospital mortality.

Results: Among 29,659 patients, 1,070 (3.6%) were readmitted. Readmitted patients were more likely to have diabetes, hypertension, cardiovascular disease (CVD), chronic kidney disease (CKD) vs those not readmitted ($p<0.0001$) and to present on first admission with acute kidney injury (15.6% vs. 9.2%), congestive heart failure (6.4% vs. 2.4%), and cardiomyopathy (2.1% vs. 0.8%) ($p<0.0001$). Higher odds of readmission were observed in patients age >60 vs. 18-40 (odds ratio [OR]=1.92, 95% confidence interval [CI]=1.48, 2.50), and admitted in the Northeast vs. West (OR=1.43, 95% CI=1.14, 1.79) or South (OR=1.28, 95% CI=1.11, 1.49). Comorbidities including diabetes (OR=1.34, 95% CI=1.12, 1.60), CVD (OR=1.46, 95% CI=1.23, 1.72), CKD stage 1-5 (OR=1.51, 95% CI=1.25,1.81) and stage 5 (OR=2.27, 95% CI=1.81, 2.86) were associated with higher odds of readmission. 12.3% of readmitted patients died during second hospitalization.

Conclusions: Among this large US population of patients hospitalized with COVID-19, readmission was associated with certain comorbidities and acute conditions during first hospitalization. These findings may inform strategies to mitigate risks of readmission due to COVID-19 complications.

Keywords: COVID-19, Real World Evidence, Readmission

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Introduction

The COVID-19 pandemic has led to large numbers of hospitalizations and deaths throughout the world. A total of 124,006 laboratory-confirmed COVID-19-associated hospitalizations were reported to the CDC through the COVID-19-Associated Hospitalization Surveillance Network March 1, 2020-January 16, 2021,[1] while the overall cumulative COVID-19-associated hospitalization rate was 380.3 hospitalizations per 100,000 population. Inpatient mortality rates throughout the world have varied significantly, though data from the United States have revealed that over 20% of patients did not survive hospital admission in some large cohorts. Several demographic and clinical risk factors for both hospitalization and inpatient mortality have been identified, including advanced age, race, and comorbid conditions such as hypertension, diabetes, and chronic end organ disease.[2-4]

It is likely that survival of the initial hospitalization fails to capture the true morbidity of severe forms of COVID-19. A significant proportion of patients are hospitalized for prolonged periods with numerous end organ complications of the virus itself or complications of critical illness. Many patients who survive are discharged to hospice or skilled nursing facilities with variable degrees of debilitation. In addition, the long-term consequences of the COVID-19 syndrome remain largely undescribed, but may be significant.[5]

Hospital readmission has emerged as an important quality indicator in health care delivery.[6, 7] Patients admitted for COVID-19 may have an increased risk of readmission given that they often experience one or more of the risk factors associated with readmission as documented in national datasets including: advanced age, medical comorbidities, socioeconomic factors, prolonged length of stay and skilled nursing facility residence.[8] Quantifying the rate of readmission for COVID-19 and identifying risk factors associated with readmission is crucial in providing accurate prognosis as well as appropriate therapies and treatments for preventing readmission-associated morbidity and mortality.[9-11] The aim of this study was to estimate the rate of readmission among patients

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discharged with confirmed COVID-19, and identify risk factors for readmission to target for intervention.

Methods

Data Acquisition and Study Population

Data for these analyses were acquired from the hospital chargemaster, a comprehensive electronic claims database of all billable products, procedures, and services incurred during hospitalization.[4] As described previously, deidentified hospital chargemaster data consist of coding recorded by experts in accordance with the criteria established by Centers for Medicare and Medicaid Services.[12] based upon review of each patient's hospital chart at or near discharge. These data were iteratively analyzed by a multidisciplinary team including a coding specialist, physicians, data scientists, an epidemiologist, scientist, and statistician.[4][13] By incorporating the detailed information included in billing, procedure, and ICD-10 codes, as well as text searches, specific variables were created to allow for analysis of the conditions and journeys of patients hospitalized for COVID-19.

Patients with COVID-19 infection were identified using the U07.1 code to indicate COVID-19 confirmed by laboratory testing, or earlier codes prior to the availability of U07.1 (B97.2 or B34.2). A list of ICD-10 codes utilized to identify patients with COVID-19, comorbidities, oxygen support level, and discharge disposition, is provided in **Supplemental Table 1**.

Data from adult patients (age ≥18 years) hospitalized with COVID-19 infection in 297 hospitals across 40 states, admitted for the first time between February 15-June 9, 2020, were included. Patients were required to have a known clinical disposition from their first hospitalization, including vital status. Patients discharged to hospice or died during the first hospitalization were excluded. Because data were stripped of all identifiers prior to acquisition, this study was not subject

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to institutional review board oversight in accordance with regulation 45 CFR 46 for the ethical conduct of human subjects research.

Each institution used a common framework with consistent processing to compile data. A unique token was generated for each patient in order to ensure protection of Protected Health Information (PHI); this was compliant with the independent expert determination of compliance allowed for under 45 CFR Part 164.514(b). These tokens can be used to trace the data back to the original data sources and are part of the dataset used for this research. All parties assert that (a) the traceability of the data as a chain of custody from Target RWE to the individual institutions is maintained, and (b) that commercialization and licensing of said data for this use is permitted.[4][13]

Patient Characteristics

Patient demographics for analysis were: age (18-40, 41-60, >60), sex, insurance type, census region of hospital and type of hospital.

Comorbidities present on each admission and from hospital encounters within 12 months up to the date of admission were ascertained from ICD-10 codes and classified by expert opinion consistent with standard definitions commonly used in health services research.[14] All chronic and acute conditions were binary variables with a 'yes' value indicating that the condition was documented in the patient's claim records.

Factors related to disease severity and clinical care were assessed for the first hospital admission using billing codes, ICD-10 codes, and text searches as previously described.[4] Factors such as length of stay, ICU admission, level of oxygen support, presence of pneumonia and discharge disposition were assessed.

Outcomes

The primary and secondary endpoints were 30-day readmission after discharge from initial hospitalization for COVID-19 associated illness and death during the second hospitalization, respectively.

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Statistical Analysis

Patient and hospitalization characteristics corresponding to first hospitalization were examined according to readmission status. Bivariate associations were assessed using chi-square tests for categorical data (Fisher's Exact for sparse data) and Kruskal-Wallis test for continuous data. Multivariable logistic regression was used to estimate the adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the outcomes of interest in relation to age, sex, census region of hospital, insurance, comorbidities, length of stay, and complications developed during hospitalization.

To ensure that results were not biased toward selection of patients with shorter time to relapse or complications requiring readmission, all analyses were repeated excluding patients with <30 days follow-up after their initial discharge. All statistical tests were 2-sided with type 1 error (alpha)=0.05. SAS version 9.4 was used for all analyses. SAS JMP® 15.1.0 was used to produce forest plots.

Results

Clinical and Demographic Characteristics of Readmitted Patients:

A total of 30,054 patients were admitted between February, 15 and June 9, 2020 with COVID-19; 380 patients <18 years old were excluded from this analysis as were 15 adults with unknown sex (**Figure 1**). The final analytic cohort comprised 29,659 adult inpatients with confirmed COVID-19, of whom 1,070 (3.6%) were readmitted within 30 days of first hospitalization discharge (**Table 1**). Patients who were readmitted were significantly more likely to be older than age 60 years compared to those not readmitted (69.7% vs. 53.7%, respectively, p<0.0001), more likely to have Medicare or Medicaid-based insurance (67.5% vs. 45.6%), and more likely to be hospitalized in the Northeast region of the US (59.1% vs. 47.5%). Most patients were readmitted within 10 days of discharge following the first hospitalization (**Supplemental Figure 1)** with the Northeast reporting 271 (25.3%) and 441 (41.2%) of 1,070 readmissions within 5 and 10 days of discharge, respectively (**Supplemental Table 2**).

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Patients who were readmitted had significantly higher rates of baseline comorbidities including diabetes mellitus (39.2% vs. 29.1%, p<0.0001), hypertension (60.9% vs. 48.7%, p<0.0001), CVD (34.1% vs. 18.2%, p<0.0001), pulmonary disease (20.1% vs. 14.9%, p<0.0001) and CKD (stage 1 to 5) (30.2% vs. 14.9%, p<0.0001) (**Table 1**). Number of comorbidities was associated with higher risk of readmissions, where patients with 3 or 4 comorbidities had 20% higher odds of being readmitted compared to patients with none (OR=1.26, 95% CI=1.03, 1.55 and OR=1.99, 95% CI=1.68, 2.36, respectively) (data not shown).

Features of First COVID-19 Hospitalization and Treatment:

Among the 29,659 patients with an initial COVID-19 related hospitalization, the overall median length of initial hospitalization was 8 days. Most of the patients were discharged home (70.1%), while 23.8% were discharged to a long-term/skilled care facility; 5.1% transferred to another hospital. Overall, 12.1% of patients required intensive care unit (ICU) care, 1.8% high-flow oxygen within 24 hours and 3.7% mechanical ventilation or ECMO during hospitalization (**Table 2**).

Patients who were readmitted were more likely to have initially been discharged to a long-term/skilled care facility compared to patients who were not readmitted (30.7% vs. 23.5%, p<0.0001). However, patients who were readmitted had significantly shorter initial length of stay (median 7 days (range:2-54) vs. 8 days (range:2-107) days, p<0.0001), and were less likely to have required ICU level care (7.9% vs. 12.2%, p<0.0001), mechanical ventilation or ECMO at any time during the first hospitalization (4.8% vs. 8.9%, p<0.0001) (**Table 2**).

Acute conditions of COVID-19 experienced during initial hospitalization are summarized in **Tables 2 and 3**. Respiratory conditions were common with 78.5% of patients experiencing pneumonia during hospitalization, 16.5% acute respiratory failure and 1.7% ARDS. Patients who were readmitted were less likely than those who were not to have been diagnosed with pneumonia during their initial hospitalization (71.1% vs. 78.7% respectively) though the rates of acute respiratory failure (17.3% vs. 16.5%) and ARDS (1.2% vs. 1.7%) were similar between those who were and were not readmitted.

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Several extra-pulmonary manifestations of COVID-19 were more common during the first hospitalization among patients who were readmitted vs. not readmitted, including AKI (15.6% vs. 9.2%, p<0.0001), cardiomyopathy (2.1% vs. 0.8%, p<0.0001) and congestive heart failure (6.4% vs. 2.4%, p<0.0001). Disseminated intravascular coagulation (DIC) (0.3% vs. 0.1%, p=0.03) and venous thromboembolism (2.1% vs. 1.3%, p=0.03) were significantly more common in the first admission for those who were readmitted (**Table 3**).

Factors Associated with Readmission

Risk factors associated with readmission are displayed in **Figure 2**. In the multivariable model, age (>60 years, OR=1.92, 95% CI=1.48,2.50; 41-60 years, OR=1.31, 95% CI=1.01,1.70, compared to 18-40 years), length of stay in initial hospitalization (OR=0.96, 95% CI=0.95,0.97 per day), region of hospital (South, OR=0.78, 95% CI=0.67,0.90; West, OR=0.70, 95% CI=0.56,0.88; Midwest, OR=0.91, 95% CI=0.70,1.19, compared to Northeast), insurance (Medicaid, OR=1.94, 95% CI=1.54, 2.43; Medicare, OR=1.59, 95% CI=1.29,1.95, compared to commercial), history of CKD (stage 5, OR=2.27, 95% CI=1.81, 2.86; stage 1-5, OR=1.51, 95% CI=1.25,1.81, compared to no CKD), CVD (OR=1.46, 95% CI=1.23,1.72), hypertension (OR=0.80, 95% CI=0.68,0.94), diabetes (OR=1.34, 95% CI=1.12,1.6), smoking (OR=1.19, 95% CI=1.02,1.39), and respiratory illness during the initial hospitalization (OR=0.73, 95% CI=0.63,0.84) were significantly associated with risk of rehospitalization.

Characteristics and Outcomes of Readmission

The principal diagnosis at the time of readmission was COVID-19 in 461 (43.1%) patients. Among these patients, pneumonia (83.9%) and acute respiratory failure (49.2%) were the most common secondary diagnoses, followed by acute heart conditions or heart failure (31.2%), AKI (27.3%) and thrombosis (11.9%) (**Supplemental Table 3**). In addition, 230 (21.5%) were readmitted with a principal diagnosis of sepsis. Of these, 29.1% had a secondary diagnosis of severe sepsis with septic shock. The most common acute conditions present on admission or during the second

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hospitalization were acute respiratory failure (30.0%, n=321), AKI (21.4%, n=229), and sepsis (17.6%, n=188) (**Supplemental Table 4**).

At the end of follow up, 49.8% of readmitted patients were discharged to home, 29.6% to a long-term/skilled care facility, 12.3% died, 3.4% were discharged to hospice, 3.2% were transferred to another hospital, and 0.2% were still hospitalized (data not shown). Dispositions at the first and second hospitalizations are summarized in **Table 2** and **Supplemental Table 5**. Nearly 31% of patients who were readmitted were discharged to a long-term/skilled care facility following the first admission, and 19.1% of patients were discharged to a long-term/skilled care facility following both the first and second hospitalizations.

Factors Associated with Death in Second Hospitalization

Results from multivariable logistic regression analysis of death during readmission are displayed in **Figure 3**. In this model, factors significantly associated with death included age (OR=1.04, 95% CI=1.02,1.07), maximum level of oxygen support during readmission (mechanical ventilation, OR=19.15, 95% CI=8.24,44.50; high-flow oxygen, OR=3.00, 95% CI=1.10,8.22; vs. no oxygen), census region (South, OR=0.46, 95% CI=0.25, 0.84; West, OR=0.28, 95% CI=0.09,0.84; Midwest, OR=0.48, 95% CI=0.18,1.32, compared to Northeast), and the presence of sepsis/SIRS (OR=3.03, 95% CI=1.83,5.02) or AKI (OR=1.85, 95% CI=1.11,3.1) during readmission.

Sensitivity Analysis

A total of 6,819 patients were discharged <30 days prior to the study end date, including 92 who were readmitted. Sensitivity analyses excluding these patients did not alter results (data not shown).

Discussion

This study includes a broad U.S. representation of hospitals and a large-scale analysis of COVID-19 readmissions. The 30-day readmission rate with 29,659 patients hospitalized for COVID-19 was 3.6%, and the rate of readmission was highest within 10 days of discharge from first

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hospitalization. Readmitted patients were older, more likely to have Medicare/Medicaid-based insurance, and more often from the Northeast. The Northeast reported 271 readmissions within 5 days after discharge (25.3%), perhaps reflecting greater acuity of illness in the early period of hyperendemic transmission in the Northeast, and a lack of understanding of the natural history of COVID-19 infection.

Readmitted patients had significantly higher rates of baseline comorbidities, including diabetes, hypertension, cardiovascular disease, cerebrovascular disease, pulmonary disease, chronic kidney disease, smoking, liver disease, solid organ transplant, history of non-skin cancer malignancy, history of HIV/AIDS, and history of peripheral vascular disease. Of interest, higher rates of baseline hypertension and pulmonary disease have also been noted in smaller retrospective studies in New York City,[15] Rhode Island,[16] and Spain,[11] suggesting that patients with these conditions who are hospitalized for COVID-19 may need extra monitoring post-discharge.

Additionally, the proportions of patients with extra-pulmonary manifestations of COVID-19 during their first admission including AKI, cardiomyopathy, and congestive heart failure were significantly higher in readmitted patients, suggesting that for patients with respiratory stability that allows for initial discharge, other organ damage must also be carefully considered.

Compared to patients who were not readmitted, a greater proportion of readmitted patients had been discharged to a long-term/skilled-care facility after first hospitalization. The high rate of readmission in patients discharged to skilled-care facilities is consistent with findings from previous studies,[8, 17] suggesting that strategies to reduce readmissions in COVID-19 patients should include careful assessment of the level of care that can be provided in a long-term care facility. Furthermore, readmitted patients had a shorter average length of stay during first hospitalization than those who were not readmitted. This is similar to patterns in other acute care hospitalizations, such as for heart failure, where decreased length of initial hospital stay may increase readmission risk.[18] In addition to having decreased average length of stays, readmitted patients in this cohort were also less likely to have received ICU level of care, which may indicate the need for longer and more escalated care

strategies or more gradual de-escalation prior to discharge for hospitalized COVID-19 patients to prevent readmission.

The final discharge disposition of readmitted COVID-19 patients in this study was death or hospice in nearly 16% of cases, which is higher than mortality rates previously published in studies of readmission following hospitalizations for heart failure and major cancer surgery.[19, 20]

On multivariable analysis, conditions noted with readmission included CKD and cardiovascular disease. Notably, CKD has been shown to predict readmissions in patients with sepsis as well,[21] and stage 5 CKD very strongly predicted readmission in this study, suggesting the need for close post-discharge monitoring of patients with this and other predictors of readmission. Patients who are insured by Medicare and Medicaid also had higher odds of readmission compared to those with commercial insurance, which may be an indication of illness, age, and/or socioeconomic status. Older age was itself found to be a risk factor for readmission. Additionally, the presence of 3 or more comorbidities was predictive of readmission, which supports the use of comorbid disease burden in risk assessment models for all-cause readmissions.[22]

Overall in-hospital mortality on readmission was 12.3%. In adjusted analysis, significant predictors of inpatient mortality were oxygen therapy, sepsis and acute kidney injury. Sepsis and AKI have been notorious causes for readmission and mortality.[23, 24] This is not surprising as several immune dysfunction mechanisms may be predisposing to sepsis in debilitating conditions of cirrhosis, AKI, and heart failure, and those infected with SaRS-COv2.[25]

A recent report from CDC found a higher rate of readmission than was found in the current study (~9% vs. 3.6%), possibly due to the longer window considered for readmissions of 60 days vs. 30 days, respectively, although most patients were readmitted within 10 days of discharge from their first hospitalization. This result is consistent with a study in Veterans Affairs showing patients were more likely to be readmitted within 10 days.[10] Nevertheless, both studies demonstrated that comorbid medical conditions and older age were associated with a higher likelihood of readmission

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and provide insights that may help mitigate risks for readmission. Several smaller studies have also evaluated rates of readmission in cohorts ranging from 19-328 patients.[16, 26][27]

The identification of predictors and patterns of readmission will allow for the development of targeted interventions for hospitalized COVID-19 patients. For example, in Medicaid patients with one or more chronic conditions, post-discharge engagement was associated with decreased likelihood of readmissions.[28] Given the need for social distancing measures due to the COVID-19 pandemic, telehealth platforms may be useful for post-discharge monitoring of high-risk patients. A 2017 study evaluating a telehealth protocol to prevent readmissions among high-risk congestive heart failure patients reported excellent patient adherence, indicating that discharged patients may benefit from this type of intervention.[29]

The COVID-19 chargemaster data provide a substantial geographic and longitudinal distribution of inpatient data with a large sample size that allows for retrospective, longitudinal analysis of hospitalized patients, including an assessment of comorbidities, complications, and outcomes. A potential limitation of this study is that these admissions largely occurred in the early phase of the pandemic in the US, when there may have been regional differences in outcomes when hyperendemic transmission in the Northeast overwhelmed some hospital systems. Although used extensively for database research, use of ICD-10 codes also has the potential for misclassification and underrepresentation of comorbid conditions, therapies, and procedures. Data such as race, vital signs and laboratory test results were not available within the chargemaster data set.

In conclusion, in this large national cohort of patients who survived an initial admission for complications of COVID-19, readmissions demonstrate the presence of significant ongoing morbidity and mortality that may occur following initial hospital discharge and identified populations in whom additional targeted interventions are warranted to improve post-hospitalization outcomes.

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NOTES

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References:

1. https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html#hospitalizations.
2. Price-Haywood, E.G., et al., *Hospitalization and Mortality among Black Patients and White Patients with Covid-19.* N Engl J Med, 2020. **382**(26): p. 2534-2543.
3. Richardson, S., et al., *Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area.* JAMA, 2020.
4. Fried, M.W., et al., *Patient Characteristics and Outcomes of 11,721 Patients with COVID19 Hospitalized Across the United States.* Clin Infect Dis, 2020.
5. Marshall, M., *The lasting misery of coronavirus long-haulers.* Nature, 2020. **585**(7825): p. 339-341.
6. Fischer, C., et al., *Is the readmission rate a valid quality indicator? A review of the evidence.* PLoS One, 2014. **9**(11): p. e112282.
7. Fung, C.H., et al., *Systematic review: the evidence that publishing patient care performance data improves quality of care.* Ann Intern Med, 2008. **148**(2): p. 111-23.
8. Gohil, S.K., et al., *Impact of Hospital Population Case-Mix, Including Poverty, on Hospital All-Cause and Infection-Related 30-Day Readmission Rates.* Clin Infect Dis, 2015. **61**(8): p. 1235-43.
9. Anesi, G.L., et al., *Characteristics, Outcomes, and Trends of Patients With COVID-19-Related Critical Illness at a Learning Health System in the United States.* Ann Intern Med, 2021.
10. Donnelly, J.P., et al., *Readmission and Death After Initial Hospital Discharge Among Patients With COVID-19 in a Large Multihospital System.* JAMA, 2021. **325**(3): p. 304-306.
11. Parra, L.M., et al., *Hospital Readmissions of Discharged Patients with COVID-19.* Int J Gen Med, 2020. **13**: p. 1359-1366.
12. CMS/NCHS, *ICD-10-CM Official Guidelines for Coding and Reporting.* (FY 2020 (October 1, 2019 - September 30, 2020)): p. 1-121.
13. Fried, M.W., et al., *Reply to authors.* Clin Infect Dis, 2020.
14. Schneeweiss, S. and J. Avorn, *A review of uses of health care utilization databases for epidemiologic research on therapeutics.* J Clin Epidemiol, 2005. **58**(4): p. 323-37.
15. Somani, S.S., et al., *Characterization of Patients Who Return to Hospital Following Discharge from Hospitalization for COVID-19.* J Gen Intern Med, 2020. **35**(10): p. 2838-2844.
16. Atalla, E., et al., *Readmissions among patients with COVID-19.* Int J Clin Pract, 2020: p. e13700.
17. Bueno, H., et al., *Trends in length of stay and short-term outcomes among Medicare patients hospitalized for heart failure, 1993-2006.* JAMA, 2010. **303**(21): p. 2141-7.
18. Carey, K. and M.Y. Lin, *Hospital length of stay and readmission: an early investigation.* Med Care Res Rev, 2014. **71**(1): p. 99-111.
19. Lahewala, S., et al., *Heart failure: Same-hospital vs. different-hospital readmission outcomes.* Int J Cardiol, 2019. **278**: p. 186-191.
20. Zafar, S.N., et al., *Comparison of Rates and Outcomes of Readmission to Index vs Nonindex Hospitals After Major Cancer Surgery.* JAMA Surg, 2018. **153**(8): p. 719-727.

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21. Horvath, J.S., et al., *An analysis of errors found in renal vein sampling for plasma renin activity.* Kidney Int, 1977. **11**(2): p. 136-8.
22. Robinson, R. and T. Hudali, *The HOSPITAL score and LACE index as predictors of 30 day readmission in a retrospective study at a university-affiliated community hospital.* PeerJ, 2017. **5**: p. e3137.
23. Scaglione, S.J., et al., *Early Hospital Readmissions and Mortality in Patients With Decompensated Cirrhosis Enrolled in a Large National Health Insurance Administrative Database.* J Clin Gastroenterol, 2017. **51**(9): p. 839-844.
24. Kumar, N., et al., *Thirty-Day Readmissions After Hospitalization for Hypertensive Emergency.* Hypertension, 2019. **73**(1): p. 60-67.
25. Lavery AM, P.L., 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;69:1695–1699. DOI: http://dx.doi.org/10.15585/mmwr.mm6945e2.
26. Somani, S., et al., *Characterization of Patients Who Return to Hospital Following Discharge from Hospitalization For COVID-19.* medRxiv, 2020.
27. Jeon, W.H., et al., *Analysis of Risk Factors on Readmission Cases of COVID-19 in the Republic of Korea: Using Nationwide Health Claims Data.* Int J Environ Res Public Health, 2020. **17**(16).
28. Gao, W., et al., *Postdischarge engagement decreased hospital readmissions in Medicaid populations.* Am J Manag Care, 2018. **24**(7): p. e200-e206.
29. Rosen, D., J.D. McCall, and B.A. Primack, *Telehealth Protocol to Prevent Readmission Among High-Risk Patients With Congestive Heart Failure.* Am J Med, 2017. **130**(11): p. 1326-1330.

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Table 1. Characteristics of hospitalized COVID-19 patients by re-admission type

Characteristics	Hospital readmission		Total (N=29659)	P-Value[a]
	Yes (N=1070)	No (N=28589)		
Demographics				
Age group, n (%)				<0.0001
18-40	85 (7.9)	3940 (13.8)	4025 (13.6)	
41-60	239 (22.3)	9287 (32.5)	9526 (32.1)	
>60	746 (69.7)	15362 (53.7)	16108 (54.3)	
Sex, n (%)				0.17
Female	508 (47.5)	14186 (49.6)	14694 (49.5)	
Male	562 (52.5)	14403 (50.4)	14965 (50.5)	
Insurance,[b] n (%)				<0.0001
Commercial	149 (13.9)	6385 (22.3)	6534 (22.0)	
Medicaid	171 (16.0)	3632 (12.7)	3803 (12.8)	
Medicare	551 (51.5)	9418 (32.9)	9969 (33.6)	
Other	199 (18.6)	9154 (32.0)	9353 (31.5)	
Hospital Type,[c] n (%)				<0.0001
Major Teaching	509 (47.6)	11221 (39.2)	11730 (39.5)	
Minor Teaching	204 (19.1)	6078 (21.3)	6282 (21.2)	
Non-Teaching	357 (33.4)	11290 (39.5)	11647 (39.3)	
Census Region, n (%)				<0.0001
Midwest	65 (6.1)	1587 (5.6)	1652 (5.6)	
Northeast	632 (59.1)	13594 (47.5)	14226 (48.0)	
South	277 (25.9)	9564 (33.5)	9841 (33.2)	
West	96 (9.0)	3844 (13.4)	3940 (13.3)	
Comorbid Disease				
History of diabetes mellitus, n (%)	419 (39.2)	8313 (29.1)	8732 (29.4)	<0.0001
History of obesity, n (%)	184 (17.2)	5326 (18.6)	5510 (18.6)	0.24
History of HTN, n (%)	652 (60.9)	13934 (48.7)	14586 (49.2)	<0.0001
History of cardiovascular disease, n (%)	365 (34.1)	5212 (18.2)	5577 (18.8)	<0.0001
History of cerebrovascular disease, n (%)	143 (13.4)	2227 (7.8)	2370 (8.0)	<0.0001
History of pulmonary disease, n (%)	215 (20.1)	4263 (14.9)	4478 (15.1)	<0.0001
History of chronic kidney disease,[d] n (%)	323 (30.2)	4262 (14.9)	4585 (15.5)	<0.0001
History of chronic kidney disease (Stage 5), n (%)	114 (10.7)	1222 (4.3)	1336 (4.5)	<0.0001
History of smoking, n (%)	284 (26.5)	5101 (17.8)	5385 (18.2)	<0.0001
History of liver disease, n (%)	34 (3.2)	299 (1.0)	333 (1.1)	<0.0001
History of solid organ transplant, n (%)	24 (2.2)	207 (0.7)	231 (0.8)	<0.0001
History of BMT/SCT, n (%)	2 (0.2)	30 (0.1)	32 (0.1)	0.42
History of non-skin cancer malignancy, n (%)	118 (11.0)	1825 (6.4)	1943 (6.6)	<0.0001
History of peripheral vascular disease, n (%)	53 (5.0)	752 (2.6)	805 (2.7)	<0.0001

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Characteristics	Hospital readmission		Total (N=29659)	P-Value[a]
	Yes (N=1070)	No (N=28589)		
History of HIV/AIDS, n (%)	18 (1.7)	293 (1.0)	311 (1.0)	0.04
History of autoimmune (RA/SLE), n (%)	21 (2.0)	437 (1.5)	458 (1.5)	0.26
Inflammatory bowel disease, n (%)	5 (0.5)	113 (0.4)	118 (0.4)	0.71
Current pregnancy, n (%)	18 (1.7)	668 (2.3)	686 (2.3)	0.16

Hypertension (HTN), bone marrow transplant/ stem cell transplant (BMT/SCT), human immunodeficiency virus/ acquired immunodeficiency syndrome (HIV/AIDS), rheumatoid arthritis/ systemic lupus erythematosus (RA/SLE)

[a]Chi-square test p-values reported

[b]Other includes Other insurance and Unknown

[c]Major teaching includes hospitals that are members of the Council of Teaching Hospitals; and minor includes those that are not members but that have accredited residency programs.

[d]Includes Chronic Kidney disease stages 1 to 5

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Table 2. Characteristics of the first hospitalization for patients with COVID-19 by readmission type

Characteristics	Readmitted to a Hospital		Total	P-Value[a]
	Yes (N=1,070)	No (N=28,589)	(N=29,659)	
Discharge disposition,[b] n (%)				<0.0001
AMA	19 (1.8)	291 (1·0)	310 (1·0)	
Home	672 (62.8)	20111 (70·3)	20783 (70·1)	
Hospital transfer[b]	50 (4.7)	1465 (5·1)	1515 (5·1)	
Long-term or skilled care facility	329 (30.7)	6722 (23·5)	7051 (23·8)	
Total duration of hospital stay (days)				
Median (n)	7·0 (1070)	8·0 (28589)	8.0 (29659)	<0.0001
Q1 - Q3 (IQR)	5.0 - 11.0 (6.0)	5.0 - 13.0 (8.0)	5.0 - 13.0 (8.0)	
Min - Max	2·0 - 54·0	2·0 - 107·0	2·0 - 107·0	
Mean (SD)	8·9 (6·4)	10·5 (8·5)	··	<0.0001
ICU level of care, n (%)	84 (7·9)	3497 (12·2)	3581 (12·1)	<0.0001
Highest level of O2 supplied within 24H of admission,[c] n (%)				0.004
No oxygen	476 (44·5)	11397 (39·9)	11873 (40·0)	
Low Flow	546 (51·0)	15708 (54·9)	16254 (54·8)	
High Flow	24 (2·2)	519 (1·8)	543 (1·8)	
Mechanical ventilation/ECMO	24 (2·2)	965 (3·4)	989 (3·3)	
Highest level of O2 ever,[c,d,e] n (%)				<0.0001
No oxygen	279 (26.·1)	5452 (19·1)	5731 (19·3)	
Low Flow	700 (65.·4)	19517 (68·3)	20217 (68·2)	
High Flow	40 (3·7)	1066 (3·7)	1106 (3·7)	
Mechanical ventilation/ECMO	51 (4·8)	2554 (8·9)	2605 (8·8)	
Time from date of admission to first day mechanical ventilation (days)				
Median (n)	1·0 (51)	2·0 (2554)	2·0 (2605)	0.14
Q1 - Q3 (IQR)	1.0 - 4.0 (3.0)	1.0 - 4.0 (3.0)	1.0 - 4.0 (3.0)	
Min - Max	1·0 - 13·0	1·0 - 84·0	1·0 - 84·0	
Duration on ICU (days)				
Median (n)	4·0 (84)	6·0 (3497)	6·0 (3581)	<0.0001
Q1 - Q3 (IQR)	2.0 - 8.5 (6.5)	3.0 - 13.0 (10.0)	3.0 - 13.0 (10.0)	
Min - Max	1·0 - 35·0	1·0 - 69·0	1·0 - 69·0	
Presence of Pneumonia within 24H of admission, n (%)	549 (51·3)	15581 (54·5)	16130 (54·4)	0.04
Presence of Pneumonia at any time, n (%)	761 (71·1)	22512 (78·7)	23273 (78·5)	<0.0001

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Characteristics	Readmitted to a Hospital		Total (N=29,659)	P-Value[a]
	Yes (N=1,070)	No (N=28,589)		

Against medical advice (AMA); interquartile range (IQR)

[a]Chi-square test and Kruskal-Wallis test p-values reported for categorical and continuous variables, respectively

T-test for equality of means reported

[b]Includes patients discharged to a federal hospital, designated Disaster Alternative Care Site, federal health care facility with a planned acute care hospital inpatient readmission, other short term general hospital, designated cancer center, children's hospital, another type of health care institution not defined elsewhere in the code list, hospital-based Medicare approved swing bed, Critical Access Hospital (CAH). Of the 50 readmitted patients, 1 was discharged to a designated cancer center or children's hospital, 3 to a federal hospital, 7 to a designated Disaster Alternative Care Site, 32 to another short term general hospital, and 7 to another type of health care institution not defined elsewhere in the code list.

[c]Includes 12 ECMO patients in Mechanical ventilation

[d]High flow includes high flow, CPAP, BIPAP and non-invasive methods

[e]Includes 125 ECMO patients in Mechanical ventilation

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Table 3. Acute conditions for patients hospitalized with COVID-19 present on admission or during first hospitalization by readmission type

Characteristics	Readmitted to a hospital		Total (N=29659)	P-Value[a]
	Yes (N=1070)	No (N=28589)		
AKI, n (%)	167 (15.6)	2638 (9.2)	2805 (9.5)	<0.0001
ARDS, n (%)	13 (1.2)	481 (1.7)	494 (1.7)	0.24
Acute MI, n (%)	14 (1.3)	250 (0.9)	264 (0.9)	0.14
Acute respiratory failure, n (%)	185 (17.3)	4703 (16.5)	4888 (16.5)	0.47
Cardiomopathy,[b] n (%)	23 (2.1)	216 (0.8)	239 (0.8)	<0.0001
Congestive heart failure, n (%)	69 (6.4)	686 (2.4)	755 (2.5)	<0.0001
DIC, n (%)	3 (0.3)	23 (0.1)	26 (0.1)	0.03
Meningitis encephalitis, n (%)	0 (0.0)	12 (0.0)	12 (0.0)	..
Myocarditis, n (%)	4 (0.4)	52 (0.2)	56 (0.2)	0.16
SIRS, n (%)	33 (3.1)	876 (3.1)	909 (3.1)	0.97
Sepsis, n (%)	122 (11.4)	2773 (9.7)	2895 (9.8)	0.07
Venous thromboembolism, n (%)	22 (2.1)	364 (1.3)	386 (1.3)	0.03
Vasculitis, n (%)	0 (0.0)	8 (0.0)	8 (0.0)	..

AKI (acute kidney injury), ARDS (acute respiratory distress syndrome), acute MI (acute myocardial infarction), DIC (disseminated intravascular coagulation), SIRS (systemic inflammatory response syndrome)

[a]Chi-square test p-values reported

[b]Cardiomyopathy could be acute or chronic

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FIGURE LEGENDS:

Figure 1: Clinical and Demographic Characteristics of Readmitted Patients

Figure 2: Risk factors associated with readmission

Figure 3: Results from multivariable logistic regression analysis of death during readmission

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Figure 1

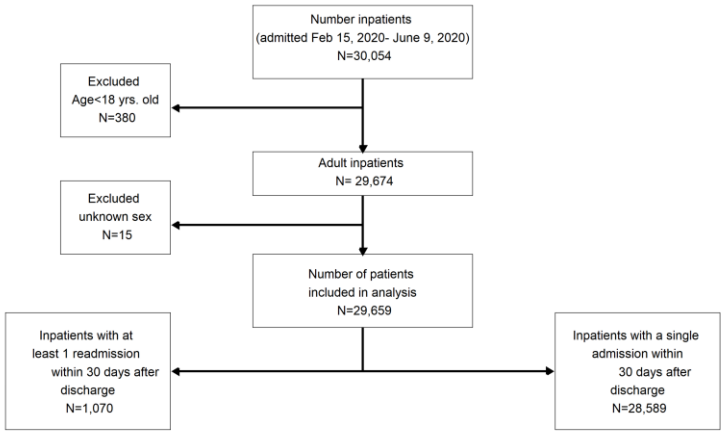

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Figure 2

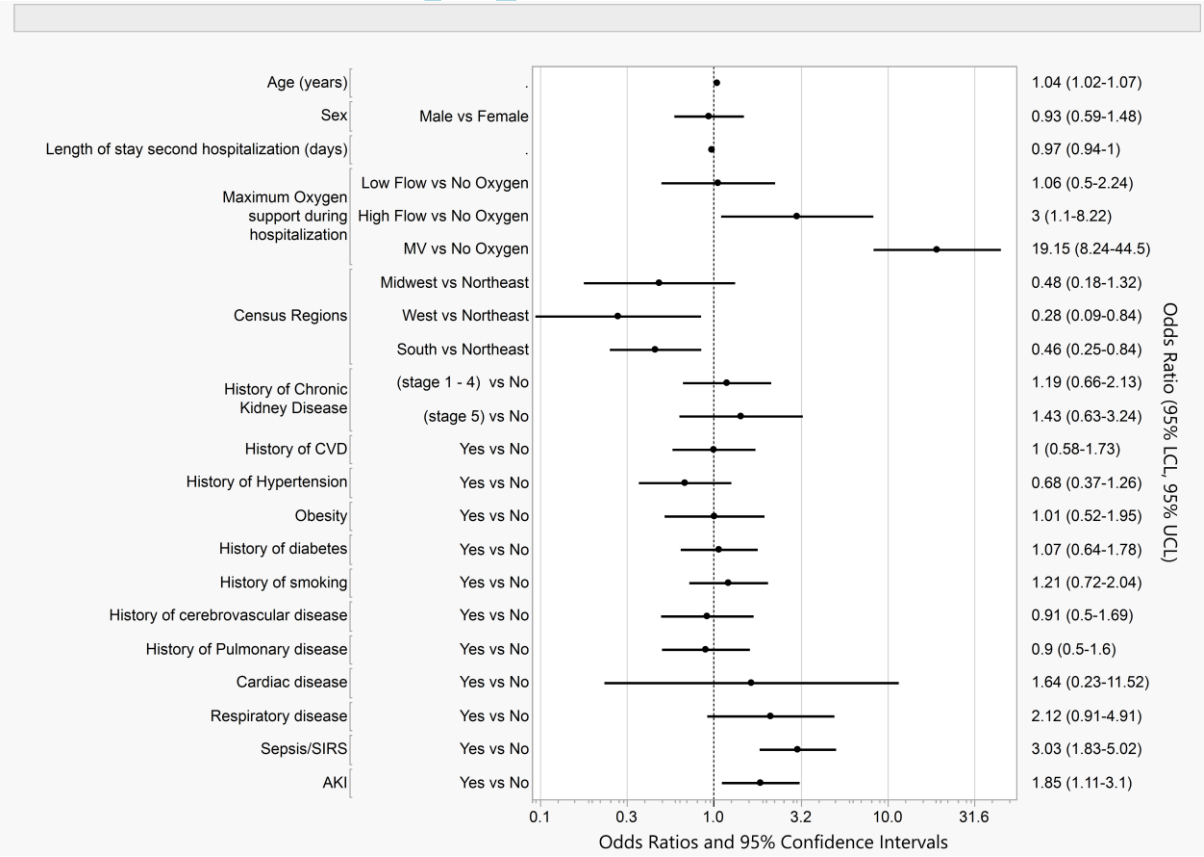
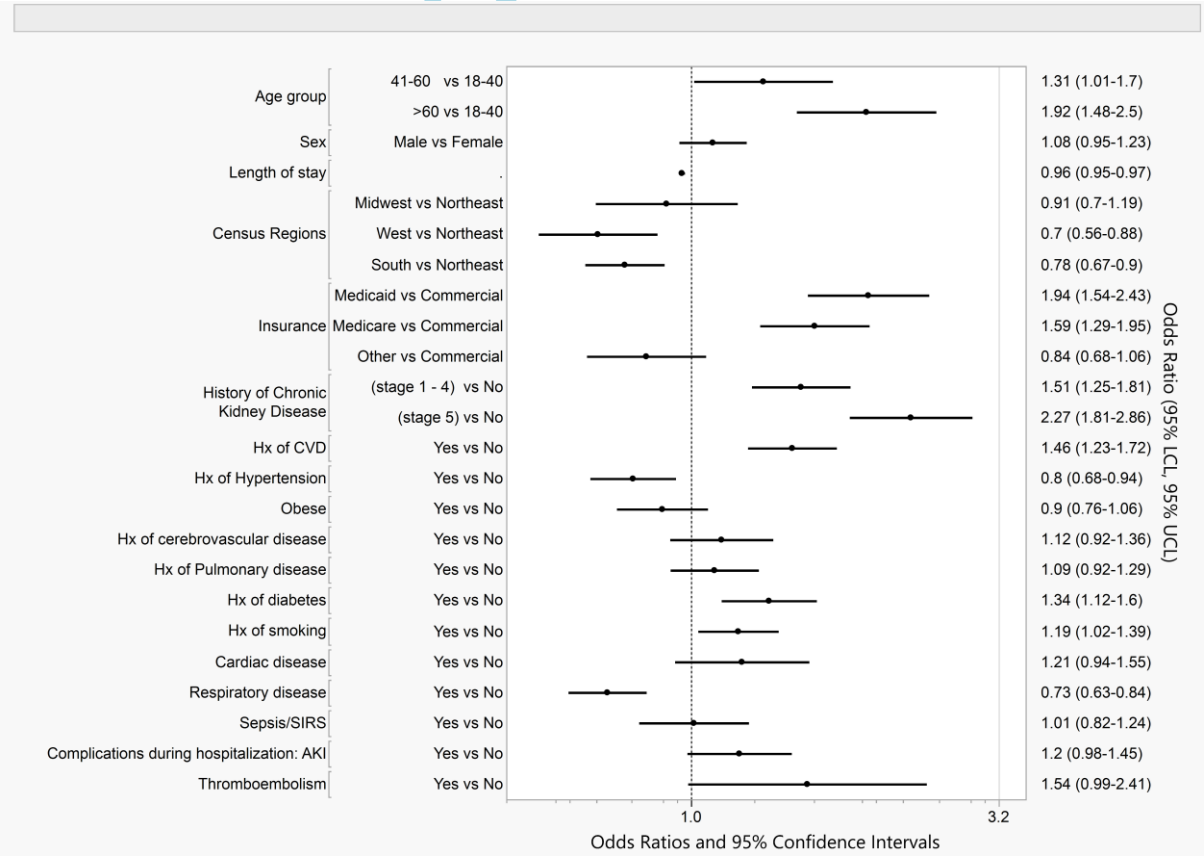

Age (years)
Sex
Length of stay second hospitalization (days)
Maximum Oxygen support during hospitalization
Census Regions
History of Chronic Kidney Disease
History of CVD
History of Hypertension
Obesity
History of diabetes
History of smoking
History of cerebrovascular disease
History of Pulmonary disease
Cardiac disease
Respiratory disease
Sepsis/SIRS
AKI
.
Male vs Female
.
Low Flow vs No Oxygen
High Flow vs No Oxygen
MV vs No Oxygen
Midwest vs Northeast
West vs Northeast
South vs Northeast
(stage 1 - 4) vs No
(stage 5) vs No
Yes vs No
1.04 (1.02-1.07)
0.93 (0.59-1.48)
0.97 (0.94-1)
1.06 (0.5-2.24)
3 (1.1-8.22)
19.15 (8.24-44.5)
0.48 (0.18-1.32)
0.28 (0.09-0.84)
0.46 (0.25-0.84)
1.19 (0.66-2.13)
1.43 (0.63-3.24)
1 (0.58-1.73)
0.68 (0.37-1.26)
1.01 (0.52-1.95)
1.07 (0.64-1.78)
1.21 (0.72-2.04)
0.91 (0.5-1.69)
0.9 (0.5-1.6)
1.64 (0.23-11.52)
2.12 (0.91-4.91)
3.03 (1.83-5.02)
1.85 (1.11-3.1)
Odds Ratio (95% LCL, 95% UCL)
0.1
0.3
1.0
3.2
10.0
31.6
Odds Ratios and 95% Confidence Intervals

Figure 3


Age group
41-60 vs 18-40
>60 vs 18-40
Sex
Male vs Female
Length of stay
.
Census Regions
Midwest vs Northeast
West vs Northeast
South vs Northeast
Insurance
Medicaid vs Commercial
Medicare vs Commercial
Other vs Commercial
History of Chronic Kidney Disease
(stage 1 - 4) vs No
(stage 5) vs No
Hx of CVD
Yes vs No
Hx of Hypertension
Yes vs No
Obese
Yes vs No
Hx of cerebrovascular disease
Yes vs No
Hx of Pulmonary disease
Yes vs No
Hx of diabetes
Yes vs No
Hx of smoking
Yes vs No
Cardiac disease
Yes vs No
Respiratory disease
Yes vs No
Sepsis/SIRS
Yes vs No
Complications during hospitalization: AKI
Yes vs No
Thromboembolism
Yes vs No
1.31 (1.01-1.7)
1.92 (1.48-2.5)
1.08 (0.95-1.23)
0.96 (0.95-0.97)
0.91 (0.7-1.19)
0.7 (0.56-0.88)
0.78 (0.67-0.9)
1.94 (1.54-2.43)
1.59 (1.29-1.95)
0.84 (0.68-1.06)
1.51 (1.25-1.81)
2.27 (1.81-2.86)
1.46 (1.23-1.72)
0.8 (0.68-0.94)
0.9 (0.76-1.06)
1.12 (0.92-1.36)
1.09 (0.92-1.29)
1.34 (1.12-1.6)
1.19 (1.02-1.39)
1.21 (0.94-1.55)
0.73 (0.63-0.84)
1.01 (0.82-1.24)
1.2 (0.98-1.45)
1.54 (0.99-2.41)
Odds Ratio (95% LCL, 95% UCL)
1.0
3.2
Odds Ratios and 95% Confidence Intervals