


Association of Surge Conditions with Mortality Among Critically Ill Patients with COVID-19

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Abstract

Objective: To determine whether surge conditions were associated with increased mortality.

Design: Multicenter cohort study.

Setting: U.S. ICUs participating in STOP-COVID.

Patients: Consecutive adults with COVID-19 admitted to participating ICUs between March 4 and July 1, 2020.

Interventions: None

Measurements and Main Results: The main outcome was 28-day in-hospital mortality. To assess the association between admission to an ICU during a surge period and mortality, we used two different strategies: (1) an inverse probability weighted difference-in-differences model limited to appropriately matched surge and non-surge patients and (2) a meta-regression of 50 multivariable difference-in-differences models (each based on sets of randomly matched surge- and non-surge hospitals). In the first analysis, we considered a single surge period for the cohort (March 23 – May 6). In the second, each surge hospital had its own surge period (which was compared to the same time periods in matched non-surge hospitals).

Our cohort consisted of 4342 ICU patients (average age 60.8 [sd 14.8], 63.5% men) in 53 U.S. hospitals. Of these, 13 hospitals encountered surge conditions. In analysis 1, the increase in mortality seen during surge was not statistically significant (odds ratio [95% CI]: 1.30 [0.47-3.58], $p = .6$). In analysis 2, surge was associated with an increased odds of death (odds ratio 1.39 [95% CI, 1.34-1.43], $p < .001$).

Conclusions: Admission to an ICU with COVID-19 in a hospital that is experiencing surge conditions may be associated with an increased odds of death. Given the high incidence of COVID-19, such increases would translate into substantial excess mortality.

Keywords

COVID-19, intensive care unit, mortality, surge, occupancy

Introduction

When reports first surfaced from Wuhan, China of a novel coronavirus (SARS-CoV-2) with both asymptomatic person-to-person transmissibility and a high incidence of acute respiratory distress syndrome (ARDS) and death, the world reacted with understandable alarm.¹⁻³ In the United States, particular concern was expressed regarding mechanical ventilator capacity. Although the U.S. maintains a national strategic reserve of ventilators, it was estimated that supply would be far less than potential demand.^{4,5} In the spring of 2020—particularly in densely populated urban areas on the U.S. East Coast—outbreaks of COVID-19 tore through communities, overwhelming many hospitals.⁶ Somewhat surprisingly, patient morbidity due to the lack of mechanical ventilators was not extensively reported. This was likely due to a number of strategies including utilization of ventilators from

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the national stockpile, repurposing non-invasive ventilatory devices as invasive mechanical ventilators, and use of alternative non-invasive ventilation strategies (eg, bi-level positive airway pressure and high-flow nasal cannula).⁷

Although ventilator shortfalls were not widely reported, providers expressed concern that other factors such as inadequate staffing, lack of ICU beds, and shortages of other essential equipment may have led to increased mortality in critically ill COVID-19 patients in the hardest hit areas.^{7,8} Increasing this concern were reports of high mortality rates in COVID-19 patients with respiratory failure who were cared for under surge conditions.^{9–11} Although these reports may have painted an overly bleak picture biased by incomplete follow-up, this mortality rate is far higher than the 26.5 to 46.3% mortality rate reported for patients with non-COVID-19 ARDS in the modern era and the 31 to 35% mortality rate for COVID-19 patients with ARDS cared for in non-surge settings.^{12–17} Finally, Bravata et al. found, in a large cohort study of COVID-19 admissions to Veteran's Administration (VA) hospitals, that high ICU caseload was associated with increased mortality; however, this study was not focused on critically ill patients and its generalizability to non-VA hospitals is unknown.¹⁸

We sought to determine whether the surge conditions during the spring of 2020 were associated with an increased mortality rate in ICU patients with COVID-19 across a diverse cohort of U.S. hospitals. We hypothesized that admission to an ICU during a period of surge would be associated with worse outcomes.

Materials and Methods

We conducted a multicenter cohort study of consecutive adults (≥ 18 years-old) admitted to U.S. ICUs with COVID-19 using the Study of the Treatment and Outcomes in Critically Ill Patients (STOP-COVID) database to evaluate the association between admission to a hospital experiencing a surge in COVID-19 ICU cases and 28-day in-hospital mortality.¹⁹ Data collection for STOP-COVID included ICU admissions from March 4 through July 1, 2020. We excluded hospitals that submitted data on fewer than 30 patients during the study period.

Data Elements

From the STOP-COVID dataset, we abstracted patient-level data on demographics (age; sex; race), chronic health information (body mass index; comorbidities—diabetes, hypertension, coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, cancer; smoking history), and acute illness information (date of ICU admission; duration of symptoms prior to ICU admission; and respiratory failure [ratio of arterial partial pressure of oxygen to inspired oxygen fraction and use of mechanical ventilation], vasopressor use, and renal, coagulation, and liver dysfunction [assessed by sequential organ failure assessment score²⁰] on ICU

admission). Hospital-level data included the number of ICU beds at baseline (prior to COVID-19 admissions) and American Hospital Association region.²¹

Exposure

Surge status at a given hospital was defined on each calendar day as having a COVID-19 ICU census that was greater than or equal to the number of ICU beds at baseline. The study period was divided into 3 time periods—pre-surge (before any hospital surged), surge (while at least one hospital was surging), and post-surge (after all hospitals were no longer surging).

Outcome

Our primary outcome was in-hospital 28-day mortality. Patients discharged alive prior to day 28 were considered alive at 28 days.

Statistical Analysis

We described the cohort using standard summary statistics. Characteristics of patients admitted on surge or non-surge days were compared using Chi-square and t-testing as appropriate.

To evaluate the association of admission during surge and 28-day in-hospital mortality, we employed three analytic approaches. Our initial approach was a difference-in-differences (DiD) analysis including patients admitted to *any* study hospital. Patients admitted to hospitals that experienced surge during the surge epoch were considered “exposed”; patients admitted to hospitals that never surged served as temporal controls (e Figure 1a). Post-surge patients were excluded and, to limit misclassification, we also excluded patients who were admitted during the surge epoch to hospitals that experienced surge conditions, but whose hospital was not surging on their day of admission. All aforementioned covariates (other than ICU bed number) were included in the model and standard errors were clustered by hospital. However, the parallel trends assumption was not met. Thus, we could not conduct this analysis and moved on to two alternate approaches.

To identify a more comparable control group for our DiD analysis, we next excluded patients admitted to ICUs in U.S. states where no participating hospital ever surged. Among this group, we conducted an inverse probability weighted (IPW) DiD analysis.²² Weights were based on each patient's propensity to be in a given exposure group (1: surge hospital, pre-surge; 2: surge hospital, during surge; 3: non-surge hospital, pre-surge; 4: non-surge hospital, during surge; eFigure 1b). The parallel trends assumption was tested and met using this approach (e Figure 2).

In a final approach that sought to minimize patient and hospital exclusions (eFigure 1c), we re-defined surge periods at the hospital level, rather than across the entire cohort. Each of the

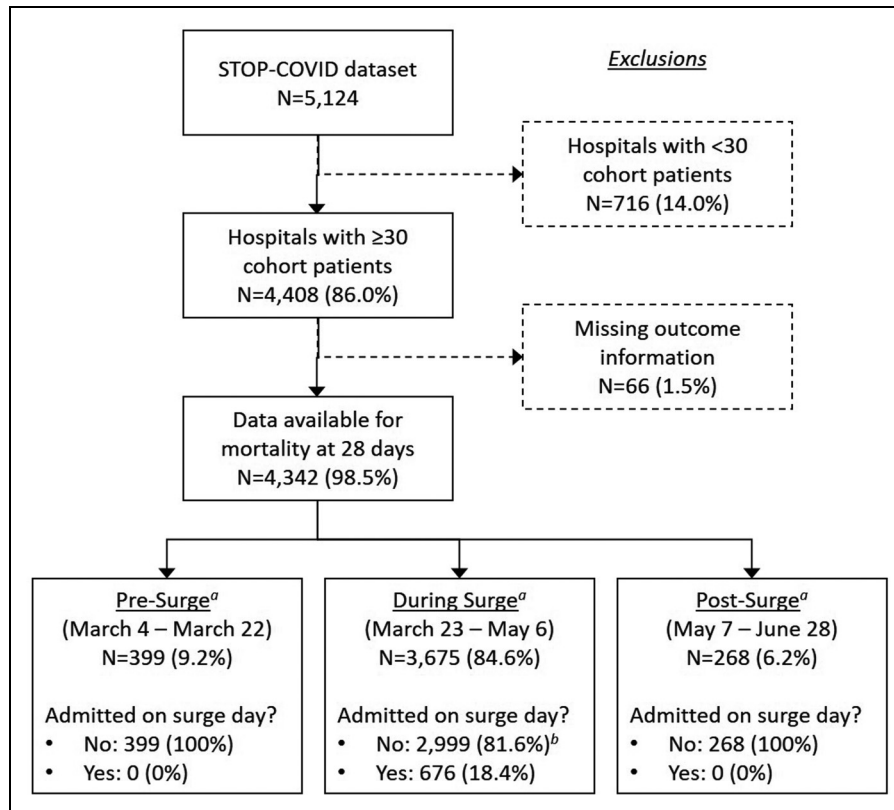


Figure 1. Cohort creation.

a surge period includes first day any hospital experienced surge through the last day any hospital experienced surge

b 408 (13.6% of 2999) admissions were to surge hospitals during the surge period but on days in which their hospital did not experience surge; these are excluded from first primary analysis.



Figure 2. Distribution of surge and non-surge days for each Cohort hospital.^a

^aEach row represents a unique cohort hospital (grouped by US State), each column a unique calendar day from March 4 to June 28. Blank squares represent days in which no new ICU admission was recorded in the cohort. Of days with ICU admissions, green squares represent non-surge days (COVID-19 ICU occupancy <100% of baseline ICU capacity) and red squares represent surge days (COVID-19 ICU occupancy ≥100% of baseline ICU capacity).

Table 1. Cohort Baseline Characteristics and Outcomes.

	Not admitted on surge day, N(%)	Admitted on surge day, N(%)	p-value ^a
# of patients, N(row %)	3666 (84.4)	676 (15.6)	
Admission period			<.001
Pre-surge (March 4 - March 22)	399 (10.9)	0 (.0)	
During surge (March 23 - May 6)	2999 (81.8) ^b	676 (100.0)	
Post-surge (May 7 - June 28)	268 (7.3)	0 (.0)	
Hospital ever experienced surge	589 (16.1)	676 (100.0)	<.001
Age (years)			<.001
≤39	377 (10.3)	40 (5.9)	
40 to 49	460 (12.5)	66 (9.8)	
50 to 59	793 (21.6)	137 (20.3)	
60 to 69	1007 (27.5)	207 (30.6)	
70 to 79	680 (18.5)	159 (23.5)	
80+	349 (9.5)	67 (9.9)	
Male gender	2321 (63.3)	436 (64.5)	.56
Race			<.001
White	1365 (37.2)	267 (39.5)	
Black	1209 (33.0)	127 (18.8)	
Other	291 (7.9)	49 (7.2)	
Unknown	801 (21.8)	233 (34.5)	
Body mass index			.004
<25	664 (18.1)	101 (14.9)	
25-<30	1028 (28.0)	224 (33.1)	
30-<35	861 (23.5)	159 (23.5)	
35-<40	464 (12.7)	72 (10.7)	
40+	525 (14.3)	84 (12.4)	
Unknown	124 (3.4)	36 (5.3)	
Comorbidities			
Diabetes	1546 (42.2)	297 (43.9)	.39
Hypertension	2234 (60.9)	418 (61.8)	.66
Coronary artery disease	494 (13.5)	94 (13.9)	.76
Congestive heart failure	378 (10.3)	55 (8.1)	.08
Chronic obstructive pulmonary disease	311 (8.5)	55 (8.1)	.77
Cancer	154 (4.2)	38 (5.6)	.10
Current smoker	198 (5.4)	27 (4.0)	.13
Symptoms started ≤3d pre-ICU admission	829 (22.6)	127 (18.8)	.027
Week of study ^c , mean(sd)	5.31 (2.44)	5.37 (1.35)	.53
28-day in-hospital mortality	1238 (33.8)	398 (58.9)	<.001

d: days; ICU: intensive care unit; sd: standard deviation.

aChi-square testing for categorical and t-testing for continuous variable comparisons.

b2,999 patients were admitted during the surge period (March 23 to May 6), yet on days where their individual hospital did not experience surge (ie, total COVID-19 ICU census was <100% baseline ICU capacity).

cThe study period was divided into weeks, week 1 (March 4 through March 11) to week 17 (June 25 to June 28, a partial week).

40 non-surge hospitals was then randomly matched to one of the 13 surge hospitals, 3 to 4 non-surge hospitals per surge hospital. The surge period for each non-surge hospital was defined as that of the surge hospital to which it was matched. This process of random matching was repeated to create 50 sets of matched surge and non-surge hospitals for which the parallel trends assumption was met (e Figure 3 and e Table 1). We then constructed a multivariable DiD model to assess the association of surge with mortality for each of the 50 matched sets. Finally, we combined effect estimates across these sets using meta-regression with robust variance estimation to account for the repeated use of observations.²³ In all models, all cohort hospitals were included; the number of patients included varied (as “post-surge” exclusions for non-surge hospitals differed across matched sets).

We additionally performed two pre-planned sensitivity analyses using the simple exposures of (1) “admitted on a surge day” or (2) “admitted during a hospital’s surge period”. To accomplish this, we constructed a pair of multivariable mixed-effects models inclusive of all aforementioned covariates; hospital of admission was included as a random effect. Both analyses were performed on the full cohort and, separately, on only patients admitted to surge hospitals. Post-hoc, we conducted three additional sensitivity analyses to evaluate the robustness of our results to our definition of surge: (1) the IPW DiD approach with different values of percent of baseline ICU capacity used to define surge; (2) the simple exposure (non-DiD) model with surge included as a continuous variable (modeled linearly); and (3) the simple exposure model with surge included as a categorical variable (by 25% of baseline ICU capacity increments).

All statistical analyses were performed using StataMP 16 (StataCorp, College Station, Texas), R (www.R-project.org), and Microsoft Excel (Microsoft, Redmond, Washington). Institutional Review Board approval was obtained from the University of Miami (#20200750) and from each participating site.

Results

Our primary cohort consisted of 4342 critically ill adult patients admitted to 53 U.S. hospitals (Figure 1). Thirteen hospitals across Louisiana, Massachusetts, New Jersey, New York, Ohio, and Pennsylvania experienced at least 1 day of surge and all surge days occurred between March 23 and May 6 (Figure 2). A total of 676 of the 4342 patients (15.6%) were admitted to the ICU on a surge day (Table 1). Patients admitted on surge days tended to be older (64.0% vs. 55.5% were ≥60 years-old), less commonly of Black race (18.8% vs. 33.0%), and more commonly received invasive mechanical ventilation (75.5% vs. 59.4%) and vasopressor support (49.4% vs. 39.8%) on ICU day 1 (e Table 2). In-hospital 28-day mortality was higher in patients admitted on surge (58.9%) versus non-surge (33.8%) days (p < .001).

Table 2. Adjusted Association of Admission During Surge with 28-Day In-Hospital Mortality.^a

Difference-in-Differences Models				
	N (%)		OR (95% CI) ^a	p-value ^b
Primary Analysis 1: IPW Model	2052		1.30 (.47,3.58)	.61
Primary Analysis 2: Meta-Analysis	3041 - 3,422 ^c		1.39 (1.34,1.43)	<.001
Simple Surge/Not Surge Models				
	Not exposed, N (%)	Exposed, N (%)	OR (95% CI) ^d	p-value ^d
Primary Surge Definition				
All Hospitals (N = 4342)				
Individual patient experienced surge	3666 (84.4)	676 (15.6)	1.49 (1.10,2.02)	.009
Admitted during hospital Surge	3655 (84.2)	687 (15.8)	1.46 (1.08,1.96)	.014
Only Surge Hospitals (N = 1265)				
Individual patient experienced surge	589 (46.6)	676 (53.4)	1.23 (.88,1.73)	.23
Admitted during hospital Surge	578 (45.7)	687 (54.3)	1.21 (.87,1.69)	.26
Alternative Surge Definitions				
All Hospitals (N = 4342); Individual patients experienced surge				
Model 1: surge as a patient-level continuous exposure (per 1% increase in ICU occupancy)	3666 (84.4)	676 (15.6)	1.003 (1.001,1.005)	.008
Model 2: surge as a patient-level categorical exposure	3666 (84.4)	676 (15.6)		
<25%			Reference	
25 to 49%			1.02 (.81,1.29)	.87
50 to 74%			1.07 (.81,1.42)	.62
75 to 99%			1.29 (.90,1.84)	.17
100 to 124%			1.44 (.95,2.18)	.09
125 to 149%			1.89 (1.01,3.53)	.046
150 to 174%			2.46 (1.27,4.77)	.008
175 to 199%			1.85 (.76,4.48)	.17
200 to 224%			.79 (.24,2.62)	.70
225 to 249%			2.26 (.87,5.90)	.10
250 to 274%			2.36 (1.12,4.97)	.024
275 to 299%			2.90 (1.01,8.34)	.049
300 to 324%			1.83 (.88,3.83)	.11
325 to 349%			1.78 (.68,4.69)	.24

CI: confidence interval; IPW: inverse probability weighted; OR: odds-ratio.

^aAll multivariable models included adjustment by the following covariables: age (grouped as <40, 40-49, 50-59, 60-69, 70-79, and 80+); male gender; race (categorized as White, Black, other, or unknown); body mass index (grouped as <25, 25-29, 30-34, 35-39, 40+, and unknown); presence of diabetes mellitus; presence of hypertension; presence of coronary artery disease; presence of congestive heart failure; presence of chronic obstructive pulmonary disease; presence of cancer; current smoker; symptoms starting ≤ 3 days prior to intensive care unit admission; respiratory status at intensive care unit admission (not mechanically ventilated [MV]; MV with $\text{paO}_2/\text{FiO}_2 \geq 300$; MV with $\text{paO}_2/\text{FiO}_2$ 200-299; MV with $\text{paO}_2/\text{FiO}_2$ 100-199; MV with $\text{paO}_2/\text{FiO}_2 < 100$; and MV with unknown $\text{paO}_2/\text{FiO}_2$); use of vasopressors on intensive care unit day 1; renal sequential organ failure assessment (SOFA) score (grouped as 0/unknown, 1, 2, 3, or 4); coagulation SOFA score (grouped as 0/unknown, 1, 2, 3, or 4); liver SOFA score (grouped as 0, 1, 2, 3, 4, or unknown); and week of the study period for intensive care unit admission date. For the IPW model to create the propensity score, we also included adjustment for American Hospital Association geographic region (grouped as region 1 [Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont], 2 [New Jersey, New York, Pennsylvania], and 3-9 [all other states]).

^bfor the interaction term of time period (pre-surge vs surge) and hospital surge status.

^cvaries across 50 matched surge/non-surge hospital sets.

^dfor the surge (vs not-surge) term in the model.

Association of Surge and 28-Day In-Hospital Mortality

Inverse probability weighted DiD modeling. The restricted cohort used for IPW DiD modeling consisted of 2052 ICU admissions across 30 hospitals (13 that surged on at least one day, 17 that did not; eTable 3). The adjusted odds of death associated with being admitted during surge was not statistically significantly different than being admitted pre-surge after adjusting for temporal trends (odds-ratio, OR [95% confidence interval, CI] for interaction term of hospital surge status and time period: 1.30 [0.47-3.58]; Table 2). These results were

robust to varying the ICU occupancy used to define surge (eTable 4).

Meta-regression of DiD modeling of 50 matched hospital sets. The 50 matched surge/non-surge hospital sets each included 1185 patients admitted to 13 hospitals which ever surged; the number of patients included in the 40 non-surge hospitals ranged from 3041 to 3422 (Figure 3). After meta-regression with robust variance estimation, we found a significant association with being admitted during surge and 28-day in-hospital

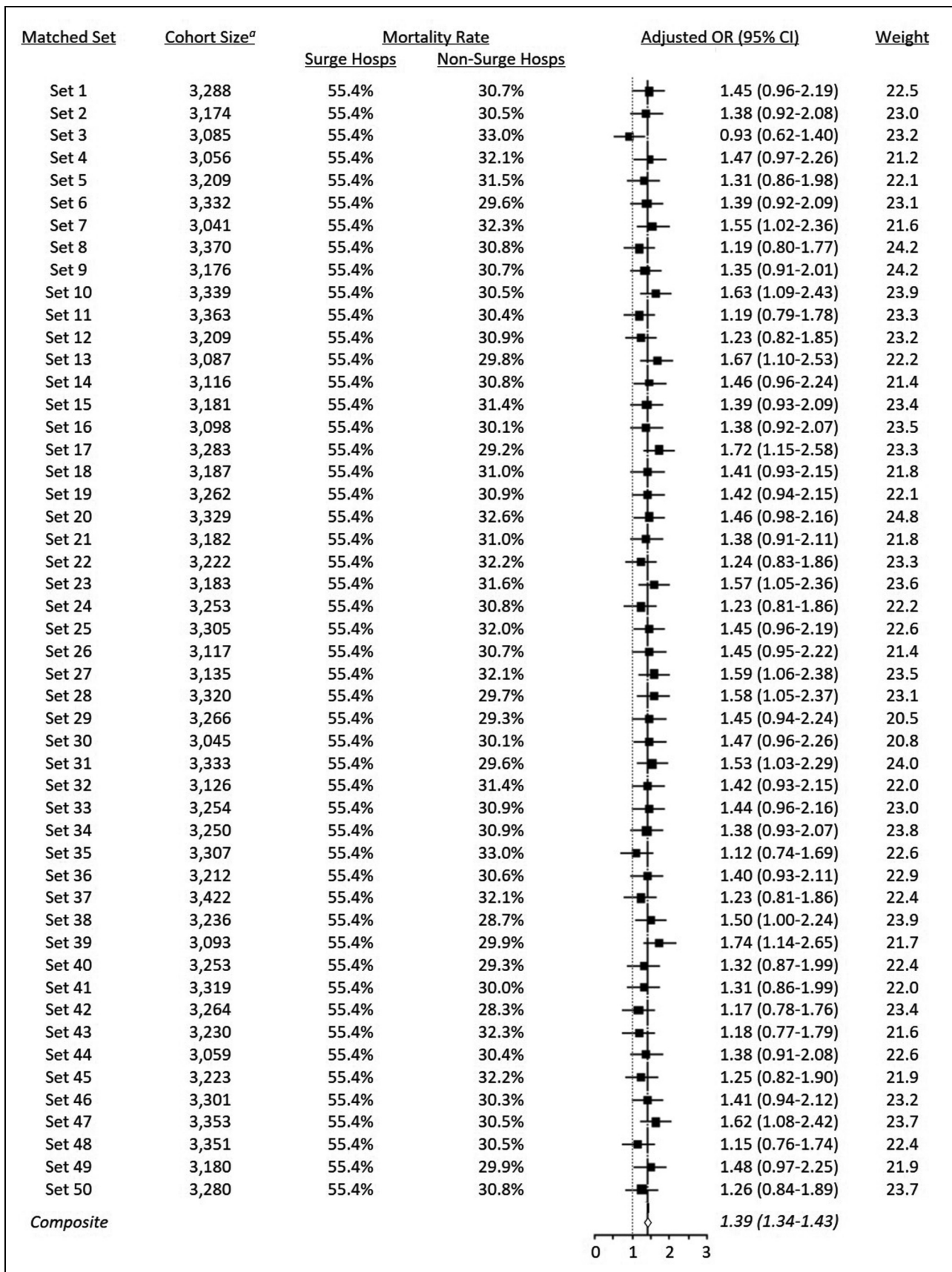


Figure 3. Meta-analysis of difference-in-differences models on 50 randomly matched surge/non-surge hospital sets.

CI: confidence interval; hosps: hospitals; OR: odds-ratio

A each cohort includes 13 surge hospitals (with 1185 patients) and 40 non-surge hospitals.

death (meta-analysis OR for interaction term of hospital surge status and time period: 1.39 [95% CI, 1.34-1.43], $p < .001$).

Sensitivity Analyses

In our simplified models, we found that admission on a surge day (OR 1.49 [95% CI, 1.10-2.02], $p = .009$) and admission during a given hospital's surge period (OR 1.46 [95% CI, 1.08-1.96], $p = .014$) were each associated with increased 28-day in-hospital mortality. These results were robust to modeling surge as a continuous variable (OR 1.003 [95% CI, 1.001-1.005] for each 1% increase in ICU occupancy, $p = .008$). When the cohort was limited to only hospitals that experienced at least one surge day, the effect size was smaller and not statistically significant (Table 2).

Discussion

Using several approaches to assess the association between being admitted to an ICU at a hospital that was concomitantly experiencing a surge in ICU COVID-19 cases and mortality, we found that admission during times of surge may be associated with higher odds of in-hospital mortality by 28 days. Specifically, across analytic strategies, there was a 21 to 49% increased odds of death. In our more conservative approach, however, we could not exclude the possibility that this difference was due to chance.

Limitations in resources (eg, ICU nurses,²⁴⁻²⁷ intensivist staffing,²⁸⁻³⁰ overall staffing,³¹⁻³⁴ and ICU beds^{35,36}) have been shown to have variable but generally negative effects on the care and outcomes of critically ill patients without COVID-19. The COVID-19 surge in certain U.S. regions in spring, 2020 represented a "perfect storm" of resource limitations; profound deficiencies in ICU beds, clinicians, and vital equipment were reported simultaneously.^{6,7,37} To our knowledge, our study is the first to quantify the magnitude of the association of surge with critically ill COVID-19 patients' outcomes across a diverse set of U.S. civilian hospitals.

Analyzing the effects of surge required sophisticated statistical techniques. Our analysis needed to address two issues: (1) hospitals surged at variable times and (2) treatment paradigms and patient case-mix varied over our study period. Our *a priori* plan was to use a DiD strategy with a single surge period for the full cohort (from the first through the last day any hospital surged). This approach would mitigate against both concerns aforementioned. However, it was limited in that all hospitals were assumed to surge simultaneously (even though each surge hospital truly did so only on certain days). To address this issue, we planned to exclude patients admitted to surge hospitals on non-surge days during the surge period. Unfortunately, this cohort did not meet assumptions necessary for our planned analysis.

Therefore, we used alternative analytic strategies decided upon *post hoc*. Our first alternative analysis was a replication of the *a priori* planned analysis using a smaller cohort which found a non-significant association of surge status with

mortality. Our second alternative analysis excluded fewer patients and, perhaps as a result, showed a statistically significant negative association of ICU admission during surge with mortality. To complement these more complicated analyses, we performed several *a priori* planned simplified sensitivity analyses which showed similar increases in mortality for patients admitted during surge. Again, those with smaller sample sizes were not statistically significant.

The strengths of our study stem from our large, diverse cohort inclusive of many sites of COVID-19 infection as well as the robustness of our results across multiple statistical modeling techniques. Our results may be limited by confounding. However, we adjusted for several potential patient- and hospital-level confounders, selected *a priori*, and attempted to address unmeasured confounding through our DiD study design. Still, we cannot test whether other unmeasured differences exist between patients exposed to surge conditions – or the care they received – and those not exposed. Additionally, the non-statistical significance of several of our analytic results likely stems from their sample size, but may actually represent true null results. Furthermore, our cohort included only patients admitted early in the pandemic; it is unknown if our findings would differ if we had included patients hospitalized later in the pandemic (eg, with different treatment approaches, vaccinations, etc). Also, we defined our exposure, surge, based on the caseload of COVID-19 patients on the day of each patient's ICU admission rather than a larger portion of the ICU stay. We also were unable to include non-COVID-19 ICU patients in our calculations of ICU occupancy. Finally, our study was not able to identify what specific aspects of surge conditions drive the association with worse outcomes.

Our findings are consistent with those from two other retrospective studies. The first, a cohort of COVID-19 ICU admissions to VA hospitals, found higher ICU caseload during a patient's hospitalization was associated with increased death (hazard ratio [95% CI] of COVID-19 ICU caseload $>100\%$ vs. $\leq 25\%$ of baseline ICU capacity: 2.35 [1.25-4.39]).¹⁷ The second, using administrative data from a 558 U.S. hospitals' admissions (not focused specifically on ICU patients) found a dose-response in the increased odds of death associated with degrees of surge.³⁸ Both studies were limited, however, by non-adjustment for temporal changes in casemix or practice patterns as the difference-in-differences approach we employed does.

Conclusion

As the COVID-19 pandemic has proven, novel infections pose an existential threat to the health of the nation. Having shown the potential impact on survival of allowing health systems to operate in suboptimal conditions, our work highlights that pandemic preparedness extends far beyond ventilator stockpiling. Readiness for the next pandemic will require investments that are commensurate with the threat.

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Supplemental Material

Supplemental material for this article is available online.

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