Hospital-Level Variation in Death for Critically Ill Patients with COVID-19

Running title: Variation in Hospital Mortality for COVID-19

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Impact: Mortality for critically ill patients with COVID-19 varied across hospitals (0 to 82%), and interhospital variation in mortality was mostly explained by differences in

presenting physiology, hospital strain and capacity, and socioeconomic status. These results have important implications for understanding factors that cause variability in mortality risk of critically ill patients with COVID-19.

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At A Glance

What is the current scientific knowledge on this subject?

Considerable variation in hospital mortality has been described for patients admitted to the intensive care unit with coronavirus disease 2019 (COVID-19). However, the factors that explain these differences remain unclear.

What does this study add to the field?

In this study of 4,019 patients in 70 hospitals, we found significant interhospital variation in mortality for critically ill patients with COVID-19. This hospital-level variation was mostly explained by hospital-level socioeconomic status, strain, and physiologic differences, although individual mortality was driven mostly by patient-level factors.

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ABSTRACT

Rationale: Variation in hospital mortality has been described for coronavirus disease 2019 (COVID-19), but the factors that explain these differences remain unclear.

Objective: Our objective was to utilize a large, nationally representative dataset of critically ill adults with COVID-19 to determine which factors explain mortality variability.

Methods: In this multicenter cohort study, we examined adults hospitalized in intensive care units with COVID-19 at 70 United States hospitals between March and June 2020. The primary outcome was 28-day mortality. We examined patient-level and hospital-level variables. Mixed-effects logistic regression was used to identify factors associated with interhospital variation. The median odds ratio (OR) was calculated to compare outcomes in higher- vs. lower-mortality hospitals. A gradient boosted machine algorithm was developed for individual-level mortality models.

Measurements and Main Results: A total of 4,019 patients were included, 1537 (38%) of whom died by 28 days. Mortality varied considerably across hospitals (0-82%). After adjustment for patient- and hospital-level domains, interhospital variation was attenuated (OR decline from 2.06 [95% CI, 1.73-2.37] to 1.22 [95% CI, 1.00-1.38]), with the greatest changes occurring with adjustment for acute physiology, socioeconomic status, and strain. For individual patients, the relative contribution of each domain to mortality risk was: acute physiology (49%), demographics and comorbidities (20%), socioeconomic status (12%), strain (9%), hospital quality (8%), and treatments (3%).

Conclusion: There is considerable interhospital variation in mortality for critically ill

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patients with COVID-19, which is mostly explained by hospital-level socioeconomic status, strain, and acute physiologic differences. Individual mortality is driven mostly by patient-level factors.

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INTRODUCTION

As of April 2021, coronavirus disease 2019 (COVID-19) has killed more than 500,000 people in the United States.[1] When patients develop severe disease, they are typically transferred to the intensive care unit (ICU), which provides more intensive monitoring along with potentially life-saving critical care therapies such as mechanical ventilation, vasoactive agents, and extracorporeal membrane oxygenation.[2,3] Studies conducted prior to the pandemic demonstrated that outcomes of critically ill patients vary across hospitals, which may relate to differences in patient characteristics and the quality of care provided at different hospitals.[4] Emerging data suggest similar variability in outcomes across hospitals for critically ill patients admitted with COVID-19.[5-8] The causes of this variability are unclear and could include differences in demographics, comorbidities, physiologic severity of illness, socioeconomic status, resource strain, hospital quality, and treatments provided. It is also unknown how each of these domains impacts mortality risk for individual patients. A better understanding of the patient- and hospital-level factors impacting death could lead to insights into the reasons for the wide variation in reported outcomes, the determinants of individual patient outcomes, and improved healthcare delivery.

Our objective was to utilize a large, nationally representative dataset of critically ill adults with COVID-19 to determine which factors explain the variability in mortality at both the hospital and the patient level. To do this, we linked detailed patient information with hospital-level data and then explored how different domains explained variations in 28-day mortality.

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METHODS

Study design, setting, and population

We utilized the multicenter Study of the Treatment and Outcomes in Critically Ill Patients with COVID-19 (STOP-COVID) database, a cohort study of 5,154 patients with COVID-19 admitted to ICUs across the United States (**Table E1** in the **Supplementary Appendix** lists the sites included in this study).[5] We included consecutive adults (age ≥18 years) admitted to the ICU with laboratory-confirmed COVID-19 admitted between March 4 and June 29, 2020. Patients were followed until the first of hospital discharge, death, or at least 28 days after ICU admission. Patients transferred to the ICU from other hospitals, admitted to a hospital not linked to the Medicare Hospital Compare ratings, or admitted to a hospital with less than 10 COVID-19 ICU admissions in the dataset were excluded. A sensitivity analysis was performed by including patients transferred from outside hospitals. The study was approved by Institutional Review Boards at each site with a waiver of informed consent.

Data collection and outcome

Manual chart review was performed at each site using a standardized case report form, as previously described.[5] Patient-level data collected included admission day, demographic information, comorbidities, vital signs on ICU admission, laboratory values, medications, non-medication treatments, and organ support in the first two weeks of ICU admission, and outcomes, including in-hospital mortality. The STOP-COVID dataset also included what type of ICU bed the patient was admitted to (e.g.,

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medical-surgical), whether the patient was admitted to a COVID-specific ICU or surge unit, and the number of ICU beds at each hospital prior to the COVID-19 pandemic.

Additional hospital-level variables were collected by linking each study hospital to data from the following sources: the American Hospital Association Annual Survey 2020 database for hospital strain and capacity variables; the 2017 Medicare Hospital Compare ratings for hospital quality ratings; the Healthcare Cost Report Information System; and the 2015 American Community Survey for socioeconomic status data, which incorporates information from communities surrounding each hospital by utilizing a previously described methodology (**Table E2** in the **Supplementary Appendix**).[9-11] Furthermore, time-varying variables describing hospital-level strain were collected from the STOP-COVID dataset (i.e., number of other patients with COVID-19 currently in the ICU at a given hospital when a patient was admitted) and from publicly available data on the number of new COVID-19 cases from the past 30 days for the county where each hospital was located.[1]

The primary outcome of the study was in-hospital death within 28 days of ICU admission. If a patient was discharged alive before day 28, they were assumed to be alive at day 28. This assumption was confirmed in a sample of patients in a previous study.[5] A sensitivity analysis was performed using in-hospital mortality as the outcome.

Statistical analysis

Explanatory variables were categorized into six domains, including three patient-level and three hospital-level domains. The individual variables and domains were chosen *a priori* based on prior literature and availability. Patient-level domains included: acute

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physiology and severity of illness in the first 48 hours of ICU admission (e.g., vital signs, laboratory values, ventilatory support, number of vasopressors, and renal replacement therapy); demographics and comorbidities (e.g., age, sex, race, body mass index, smoking status, and pre-existing conditions); and treatments provided in the first 48 hours of ICU admission (e.g., corticosteroids, remdesivir, tocilizumab, prone position ventilation). Hospital-level treatment intensity was also included as a variable in the treatment domain by calculating the percentage of mechanically ventilated patients with a PaO_2/FiO_2 ratio<150 who were treated with extracorporeal membrane oxygenation, inhaled pulmonary vasodilators, tocilizumab, prone positioning, or neuromuscular blockade. Hospital-level domains included: socioeconomic factors at the hospital level (e.g., % high school diploma, % unemployed, % English speaking, % travel to work >45 minutes); hospital strain (e.g., number of ICU beds prior to COVID-19, time-varying number of ICU beds filled with COVID-19 patients, whether the patient was admitted to a COVID-specific ICU or surge unit, total number of medical-surgical beds, ICU occupancy rate pre-pandemic, number of hospital beds in the county, number of COVID-19 cases in the county from the prior 30 days); and hospital quality scores (mortality, readmission, safety, timeliness, patient experience, and effectiveness). ICU admission day was used to create a variable that denotes the “days since study start” that a patient was admitted to the ICU, which was assigned to each patient to account for possible longitudinal changes in hospital quality.[12] The full variable list for each domain, along with additional descriptions, is provided in **Table E2** in the **Supplementary Appendix**. Missing values were imputed using bagged forests from the caret package in R, which builds ensembles of decision trees, with each tree fit to a

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randomly selected bootstrapped sample of the dataset, using non-missing variables to impute missing variables (see **Table 1** for the amount of missing data for each variable). This approach has the advantage of automatically modeling non-linearities and interactions that may be important for accurate variable imputation.[13] Comparisons between patients who survived vs. died within 28 days were made for all study variables using Wilcoxon rank-sum tests and chi-squared tests.

Next, mixed-effects logistic regression models were fit, first with an empty model with a random effect for each hospital, and then by sequentially adjusting for variables from each domain in the order described above, which moves from patient-level to hospital-level factors. This ordering allowed for the separation of patient- and hospital-level variables to determine their contributions to interhospital variation in mortality. The change in the adjusted variation of 28-day mortality was calculated, moving from one model to the next, by examining the median odds ratio for each model. The median odds ratio can be interpreted as the difference in odds between a randomly selected lower-risk hospital and a randomly selected higher-risk hospital. It can be conceptualized as the increased risk that a subject would have if he/she was admitted to a higher risk hospital.[14,15] Pseudo-R^2 values were also calculated for each individual domain using Efron's R^2, which is calculated by taking the sum of the squared model residuals divided by the total variability in the dependent variable.

Finally, to calculate the contribution of the domains to an individual's risk of mortality, a gradient boosted tree machine learning model was fit using all the variables from each domain.[16] Ten-fold cross-validation was used to optimize the model's area under the receiver operating characteristic curve. Shapley values were then calculated for each

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individual patient, which estimate the contribution of each variable for that individual patient's risk of 28-day mortality.[17] The individual Shapley values were then combined across all patients in the dataset using the mean of their absolute value to determine the percent mortality risk explained by each domain. All analyses were performed using Stata version 16.1 (StataCorps, College Station, TX) and R version 4.2 (R Foundation for Statistical Computing, Vienna, Austria) with the caret, xgboost, and iml packages. A two-sided p-value <0.05 denoted statistical significance.

RESULTS

Patient characteristics

A total of 4,019 patients (median age [IQR] 63 [53-72]; 63% male (n = 2532)) from 70 hospitals were included in the analysis after exclusion criteria were applied (**Figure E1** and **Table E1** in the **Supplementary Appendix**), and 1,537 (38%) died by 28 days. The median number of patients at a given hospital was 34 (IQR 20-79; **Figure E2** in the **Supplementary Appendix**). Patients who died were older (median [IQR] 68 [59-76] vs. 60 [49-68] years), more likely to be male (66% vs. 61%), more likely to be current or former smokers (30% vs. 23%), and had higher frequencies of most comorbidities compared to those who survived at 28 days (**Table 1**). Most vital signs and laboratory results were significantly different during the first 48 hours of ICU admission between those who died compared to those who survived (**Table 1**). Patients who died were also more likely to have received invasive mechanical ventilation (80% vs. 58%) and renal replacement therapy (9% vs. 5%) during the first 48 hours of ICU admission. Finally, certain medications were more often provided to those who died, such as

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neuromuscular blocking agents (25% vs. 17%), hydroxychloroquine (63% vs. 59%), and corticosteroids (35% vs. 21%) (**Table 1**).

Hospital-level analysis

Patients who died were admitted to hospitals with a higher percentage of ICU beds occupied by COVID-19 patients (48% vs. 31%), a higher percentage of the population traveling >45 minutes to work (23% vs. 18%), a lower pre-pandemic ICU occupancy rate (69% vs. 74%), lower number of pre-COVID-19 ICU beds (median [IQR] 53 [47-98] vs. 98 [54-115]), higher number of COVID-19 cases in the county in the prior 30 days (median [IQR] 2,279 [640-7,268] vs. 1,416 [398-4,585]), and lower hospital quality scores as compared to patients who survived (**Table 2**).

Twenty-eight-day mortality varied widely across hospitals, from 0% at the lowest risk hospital to 82% at the highest. In the mixed-effects regression model, the median odds ratio decreased from 2.06 (95% CI, 1.73-2.37) in the unadjusted model to 1.22 (95% CI, 1.00-1.38) in the fully adjusted model (**Figure 1**). This was associated with a change in the range of mortality across hospitals from 12-91% (random effects only) to 32-44% (fully adjusted model). Model adjustment with variables from the physiology, socioeconomic status, and strain domains were associated with the greatest change in the median odds ratio (all >0.20 change in the point estimate). The fully adjusted model explained nearly all the variability across hospitals (p-value for random effect term=0.73; see **Table E3** in the **Supplementary Appendix** for model coefficients). Pseudo-R^2 values for each individual domain demonstrated similar results, with physiology (0.2),

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demographics (0.11), socioeconomic status (0.10), and strain (0.09) having the highest values, followed by quality (0.06) and treatments (0.04).

Patient-level analysis

The Shapley values calculated from the XGBoost model using variables from all the domains found that physiology (49%), demographics and comorbidities (20%), hospital socioeconomic status (12%), strain (9%), hospital quality (8%), and treatments (3%) all contributed to mortality risk (**Figure 2**). The mean contributions of the individual variables in each domain are shown in **Figures E3-E8** in the **Supplementary Appendix**. Thus, for patients in the dataset, on average their presenting physiology explained half of their quantifiable individual risk of mortality, while external factors such as hospital socioeconomic status, hospital capacity and strain, hospital quality, and the treatments clinicians provided explained over one-quarter (31%) of their mortality risk. Among patient demographics, age had the highest contribution, explaining 12% of the mortality risk, while co-morbidities explained 4% of a patient's mortality risk. Temporal trends captured by the "days since study start" variable only explained a small percentage of a patient's mortality risk (1%).

Sensitivity analysis

Performing the analyses using in-hospital mortality (n=3,904 (97.1%) with complete hospital follow-up) demonstrated similar results to the main analysis that used 28-day mortality (**Figures E9** and **E10** in the **Supplementary Appendix**). For example, the median odds ratio decreased from 2.10 (95% CI, 1.76-2.41) in the unadjusted model to 1.18 (95% CI, 1.00-1.36) in the fully adjusted model, and adjustment with variables from

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the physiology, socioeconomic status, and strain domains were associated with the greatest change in the median odds ratio. The ordering and magnitude of the domains regarding their contribution to individual risk was also similar. Adding outside hospital transfers back into the cohort also demonstrated similar results to the primary analysis (**Figures E11** and **E12** in the **Supplementary Appendix**).

DISCUSSION

In this multicenter cohort study of 4,019 critically ill adults with COVID-19 admitted to ICUs at 70 geographically-diverse hospitals across the United States, we found wide variation in 28-day mortality across hospitals. This hospital-level variability was mostly explained by differences in socioeconomic status of the hospital population, hospital capacity and strain, and presenting ICU physiology. Further, the mortality risk for individual patients was largely explained by demographic characteristics and co-morbidities as well as acute physiology. To our knowledge, this is the first manuscript of its kind investigating both hospital- and individual-level contributors to variation in mortality from a large, nationally representative cohort of critically ill patients with COVID-19. Our results help explain the wide variation in published mortality rates for critically ill COVID-19 patients and quantify how different factors contribute to an individual patient's mortality.

Published reports on the outcomes of critically ill COVID-19 patients have shown wide variations in mortality. For example, an early report by Arenz et al. reported an in-hospital mortality rate of 67% for patients admitted to the ICU at one hospital in Washington State.[18] In contrast, a study by Cummings et al. reported a mortality of 39%

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in a study from two hospitals in New York City.[19] This variability was summarized in a recent systematic review by Serafim and colleagues, which reported an in-hospital mortality range of 1% to 62%.[8] The cause of this variation has been hypothesized to be related to various factors such as hospital strain, patient characteristics, and variability in treatment practices.[5,20-23]

Our findings provide important insights into the reasons for this wide variation in hospital-level mortality. We found that hospital socioeconomic status, physiology, and hospital strain were the most important factors explaining this variability, while treatments provided to patients contributed least. To our knowledge, we are the first to show that the socioeconomic status of the community surrounding a hospital is an important contributor to hospital-level variability in outcomes in a geographically representative sample of critically ill COVID-19 patients. This finding could be due to factors related to either the impact of socioeconomic status on the health status of individual patients in the study or unobserved variability in the quality of care that hospitals provide for a population with a lower socioeconomic status.[22,24] Interestingly, the most important individual variable from the socioeconomic status domain was the percentage of patients at the hospital who traveled >45 minutes to work. This variable has been previously used to capture the spatial mismatch hypothesis theory,[25,26] which relates to discrepancies between the location of low-income neighborhoods and the locations of employment opportunities. This variable was also found to be one of the most important metrics of social risk in a study investigating hospital ratings and neighborhood disadvantage.[9] Our findings of increased mortality related to hospital

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population socioeconomic status suggest that COVID-19 may be exacerbating existing healthcare disparities in the US.[27]

The majority of an individual's risk of mortality was related to presenting physiology, demographics, and pre-existing conditions. Only one-quarter of a patient's quantifiable mortality risk was related to other factors such as hospital capacity and strain, hospital socioeconomic status, hospital quality, and treatments. Prior work suggested that the number of pre-existing ICU beds is an important predictor of mortality among critically ill patients with COVID-19,[5] suggesting a correlation between ICU capacity and outcomes.

However, additional factors such as the baseline occupancy rate prior to the pandemic and the number of patients with COVID-19 currently admitted to the ICU are important to consider when determining the strain on critical care resources. By including these variables and other related factors into one domain, we were able to show that strain and capacity contribute to both hospital-level variability and individual mortality. This contribution to mortality risk may be related to rationing, more aggressive goals of care discussions, and treatment of critically ill patients outside the normal ICU or by less experienced providers. Hospital quality scores also had some explanatory power, albeit less than hospital socioeconomic status or strain. This suggests that the quality of the hospital a patient with COVID-19 goes to has a small but measurable effect on their outcome, which is consistent with prior work in all hospitalized patients.[28]

Of all the domains studied, the treatments provided to patients had the least impact on hospital-level variability and individual-level mortality risk. This may be explained by the fact that few treatments have shown a mortality benefit for critically ill patients with

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COVID-19.[29-32] Notably, the three treatments that contributed the most to improved mortality – neuromuscular blockade, aspirin, and Tocilizumab – are all therapies that have previously been shown to improve outcomes for patients with COVID-19 or acute respiratory distress syndrome.[33-35]

This study has several strengths. Our cohort consisted of a geographically diverse sample of critically ill adults with COVID-19. We had access to detailed patient characteristics, physiology, interventions, and medications during their ICU stay. In addition, we were able to link the hospitals where these patients were admitted to quality scores and hospital-level socioeconomic status. Furthermore, by linking patients to the American Hospital Annual Survey data and time-varying county-level COVID-19 data, we were able to better quantify capacity and strain. Finally, in addition to standard mixed-effects regression models, we also used a state-of-the-art machine learning approach to determine the contribution of individual variables to patient mortality.[17]

This study also has several limitations. First, although we were able to identify variables associated with mortality, our study design does not lend itself to inferring causality. In addition, our findings only apply to patients admitted to ICU, as we did not have data on patients who were critically ill but were not admitted to an ICU (e.g., due to bed rationing or goals of care). Furthermore, there may be additional variables that contribute to mortality risk that we did not account for in our study. For example, best practices and supportive care interventions, such as low tidal volume ventilation for patients with acute respiratory distress syndrome, were not collected, nor were other hospital-level factors (e.g., teaching status, intensivist coverage, and nurse-to-patient ratios), nor the duration of treatments. Similarly, the Shapley values measure only quantifiable mortality that is

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explained by the variables in the model. It is also possible that some patients were discharged alive before day 28 only to die at home soon thereafter (e.g., patients discharged to home hospice). Although we verified in 50 patients at six participating hospitals that all patients discharged alive before 28 days were still alive at day 28, this might not be true at all centers. In addition, the hospital quality data was collected in 2017, which may not reflect quality of care during the present-day pandemic. Finally, we only had hospital-level socioeconomic status available as opposed to individual socioeconomic status, so we could not determine whether the impact of this domain was related to the socioeconomic status of individual patients or the resources and quality that might be associated with hospitals that provide care for patients with varying socioeconomic status characteristics.

In conclusion, we found considerable interhospital variation in death among critically ill patients with COVID-19. This variability is explained by several domains, including hospital socioeconomic status, presenting physiology, and hospital capacity and strain. Similar factors contribute to an individual patient's risk of mortality, with patient-level factors (e.g., physiology, demographics, and co-morbidities) explaining most of their mortality risk.

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FIGURES AND TABLES

Figure 1. Case-mix Adjusted Probabilities of 28-day Mortality. The graphs illustrate the change in interhospital variation in death as each domain is added to the unadjusted mixed-effects model (leftmost panel) and ending with the fully adjusted model (rightmost panel), which shows that most of the variation in mortality across hospitals can be explained by the domains included. The x-axis is hospital ranked by increasing probability of death in 28 days, and the y-axis shows the case-mix adjusted probability of death in the mixed-effects regression model, with the red dots denoting the point estimates and the whiskers denoting the 95% confidence intervals. The median odds ratio (OR) and range in mortality are presented for each model.

Abbreviations: Demo = Demographics, SES = Socioeconomic Status

Figure 2. Contributions to 28-Day Mortality Risk Based on Shapley Values. The figure illustrates the relative contribution of all variables in each domain based on Shapley values calculated from the XGBoost machine learning model (red bars; left y-axis). The cumulative contribution of the domains, moving from left to right in the figure, is shown with the line plot (right y-axis).

Abbreviations: Demo = Demographics, SES = Socioeconomic Status, Pop = Population

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Table 1. Patient Characteristics at Baseline.

Variable	All patients (N = 4019)	28-Day Survivors (N = 2482)	28-Day Non-Survivors (N = 1537)
DEMOGRAPHICS & PRE-EXISTING COMORBIDITIES			
Demographics			
Age (years) - median (IQR)	63 (53-72)*	60 (49-68)	68 (59-76)
Male - n (%)	2532 (63.0)*	1520 (61.2)	1012 (65.8)
Race- n (%)			
White	1527 (38.0%)	950 (38.3%)	577 (37.5)
Black	1238 (30.8%)	782 (31.5 %)	456 (29.7%)
Other	328 (8.2%)	213 (8.6%)	115 (7.5%)
Unknown/Not Reported	926 (23.0%)	537 (21.6%)	389 (25.3%)
Ethnicity – n (%)			
Hispanic	954 (23.7%)	601 (24.2%)	353 (23.0%)
Non-Hispanic	2600 (64.7%)	1604 (64.6%)	996 (64.8%)
Unknown/Not Reported	465 (11.6%)	277 (11.2%)	188 (12.2%)
Current or Former Smoker - n (%)	1039 (25.9)*	581 (23.4)	458 (29.8)
Body Mass Index kg/m² - median (IQR)	30.2 (26.3-35.5)*	30.6 (26.5-35.9)	29.7 (26.0-34.9)
Pre-existing Comorbidities - n (%)			
Active Cancer	190 (4.7)*	80 (3.2)	110 (7.2)
Congestive Heart Failure	425 (10.6)*	224 (9.0)	201 (13.1)
Chronic Obstructive Pulmonary Disease	356 (8.9)*	175 (7.1)	181 (11.8)
Coronary Artery Disease	567 (14.1)*	277 (11.2)	290 (18.9)
Diabetes	1713 (42.6)*	972 (39.2)	741 (48.2)
End-Stage Renal Disease	153 (3.8)*	79 (3.2)	74 (4.8)
Hypertension	2476 (61.6)*	1398 (56.3)	1078 (70.1)
PHYSIOLOGY			
Vital Signs [a]			
Altered Mental Status - n (%)	997 (24.8)*	420 (16.9)	577 (37.5)
Heart Rate (beats/min) - median (IQR)	105 (91-120)*	103 (90-118)	109 (93-125)
Respiratory Rate (beats/min) - median (IQR)	32 (26-39)*	32 (26-39)	31 (26-38)
Systolic Blood Pressure (mm Hg) - median (IQR)	97 (85-111)*	99 (88-112)	94 (82-109)
Temperature (°C) - median (IQR)	37.9 (37.2-38.8)*	38.0 (37.2-38.8)	37.8 (37.1-38.7)
Labs [b]			
Arterial pH – median (IQR)	7.3 (7.3-7.4)*	7.4 (7.3-7.4)	7.3 (7.2-7.4)
Aspartate aminotransferase (U/L) – median (IQR)	60 (39-86)*	56 (37-79)	67 (42-105)
Creatinine (mg/dl) - median (IQR)	1.2 (0.9-2.1)*	1.1 (0.8-1.6)	1.6 (1.1-2.9)
C-reactive protein (mg/L) - median (IQR)	173 (115-238)*	168 (108-229)	185 (127-250)
D-dimer (ng/mL) - median (IQR)	2340 (1015-6135)*	2024 (825-4340)	3841 (1593-9305)
Ferritin (ng/ml) - median (IQR)	1291 (661-2214)*	1177 (622-1933)	1588 (776-2682)
High Troponin Indicator [c] - n (%)	1769 (44.0)*	820 (33.0)	949 (61.7)
Lactate (mmol/L) - median (IQR)	1.7 (1.3-2.4)*	1.6 (1.3-2.1)	2.0 (1.4-2.9)
Lymphocytes (%) - median (IQR)	8.9 (5.4-13.3)*	10.0 (6.4-14.6)	7.1 (4.0-11.1)
Procalcitonin [a] (ng/ml) - median (IQR)[1]	1.3 (0.2-4.6)*	0.8 (0.2-2.3)	1.4 (0.5-8.0)
Sodium [a] (mEq/L) - median (IQR)[1]	137 (134-140)*	136 (134-139)	137 (134-141)
Urine Output (mL) - median (IQR)	716 (436-1000)*	792 (550-1050)	579 (300-875)
White Blood Cell Count (per mm³) - median (IQR)	9.6 (6.8-13.3)*	9.0 (6.5-12.1)	10.6 (7.6-15.1)
Severity of Illness [b]			
PaO2:FiO2 (P/F) Ratio [d] (mm Hg) - median (IQR)	131 (102-158)*	135 (112-159)	123 (86-155)
Invasive Mechanical Ventilation - n (%)	2681 (66.7)*	1449 (58.4)	1232 (80.2)
Renal Replacement Therapy [e]- n (%)	258 (6.4)*	118 (4.8)	140 (9.1)
Vasopressors [f] - n (%)			
One	1367 (34.0)*	790 (31.8)	577 (37.5)

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Two or more	648 (16.1)*	282 (11.4)	366 (23.8)
TREATMENTS [b] - n (%)			
Aspirin	696 (17.3)*	389 (15.7)	307 (20.0)
Azithromycin	2003 (49.8)*	1270 (51.2)	733 (47.7)
Hydroxychloroquine	2423 (60.3)*	1457 (58.7)	966 (62.8)
Neuromuscular blockade	812 (20.2)*	428 (17.2)	384 (25.0)
Prone positioning	1087 (27.0)	663 (26.7)	424 (27.6)
Remdesivir	238 (5.9)*	168 (6.8)	70 (4.6)
Statin	913 (22.7)	553 (22.3)	360 (23.4)
Corticosteroid	1057 (26.3)*	522 (21.0)	535 (34.8)
Tocilizumab	497 (12.4)*	331 (13.3)	166 (10.8)
Vitamin C	281 (7.0)*	148 (6.0)	133 (8.7)

Table 1 Legend.
*P-value <0.05 for difference between survivors and non-survivors (Wilcoxon rank sum test for continuous variables and chi-squared for categorical)

Data regarding troponin were missing for 2544 (63%).
Data regarding PaO2:FiO2 were missing for 1576 (39%).
Data regarding PEEP day 1 were missing for 1513 (38%).
Data regarding procalcitonin were missing for 1455 (36%).
Data regarding D-dimer were missing for 1233 (31%)
Data regarding urine output were missing for 1210 (30%).
Data regarding lactate were missing for 1198 (30%)
Data regarding ferritin were missing for 1054 (26%).
Data regarding CRP were missing for 926 (23%).
Data regarding arterial pH were missing for 902 (22%).
Data regarding smoking status were missing for 745 (19%).
Data regarding lymphocytes were missing for 36 (11%).
Data regarding AST were missing for 353 (9%).
Data regarding mental status were missing for 220 (5%).
Data regarding PEEP day 2 were missing for 163 (4%).
Data form BMI were missing for 152 (4%).
Data regarding WBC was missing for 77 (2%).
Data regarding creatinine were missing for 70 (2%).
Data regarding sodium were missing for 24 (<1%)
Missing data were imputed using bagImpute and are included in the table

[a] Collected upon ICU admission
[b] Worst value or if occurred anytime during day 1-2 in the ICU
[c] Troponin T or I > the 99th percentile upper reference limit of normal for that lab
[d] Refers to the PaO2:FiO2 ratio and was only recorded in patients receiving invasive mechanical ventilation. Other values imputed.
[e] Received renal replacement therapy for acute or chronic renal failure
[f] Included phenylephrine hydrochloride, epinephrine, norepinephrine bitartrate, vasopressin, dopamine hydrochloride, dobutamine, and milrinone

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Table 2. Hospital Characteristics for Patients Included in the Study.

Variable	All patients (N = 4019)	28-Day Survivors (N = 2482)	28-Day Non-Survivors (N = 1537)
SOCIOECONOMICS OF HOSPITAL POP			
% of Population for whom Commute to Work takes > 45 min– median (IQR)	18.3 (12.9-25.5)*	17.8 (11.8-21.0)	23.4 (15.9-29.3)
% of Households Speaking English Only– median (IQR)	72.6 (62.7-80.9)*	72.9 (64.3-82.4)	70.9 (61.8-78.9)
% of Population Uninsured– median (IQR)	9.1 (5.7-13.0)	9.0 (5.7-13.0)	10.0 (5.6-13.0)
% of Population who are Black– median (IQR)	15.2 (8.9-27.0)	16.2 (9.7-27.0)	15.2 (8.3-28.0)
% of Population who are Dual Eligible– median (IQR)	2.5 (1.3-3.3)	2.6 (1.5-3.2)	2.3 (1.3-3.3)
% of Population with High School Diploma– median (IQR)	88.0 (83.3-93.5)	88.1 (83.2-92.3)	87.4 (83.3-94.5)
% of the Population who are Unemployed– median (IQR)	7.3 (5.6-9.7)	7.3 (5.6-9.2)	7.3 (5.3-9.7)
% Single Parent Households– median (IQR)	17.4 (12.8-22.1)*	17.0 (12.8-22.1)	17.5 (13.1-22.2)
Mean Household Size– median (IQR)	2.5 (2.3-2.8)*	2.5 (2.2-2.7)	2.7 (2.4-2.9)
Mean Median Home Value– median (IQR)	30,5629 (212,487-519,842)*	275,506 (206,403-519,842)	392,285 (229,155-519,842)
Mean Median Income– median (IQR)	63,078 (50637-87,753)*	62,915 (51208-87,754)	64,957 (49,753-96,175)
Metro Area – n (%)	3,534 (87.9)	2,124 (85.6)	1,410 (91.7)
HOSPITAL STRAIN – median (IQR)			
% of Hospital ICU Beds w/ STOP COVID Patients [a]	37.5 (14.4-69.6)*	30.6 (12.3-53.8)	48.2 (19.0-104.3)
County Population	932,202 (798,975-1,628,706)	945,726 (593,490-1,628,706)	932,202 (798,975-1,628,706)
ICU Occupancy Rate	75.0 (58.7-83.2)*	76.4 (63.2-84.2)	69.3 (54.2-82.1)
# Hospital Medical-Surgical Beds	510 (329-718)*	555 (358-733)	437 (266-691)
Hospital Total Occupancy Rate	77.3 (69.5-84.6)*	79.5 (69.6-84.6)	74.6 (66.8-84.5)
# of ICU Beds pre-COVID-19	88 (48-112)*	98 (54-115)	53 (47-98)
Total # of County COVID Cases in the 30 days prior to Admission [a]	1,743 (475-5,845)*	1,416 (398-4,585)	2,279 (640-7,268)
Total # of Hospital Beds	682 (448-1,006)*	794 (522-1,006)	610 (355-937)
Total # of Hospital Beds in the County	3,411 (2,286-5,326)*	3,657 (2,156-5,344)	2,768 (2,310-5,069)
In COVID ICU or surge - n (%)	3047 (76)	1879 (76)	1168 (76)
HOSPITAL QUALITY – median (IQR)			
Standardized Outcomes Mortality Score	0.9 (0.4-1.9)*	1.0 (0.4-2.0)	0.5 (0.4-1.4)
Standardized Outcomes Readmission Score	-0.9 (-2.0--0.4)*	-0.9 (-1.7--0.4)	-0.9 (-2.2--0.4)
Standardized Outcomes Safety Score	-0.1 (-1.1-0.6)*	-0.1 (-1.0-0.7)	-0.3 (-1.7-0.2)
Standardized Patient Experience Score	-0.3 (-0.7-0.4)*	0.0 (-0.6-0.4)	-0.6 (-0.9-0.2)
Standardized Process Effect Score	-0.1 (-0.8-0.6)*	0.1 (-0.5-0.6)	-0.3 (-1.4-0.5)
Standardized Process Time Score	-1.6 (-2.8--0.8)	-1.6 (-2.7--0.9)	-1.6 (-2.8--0.4)
Study Day	30 (23-40)	30 (23-41)	30 (23-39)
HOSPITAL TREATMENT INTENSITY – n (%)			
% patients vented w/ P/F < 150 receiving more intense therapies	60 (47-67)*	57 (47-67)	63 (43-67)

Table 2 Legend.

*P-value <0.05 for difference between survivors and non-survivors (Wilcoxon rank sum test for continuous variables and chi-squared for categorical)
[a] Time-varying based on the date of patient admission.

Data regarding ICU occupancy rate was missing for 97 (2%)
Missing data were imputed using bagImpute and are included in the table

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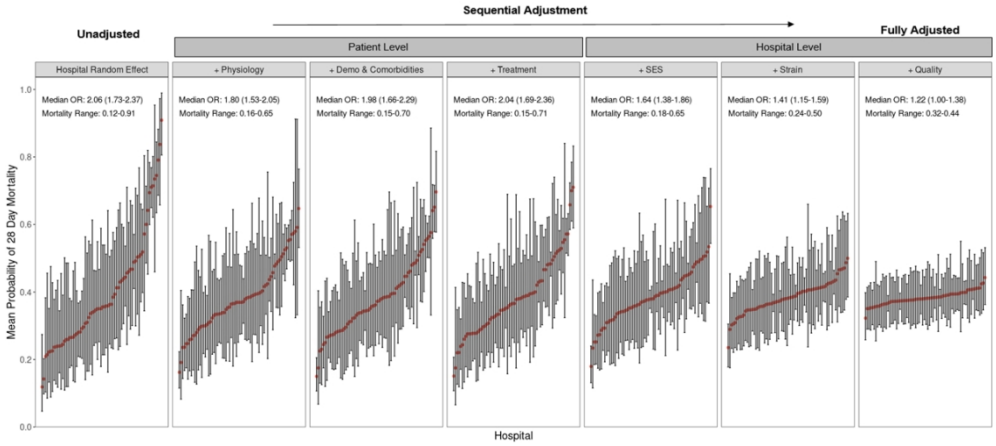

Figure 1. Case-mix Adjusted Probabilities of 28-day Mortality. The graphs illustrate the change in interhospital variation in death as each domain is added to the unadjusted mixed-effects model (leftmost panel) and ending with the fully adjusted model (rightmost panel), which shows that most of the variation in mortality across hospitals can be explained by the domains included. The x-axis is hospital ranked by increasing probability of death in 28 days, and the y-axis shows the case-mix adjusted probability of death in the mixed-effects regression model, with the red dots denoting the point estimates and the whiskers denoting the 95% confidence intervals. The median odds ratio (OR) and range in mortality are presented for each model. Abbreviations: Demo = Demographics, SES = Socioeconomic Status

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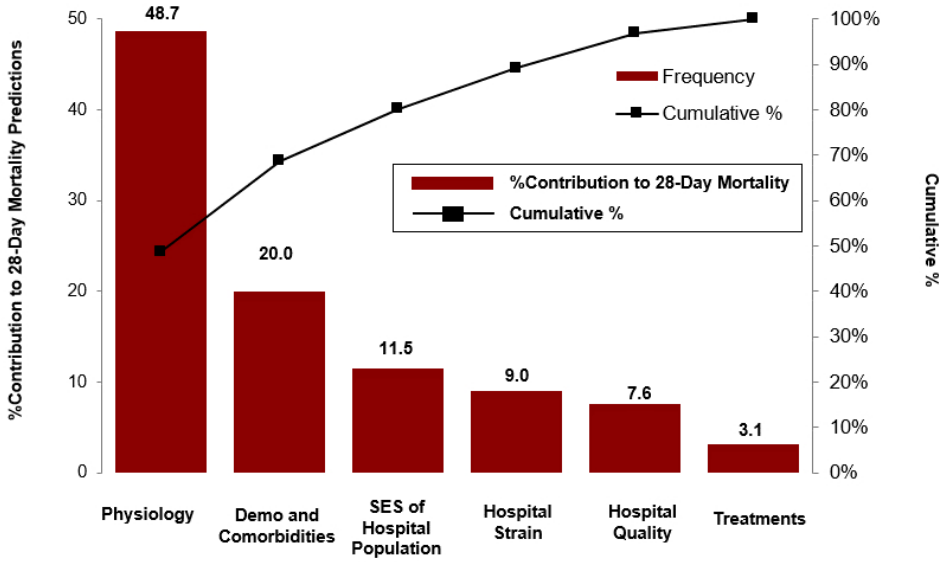

Figure 2. Contributions to 28-Day Mortality Risk Based on Shapley Values. The figure illustrates the relative contribution of all variables in each domain based on Shapley values calculated from the XGBoost machine learning model (red bars; left y-axis). The cumulative contribution of the domains, moving from left to right in the figure, is shown with the line plot (right y-axis). Abbreviations: Demo = Demographics, SES = Socioeconomic Status, Pop = Population

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Hospital-Level Variation in Death for Critically Ill Patients with COVID-19

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Supplementary Appendix

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University of Kentucky Medical Center: Javier A. Neyra*, Nourhan Chaaban

University Medical Center of Southern Nevada: Alfredo Iardino, Elizabeth H. Au, Jill H. Sharma

University of Miami Health System: Marie Anne Sosa*, Sabrina Taldone, Gabriel Contreras, David De La Zerda, Alessia Fornoni, Hayley B. Gershengorn

University of Michigan: Salim S. Hayek*, Pennelope Blakely, Hanna Berlin, Tariq U. Azam, Husam Shadid, Michael Pan, Patrick O' Hayer, Chelsea Meloche, Rafey Feroze, Rayan Kaakati, Danny Perry, Abbas Bitar, Elizabeth Anderson, Kishan J. Padalia, Christopher Launius, John P. Donnelly, Andrew J. Admon

University of North Carolina School of Medicine: Jennifer E. Flythe*, Matthew J. Tugman, Emily H. Chang

University of Oklahoma Health Sciences Center: Brent R. Brown*

University of Pennsylvania Health System: Amanda K. Leonberg-Yoo*, Ryan C. Spiardi, Todd A. Miano, Meaghan S. Roche, Charles R. Vasquez

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University of Pittsburgh Medical Center: Amar D. Bansal*, Natalie C. Ernecoff, Sanjana Kapoor, Siddharth Verma, Huiwen Chen

University of Tennessee Health Science Center and Memphis VA Medical Center/Methodist University Hospital – Csaba P. Kovesdy*, Miklos Z. Molnar*, Ambreen Azhar

University of Texas Southwestern Medical Center and Parkland Health and Hospital System: S. Susan Hedayati*, Mridula V. Nadamuni, Shani Shastri, Duwayne L. Willett

University of Vermont Larner College of Medicine: Samuel A.P. Short

University of Virginia Health System: Amanda D. Renaghan*, Kyle B. Enfield

University of Washington Medical Center: Pavan K. Bhatraju*, A. Bilal Malik

Vanderbilt University Medical Center: Matthew W. Semler

Washington University in St. Louis/Barnes Jewish Hospital: Anitha Vijayan*, Christina Mariyam Joy, Tingting Li, Seth Goldberg, Patricia F. Kao

Wellforce Health System: Lowell General Hospital **-** Greg L. Schumaker*, Tufts Medical Center - Nitender Goyal*, Anthony J. Faugno, Greg L. Schumaker, Caroline M. Hsu, Asma Tariq, Leah Meyer, Ravi K. Kshirsagar, Daniel E. Weiner

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Table E1. STOP-COVID Sites and Hospitals Included in this Study

Site	Hospitals
Northeast	
Beth Israel Deaconess Medical Center	Beth Israel Deaconess Medical Center
Brigham and Women's Faulkner Hospital	Brigham and Women's Faulkner Hospital
Brigham and Women's Hospital	Brigham and Women's Hospital
Cooper University Health Care	Cooper University Hospital
	Inspira Medical Center Vineland
Hackensack Meridian Health Hackensack University Medical Center	Hackensack Meridian Health Pascack Valley Medical
Hackensack Mountainside Hospital	Hackensack-UMC Mountainside Hospital
Johns Hopkins Hospital	Johns Hopkins Hospital
	Johns Hopkins Bayview Medical Center
Kings County Hospital Center	Kings County Hospital Center
Massachusetts General Hospital	Massachusetts General Hospital
MedStar Georgetown University Hospital	MedStar Georgetown University Hospital
Montefiore Medical Center	Montefiore Medical Center
Mount Sinai	Mount Sinai
Newton Wellesley Hospital	Newton Wellesley Hospital
New York-Presbyterian Queens Hospital	New York-Presbyterian Queens Hospital
New York-Presbyterian/Weill Cornell Medical Center	New York-Presbyterian/Weill Cornell Medical Center
New York University Langone Hospital	New York University Langone Hospital
Rutgers/New Jersey Medical School	University Hospital
Rutgers/Robert Wood Johnson Medical School	Robert Wood Johnson Medical School
Temple University Hospital	Temple University Hospital
Thomas Jefferson University Hospital	Kennedy University Hospital – Stratford Division
	Thomas Jefferson University Hospital
Tufts Medical Center	Tufts Medical Center
	Lowell General Hospital
University of Pennsylvania Health System	University Medical Center of Princeton at Plainsboro
	Penn Presbyterian Medical Center
	Hospital of University of Pennsylvania
University of Pittsburgh Medical Center	UPMC Passavant
Westchester Medical Center	Westchester Medical Center
Yale University Medical Center	Yale-New Haven Hospital
South	
Baylor College of Medicine, Houston	Harris Health System
Baylor University Medical Center/Baylor Scott White and Health	Baylor University Medical Center
Duke University Medical Center	Duke University Medical Center
Memphis VA Medical Center/ Methodist University Hospital	Methodist Healthcare Memphis Hospitals
Ochsner Medical Center	Ochsner Medical Center
Tulane Medical Center	Tulane Medical Center
University of Alabama-Birmingham Hospital	University of Alabama Hospital
University of Florida Health-Gainesville	UF Health Shands Hospital
University of North Carolina Hospitals	University of North Carolina Hospitals
University of Texas Southwestern Medical Center	Parkland Health and Hospital System
University of Virginia Health System	University of Virginia Medical Center
Midwest	
Barnes-Jewish Hospital	Barnes-Jewish Hospital
Cook County Health	John H Stroger Jr Hospital
Froedtert Hospital	Froedtert Memorial Lutheran Hospital
Indiana University Health Methodist Hospital	Indiana University Health
Mayo Clinic, Rochester Minnesota	Mayo Clinic, Rochester Minnesota
Northwestern Memorial Hospital	Northwestern Memorial Hospital
Promedica Health System	Bay Park Community Hospital
	Promedica Monroe Regional Hospital
	Toledo Hospital
Rush University Medical Center	Rush University Medical Center
University Hospitals Cleveland Medical Center	UH Cleveland Medical Center
	University Hospitals Ahuja Medical Center
University of Chicago Medical Center	University of Chicago Medical Center
University of Illinois Hospital and Health Sciences System	University of Illinois Hospital and Health Sciences System
University of Kentucky Hospital	University of Kentucky Hospital
University of Michigan Hospital	University of Michigan Hospital
West	

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Loma Linda University Medical Center	Loma Linda University Medical Center
Mayo Clinic, Arizona	Mayo Clinic, Arizona
Renown Health	Renown Regional Medical Center
Stanford Healthcare	Stanford Healthcare
University of California-Davis Medical Center	University of California-Davis Medical Center
University of California-Los Angeles Medical Center	Ronald Reagan UCLA Medical Center
University of California-San Diego Medical Center	UC San Diego Health Hillcrest - Hillcrest Med Ctr
University of California-San Francisco Medical Center	UCSF Medical Center
UCHealth University of Colorado	University of Colorado Hospital Authority
University Medical Center of Southern Nevada	University Medical Center
University of Washington Medical Center	Harborview Medical Center
	University of Washington Medical Ctr

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Table E2. Variable Descriptions and Sources

Variable	Description/Collection Notes	Source
Vitals	Collected on day 1 of ICU admission	STOP COVID dataset
Altered Mental Status		
Highest Heart Rate (beats/min)		
Highest Respiratory Rate (beats/min)		
Lowest Systolic Blood Pressure (mm Hg)		
Max Temperature (°C)		
Labs	Collected once a day for the first 14 days in the ICU – used worst value during days 1-2 in the ICU (sodium and procalcitonin were recorded on day 1 only)	
Arterial pH		
Aspartate aminotransferase - AST (U/L)		
C-reactive protein - CRP (mg/L)		
Creatinine (mg/dl)		
D-dimer (ng/mL)		
Ferritin (ng/ml)		
High Troponin Indicator		
Lactate (mmol/L)		
Lymphocytes (%)		
Procalcitonin (ng/ml)		
Sodium (mEq/L)		
Urine Output (mL)		
White Blood Cell Count (per mm3)		
Severity of Illness		
P/F Ratio (mm Hg)	Collected only on patients receiving invasive mechanical ventilation with an arterial blood gas available	
Ventilator Status		
PEEP		
Number of Vasopressors	Maximum number of vasopressors required each day	
Renal Replacement Therapy	CRRT, intermittent hemodialysis, peritoneal dialysis, other	
Demographics		
Age (years)		
Body Mass Index (BMI)		
Current or Former Smoker	Per chart review; does not include vaping or smoking of non-tobacco products. Non-smoker, former smoker, current smoker	
Race and Ethnicity		
Sex (Male)		
Pre-existing Comorbidities		
Active Cancer	Per manual chart review of the electronic health record.	
Congestive Heart Failure		
Chronic Obstructive Pulmonary Disease (COPD)		
Coronary Artery Disease		
Diabetes		
End Stage Renal Disease (ESRD)		
Hypertension		
Treatments		
Aspirin	Date recorded for day of treatment initiation. Indicated as present if date of initiation was either before ICU admission or on ICU days 1 or 2.	
Azithromycin		
Corticosteroid		
Hydroxychloroquine		
Neuromuscular Blockade		
Prone positioning		
Remdesivir		
Statin		
Tocilizumab		
Vitamin C (IV or PO)		
Hospital Level Treatment Intensity	Percentage of mechanically ventilated patients with a PaO2/FiO2 ratio<150 who were treated with extracorporeal membrane oxygenation, inhaled pulmonary vasodilators, tocilizumab, prone positioning, or neuromuscular blockade.	
SES of Hospital Population		
% of Households Speaking English Only	Geographic catchment regions were calculated for each hospital based on the number of hospital beds. American Community Survey results where then combined across the closest block groups containing this population.	American Community Survey 2015 summarized over each hospital's local geographic catchment area. US Census Bureau. American Community Survey 5-Year Estimates. 2015. Available at: https://www.nhgis.org. Accessed March 22,
% of Population for whom Work Commute takes > 45 min		
% of Population Uninsured		
% of Population who are Black		
% of Population who are Dual Eligible		

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% of Population with High School Diploma		2018.
% of the Population who are Unemployed		
% Single Parent Households		
Mean Household Size		
Mean Median Home Value		
Mean Median Income		
Metro Area		USDA Rural-Urban Continuum Codes https://www.ers.usda.gov/data-products/rural-urban-continuum-codes.aspx
Hospital Strain		
# of COVID Cases in the County in the last 30 Days		John's Hopkins Database https://github.com/CSSEGISandData/COVID-19/tree/master/csse_covid_19_data/csse_covid_19_time_series
# of pre-COVID ICU Beds		STOP COVID Dataset
% of Hospital ICU Beds w/ STOP COVID Patients	Calculated using the total number of ICU beds in the hospital prior to the pandemic in the denominator and the current number of hospitalized COVID patients in the numerator.	
COVID-specific or Surge ICU	Whether an ICU was a COVID-specific ICU or surge ICU.	
# of Hospital Medical-Surgical Beds	From the 2018 AHA Annual Surveys of Hospitals and U.S. Census Bureau population data – published Jan 31,2020	American Hospital Association 2018 survey data https://www.aha.org/statistics/fast-facts-us-hospitals
Hospital Total Occupancy Rate		
Total # of Hospital Beds		
Total # of Hospital Beds in the County		
ICU Occupancy Rate		Healthcare Cost Report Information System, a Centers for Medicare and Medicaid Services dataset composed of the cost reports submitted by Medicare-certified hospitals
County Population		United States Census Bureau 2019 https://www.census.gov/data/datasets/time-series/demo/popest/2010s-counties-total.html#par_textimage_70769902
Hospital Quality		Medicare Hospital Compare dataset US Centers for Medicare Medicaid Services. December 2017 Hospital Compare. . Available at: www.medicare.gov/hospitalcompare/search.html. Accessed August 14, 2018.
Standardized Outcomes Mortality Score	Up to 57 quality metrics were assessed and combined into 7 quality group scores. These then determine the star rating from 1-5 used by Medicare. We use 6 of the 7 score components (efficiency excluded due to multicolinearity). Score were standardized across all hospitals in the Medicare Compare dataset.	
Standardized Outcomes Readmission Score		
Standardized Outcomes Safety Score		
Standardized Patient Experience Score		
Standardized Process Effect Score		
Standardized Process Time Score		
Study Day	Days since study start	STOP COVID Dataset
Other		
Death	Discharged, follow-up 28 + days, or death before day 28	STOP COVID Dataset
Hospital Name	Used for linking to Medicare provider ID for hospital data	

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Table E3. Final Mixed-Effects Model Coefficient Odds Ratios

Variable	Odds Ratio (95% CI)
PHYSIOLOGY	
Vitals	
Altered Mental Status	1.566 (1.287 - 1.906)
Highest Heart Rate (beats/min)	1.004 (1.000 - 1.008)
Highest Respiratory Rate (beats/min)	0.997 (0.988 - 1.005)
Lowest Systolic Blood Pressure (mm Hg)	0.999 (0.995 - 1.003)
Max Temperature (°C)	0.980 (0.900 - 1.067)
Labs	
Arterial pH	0.206 (0.079 - 0.540)
Aspartate aminotransferase - AST (U/L)	1.000 (1.000 - 1.001)
C-reactive protein - CRP (mg/L)	1.000 (0.999 - 1.001)
Creatinine (mg/dl)	1.098 (1.041 - 1.159)
D-dimer (ng/mL)	1.000 (1.000 - 1.000)
Ferritin (ng/ml)	1.000 (1.000 - 1.000)
High Troponin Indicator	1.238 (1.022 - 1.499)
Lactate (mmol/L)	1.151 (1.086 - 1.220)
Lymphocytes (%)	0.997 (0.987 - 1.007)
Procalcitonin (ng/ml)	0.997 (0.991 - 1.002)
Sodium (mEq/L)	1.019 (1.005 - 1.034)
Urine Output (mL)	1.000 (1.000 - 1.000)
White Blood Cell Count (per mm3)	0.996 (0.982 - 1.010)
Severity of Illness	
P/F Ratio (mm Hg)	0.998 (0.997 - 0.999)
Ventilator Status Day 1 (ref = not ventilated)	
Mechanical Ventilator and PEEP 5 or less	1.604 (0.970 - 2.655)
Mechanical Ventilator and PEEP 6-10	2.493 (1.685 - 3.689)
Mechanical Ventilator and PEEP 11-15	2.026 (1.405 - 2.922)
Mechanical Ventilator and PEEP > 15	2.012 (1.289 - 3.138)
BiPAP/CPAP/HFNC	2.227 (1.626 - 3.051)
Mechanical Ventilator Day 2	0.798 (0.490 - 1.300)
PEEP Day 2	1.036 (1.001 - 1.072)
Number of Vasopressors (ref = none)	
One	1.087 (0.873 - 1.353)
Two or more	1.330 (1.003 - 1.765)
Renal Replacement Therapy	1.054 (0.699 - 1.590)
DEMOGRAPHICS & PRE-EXISTING COMORBIDITIES	
Demographics	
Age (years)	1.049 (1.041 - 1.057)
Body Mass Index (BMI)	1.017 (1.006 - 1.029)
Smoker Ever	1.225 (1.013 - 1.482)
Race/Ethnicity (ref = Non-Hispanic White)	
Hispanic	1.055 (0.828 - 1.343)
Non-Hispanic Black	0.773 (0.614 - 0.972)
Unknown/Other	0.926 (0.724 - 1.184)
Sex (Male)	1.447 (1.214 - 1.725)
Pre-existing Comorbidities	
Active Cancer	2.121 (1.482 - 3.035)
Congestive Heart Failure	1.204 (0.927 - 1.564)
Chronic Obstructive Pulmonary Disease (COPD)	1.381 (1.045 - 1.825)
Coronary Artery Disease	1.113 (0.880 - 1.408)
Diabetes	1.156 (0.976 - 1.370)
End Stage Renal Disease (ESRD)	0.795 (0.461 - 1.369)
Hypertension	1.034 (0.858 - 1.246)
TREATMENTS	
Aspirin	1.246 (0.994 - 1.564)
Azithromycin	1.031 (0.865 - 1.229)
Corticosteroid	1.251 (1.022 - 1.531)
Hydroxychloroquine	0.987 (0.809 - 1.203)
Neuromuscular Blockade	1.389 (1.120 - 1.723)
Prone positioning	0.951 (0.776 - 1.165)
Remdesivir	1.235 (0.858 - 1.779)
Statin	0.983 (0.798 - 1.211)
Tocilizumab	0.733 (0.565 - 0.951)
Vitamin C (IV or PO)	0.825 (0.592 - 1.149)
Hospital Level Treatment Intensity	0.998 (0.992 - 1.005)

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SES OF HOSPITAL POPULATION	
% of Households Speaking English Only	0.969 (0.947 - 0.993)
% of Population for whom Commute to Work takes >45 min	1.021 (0.996 - 1.047)
% of Population Uninsured	1.012 (0.943 - 1.085)
% of Population who are Black	1.010 (0.988 - 1.032)
% of Population who are Dual Eligible	0.841 (0.629 - 1.123)
% of Population with High School Diploma	1.083 (1.002 - 1.171)
% of the Population who are Unemployed	1.008 (0.928 - 1.095)
% Single Parent Households	0.992 (0.907 - 1.085)
Mean Household Size	1.563 (0.454 - 5.384)
Mean Median Home Value	1.000 (1.000 - 1.000)
Mean Median Income	1.000 (1.000 - 1.000)
Metro Area	0.991 (0.590 - 1.665)
HOSPITAL STRAIN	
# of COVID Cases in the County in the last 30 Days [a]	0.998 (0.994 - 1.003)
# of pre-COVID ICU Beds (ref > 100)	
51-100	1.030 (0.757 - 1.402)
≤ 50	1.605 (0.946 - 2.723)
% of Hospital ICU Beds w/ STOP COVID Patients	1.021 (0.789 - 1.322)
# of Hospital Medical Surgical Beds	1.002 (1.000 - 1.004)
Hospital Total Occupancy Rate	0.978 (0.963 - 0.993)
Total # of Hospital Beds	0.999 (0.997 - 1.000)
Total # of Hospital Beds in the County [a]	1.004 (0.994 - 1.013)
ICU Occupancy Rate	0.999 (0.989 - 1.010)
Indictor for COVID ICU or Surge	1.162 (0.938 - 1.439)
HOSPITAL QUALITY	
Standardized Outcomes Mortality Score	0.680 (0.579 - 0.799)
Standardized Outcomes Readmission Score	0.969 (0.824 - 1.140)
Standardized Outcomes Safety Score	0.983 (0.859 - 1.124)
Standardized Patient Experience Score	0.976 (0.766 - 1.245)
Standardized Process Effect Score	0.962 (0.800 - 1.157)
Standardized Process Time Score	0.977 (0.835 - 1.143)
Study day	0.996 (0.988 - 1.005)
OTHER	
Intercept	1.120 (0 - 97905)
Hospital RE	0.043 (0.008 - 0.222)

Table E3. Legend

[a] scaled to county pop (note in XGBoost model did not scale and included county population as its own variable due to the interaction mechanisms in XGBoost)

Abbreviations: ICU = intensive care unit, RE = random effect

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Figure E1. Study CONSORT Diagram

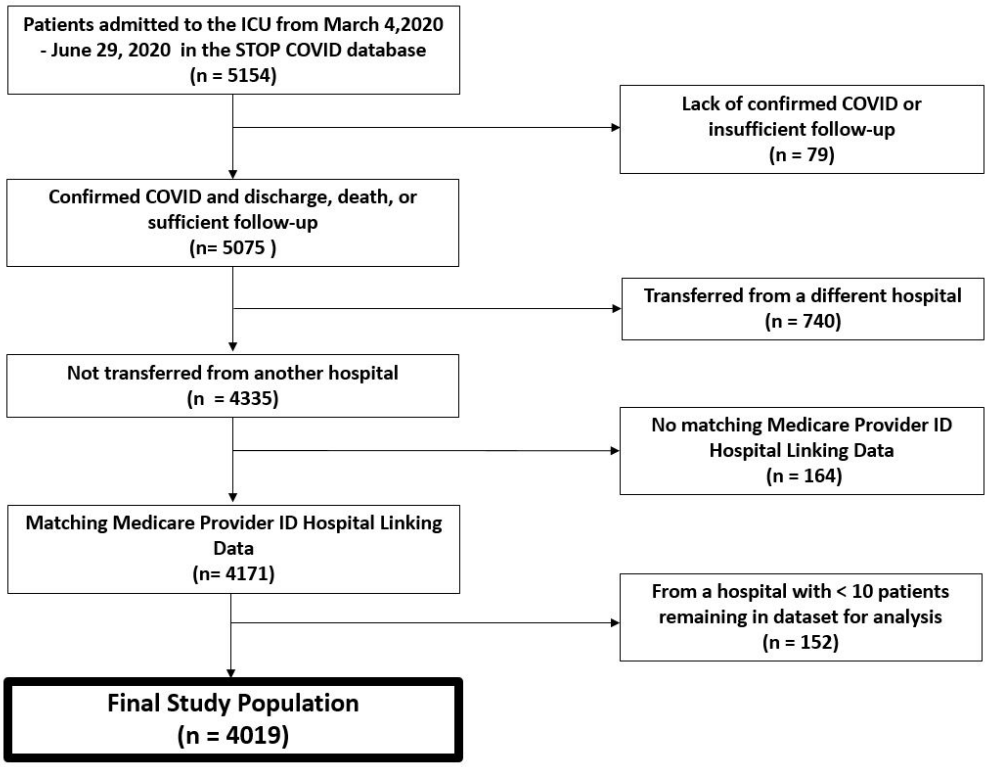

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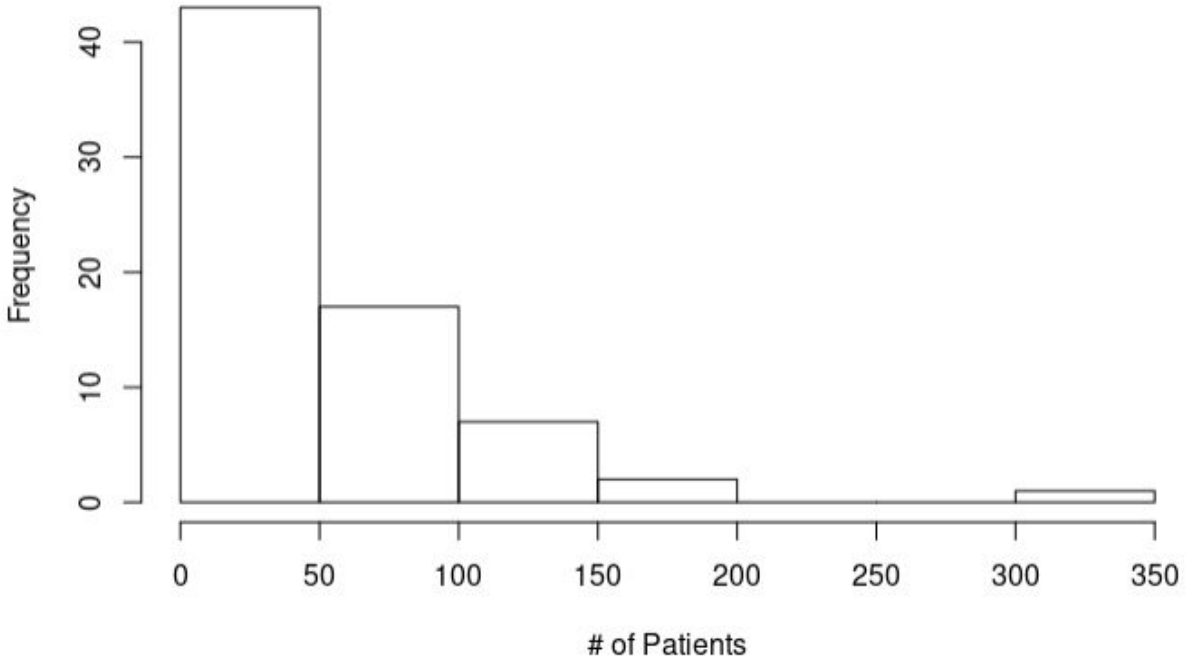
Figure E2. Histogram of the Number of Patients at each Hospital.



Abbreviations: # = Number

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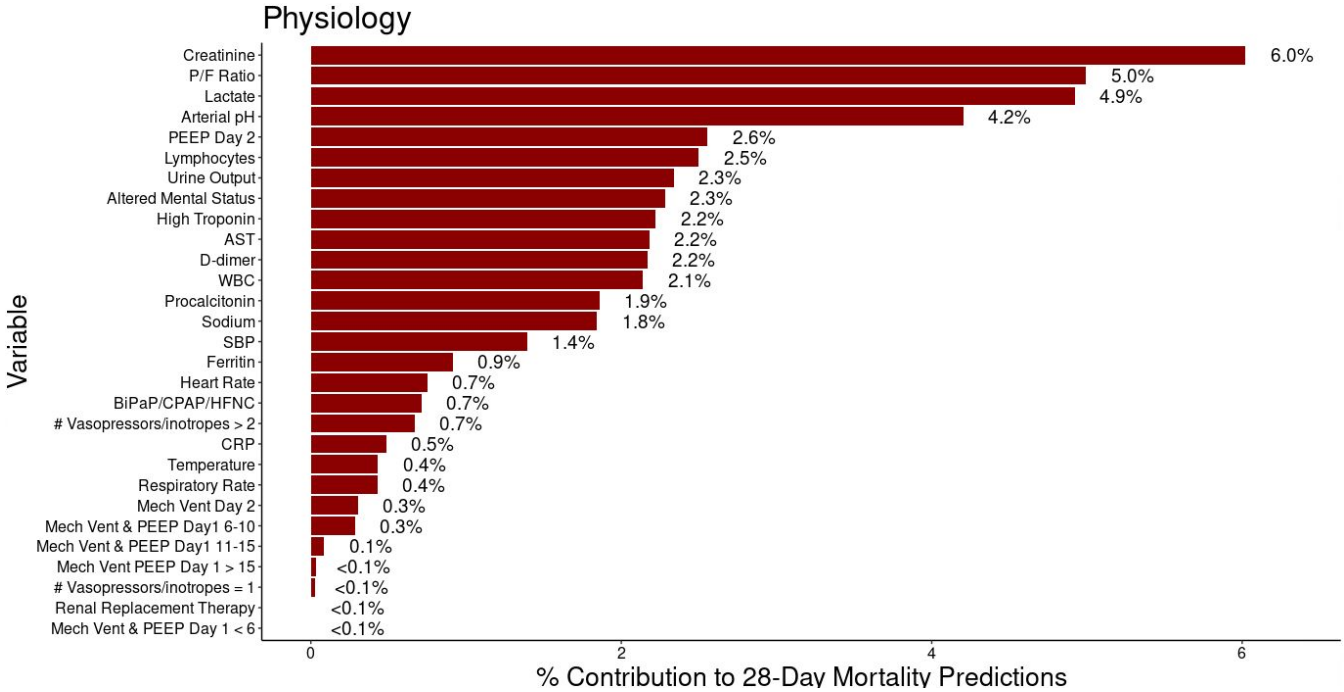
Figure E3. Shapley Value Percentage Contributions to the XGBoost Model Prediction within the Physiology Domain. The figure shows the sum of the percent contributions of each variable in the physiology domain (vitals, labs, and ventilation).



Abbreviations: WBC = white blood cell; AST = Aspartate transaminase, SBP = Systolic blood pressure, CRP = C-reactive Protein, Mech = Mechanical, Vent = Ventilation

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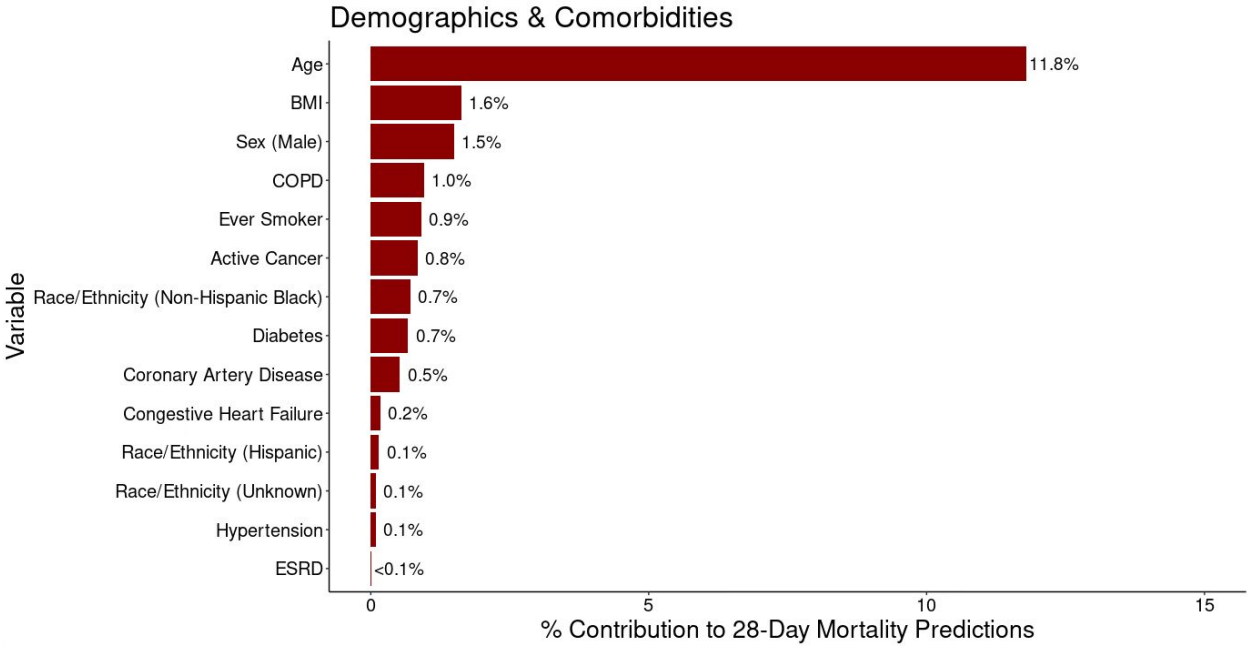
Figure E4. Shapley Value Percentage Contributions to the XGBoost Model Prediction within the Demographics and Comorbidities Domain. The figure shows the sum of the percent contributions of each variable in the demographics and comorbidities domain.



Abbreviations: BMI = Body mass index, COPD = Chronic obstructive pulmonary disease; ESRD = End stage renal disease

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Figure E5. Shapley Value Percentage Contributions to the XGBoost Model Prediction within the Socioeconomics of the Hospital Population Domain. The figure shows the sum of the percent contributions of each variable in the socioeconomics of hospital population domain.

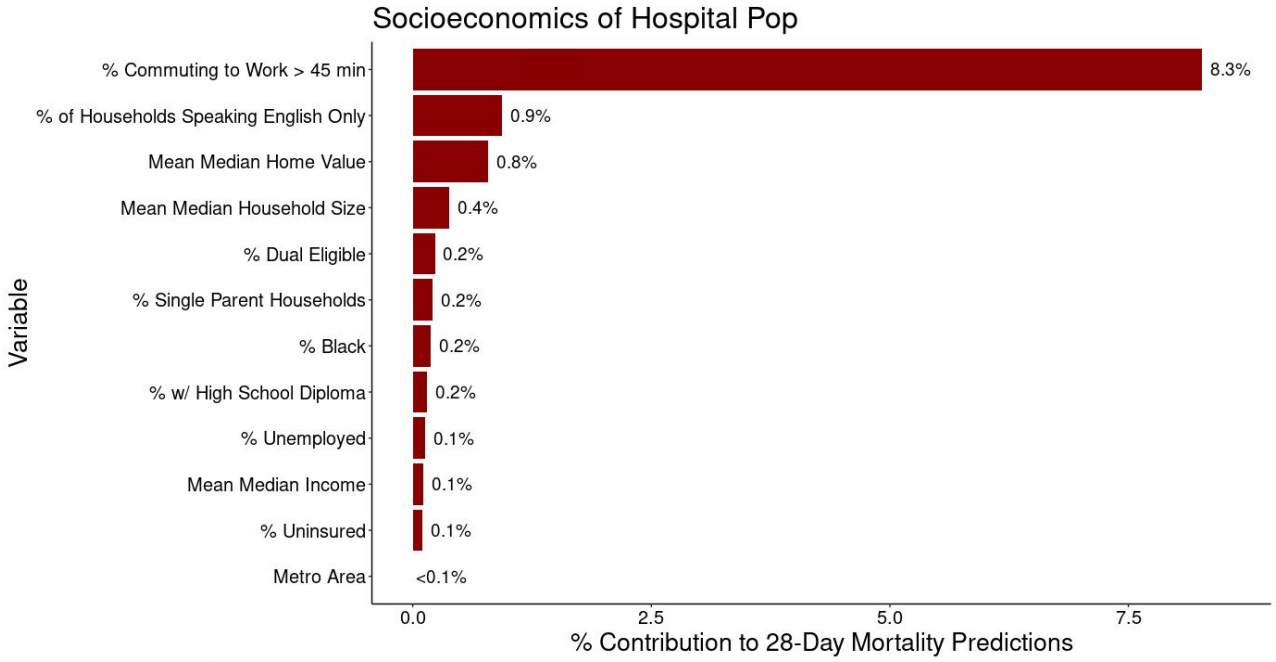

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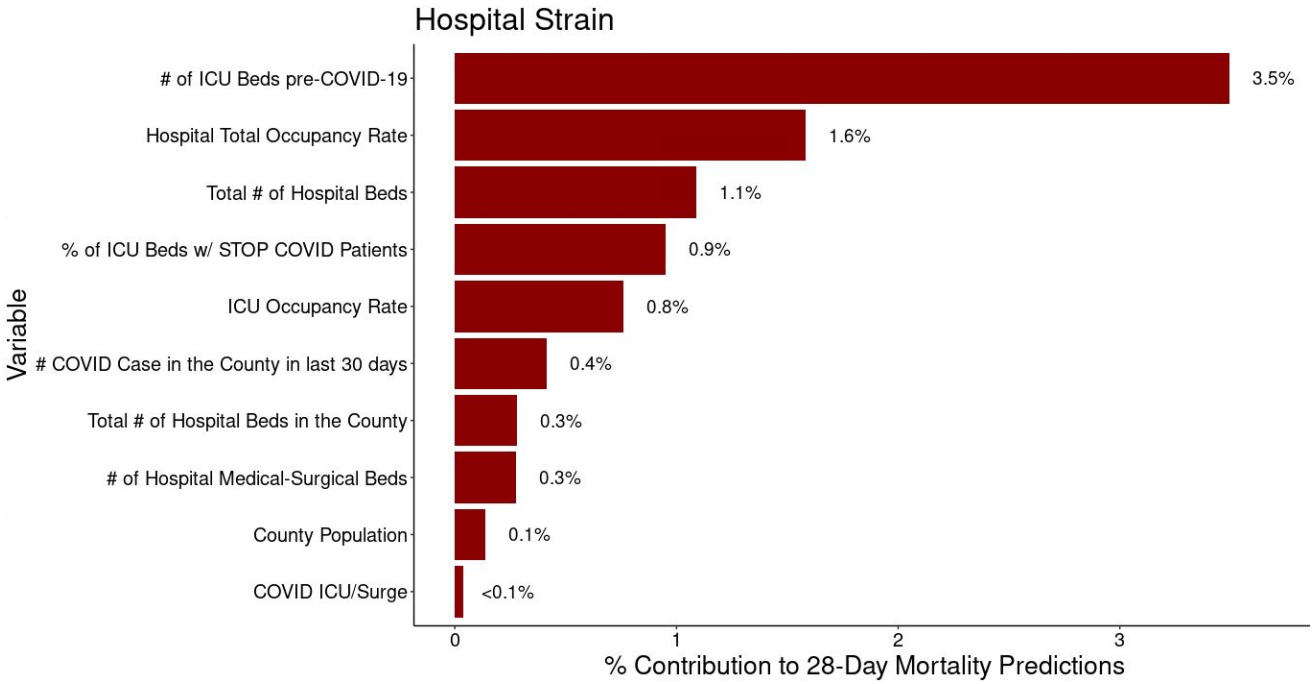
Figure E6. Shapley Value Percentage Contributions to the XGBoost Model Prediction within the Hospital Strain Domain. The figure shows the sum of the percent contributions of each variable in the hospital strain domain.



Abbreviations: # = number, ICU = intensive care unit

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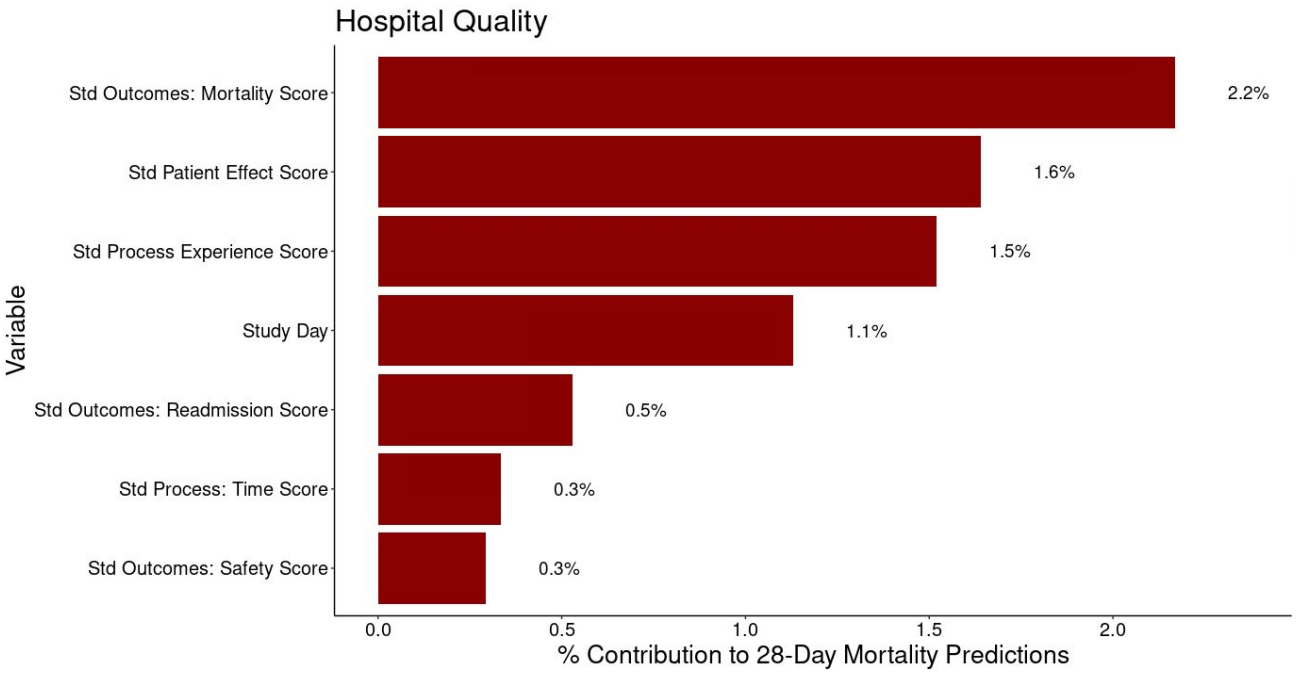
Figure E7. Shapley Value Percentage Contributions to the XGBoost Model Prediction within the Hospital Quality Domain. The figure shows the sum of the percent contributions of each variable in the hospital quality domain.



Abbreviations: Std = Standardized

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Figure E8. Shapley Value Percentage Contributions to the XGBoost Model Prediction within the Treatment Domain. The figure shows the sum of the percent contributions of each variable in the treatment domain.

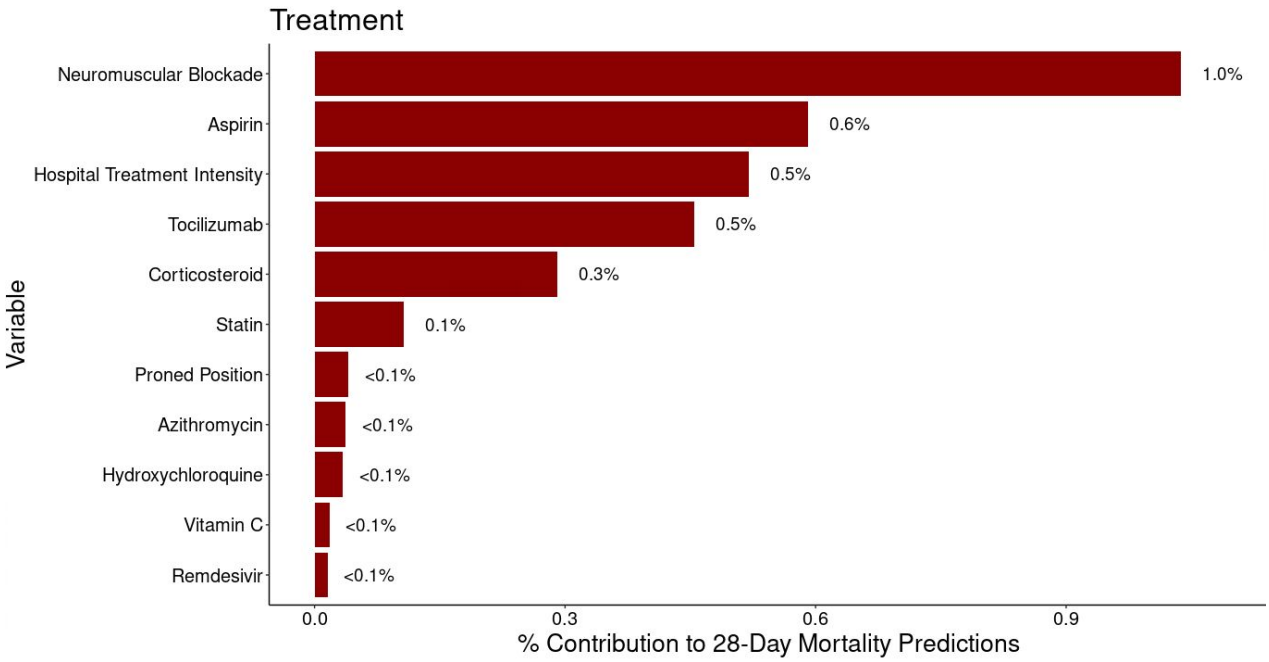

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Figure E9. Case-mix Adjusted Probabilities of In-Hospital Mortality. The graphs illustrate the change in interhospital variation in death as each domain is added to the unadjusted mixed-effects model (leftmost panel) and ending with the fully adjusted model (rightmost panel), which shows that most of the variation in mortality across hospitals can be explained by the domains included. The x-axis is hospital ranked by increasing probability of in-hospital death, and the y-axis shows the case-mix adjusted probability of death in the mixed-effects regression model, with the red dots denoting the point estimates and the whiskers denoting the 95% confidence intervals. The median odds ratio (OR) and range in mortality are presented for each model.
Abbreviations: Demo = Demographics, SES = Socioeconomic Status

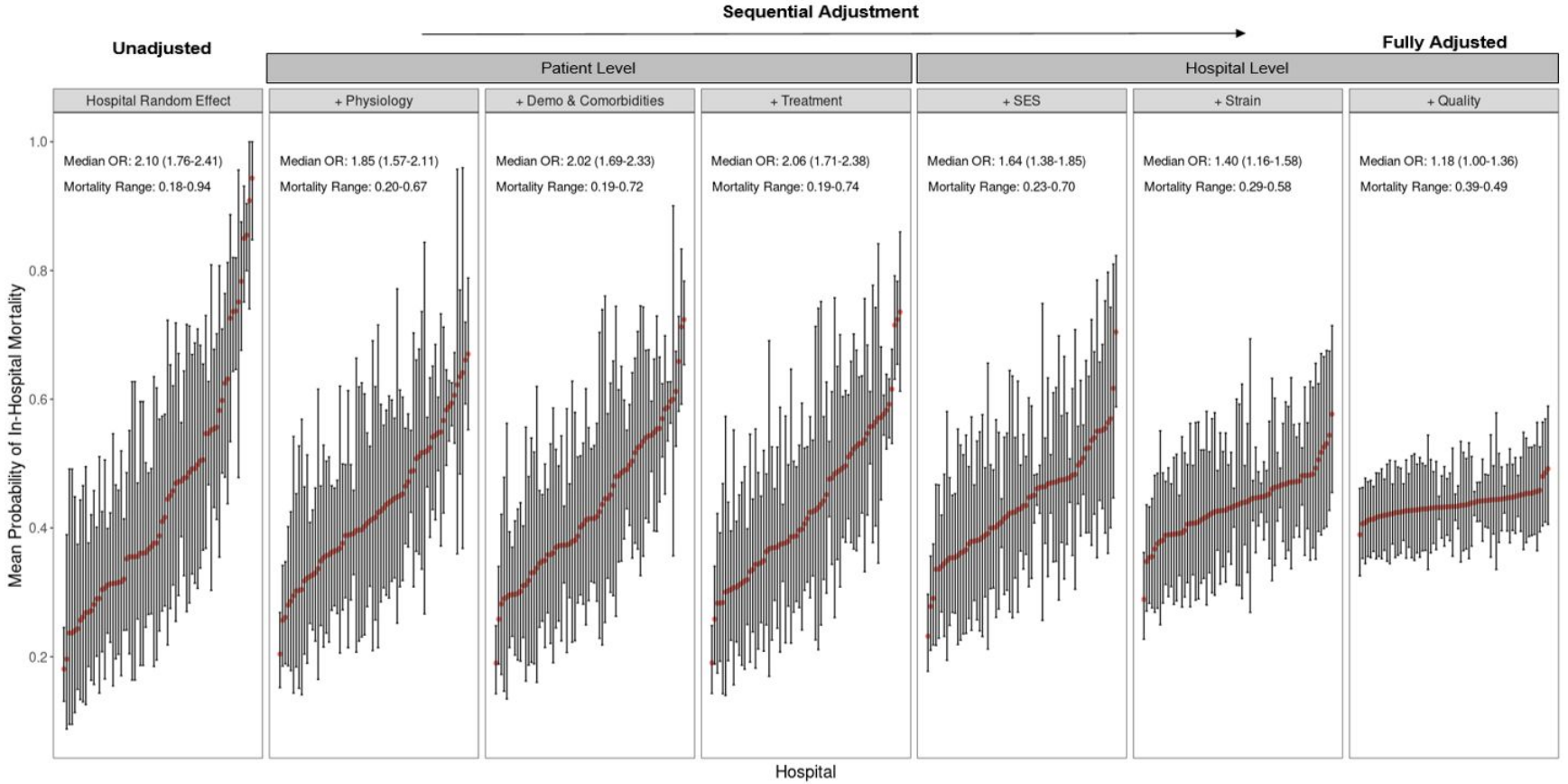

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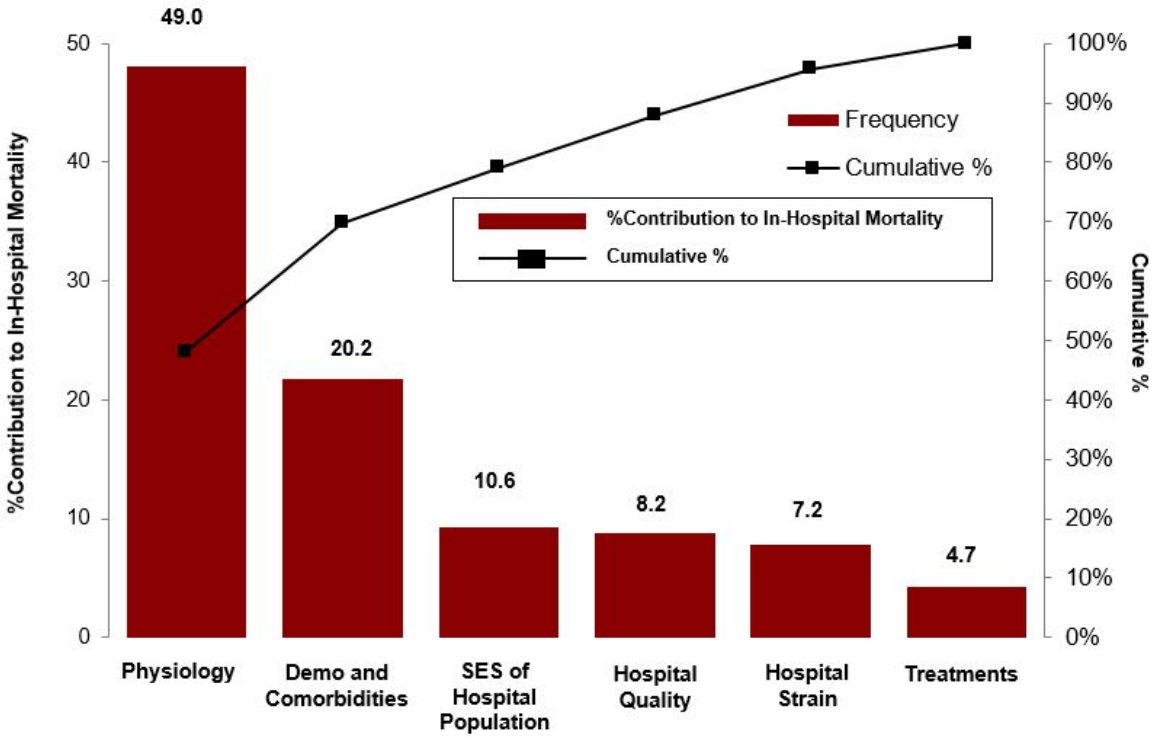
Figure E10. Contributions to In-Hospital Mortality Risk Based on Shapley Values. The figure illustrates the relative contribution of all variables in each domain based on Shapley values calculated from the XGBoost machine learning model (red bars; left y-axis). The cumulative contribution of the domains, moving from left to right in the figure, is shown with the line plot (right y-axis).



Abbreviations: Demo = Demographics, SES = Socioeconomic Status, Pop = Population

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Figure E11. Case-mix Adjusted Probabilities of 28-Day Mortality with Transfer Patients included. The graphs illustrate the change in interhospital variation in death as each domain is added to the unadjusted mixed-effects model (leftmost panel) and ending with the fully adjusted model (rightmost panel), which shows that most of the variation in mortality across hospitals can be explained by the domains included. The x-axis is hospital ranked by increasing probability of in-hospital death, and the y-axis shows the case-mix adjusted probability of death in the mixed-effects regression model, with the red dots denoting the point estimates and the whiskers denoting the 95% confidence intervals. The median odds ratio (OR) and range in mortality are presented for each model. Abbreviations: Demo = Demographics, SES = Socioeconomic Status

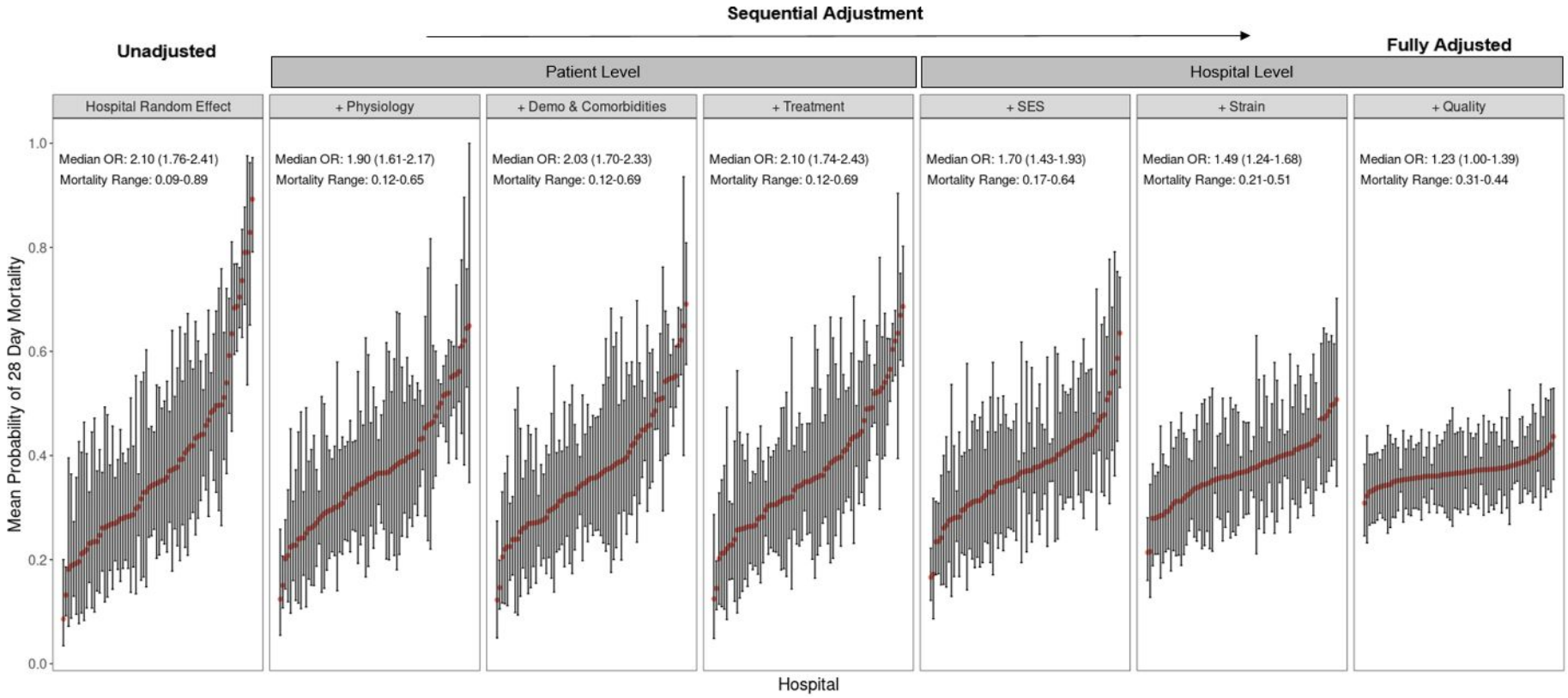

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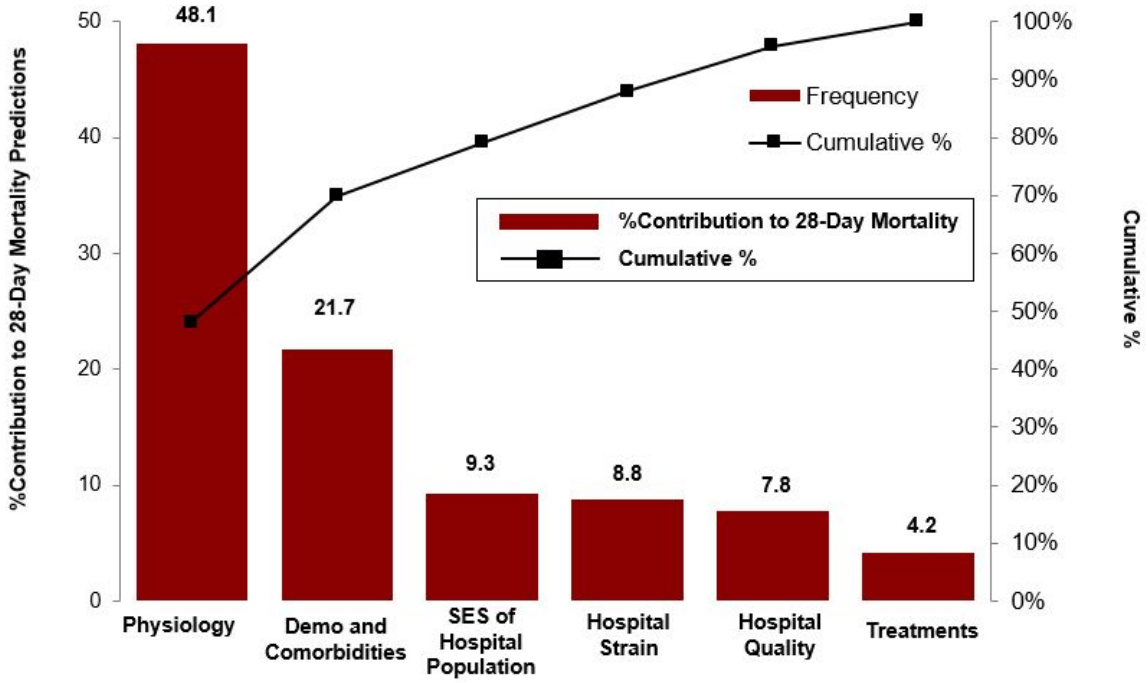
Figure E12. Contributions to 28-Day Mortality Risk with Transfer Patients included Based on Shapley Values. The figure illustrates the relative contribution of all variables in each domain based on Shapley values calculated from the XGBoost machine learning model (red bars; left y-axis). The cumulative contribution of the domains, moving from left to right in the figure, is shown with the line plot (right y-axis).



Abbreviations: Demo = Demographics, SES = Socioeconomic Status, Pop = Population

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