Factors associated with hospitalization and critical illness among 5,279 patients with COVID-19 disease in New York City: A prospective cohort study

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Abstract

Objective: To describe outcomes of hospitalized patients with COVID-19 in the United States, and the clinical and laboratory characteristics associated with severity of illness.

Design, Setting and Participants: Cross-sectional analysis of all patients with laboratory-confirmed SARS-Cov-2 infection at a single academic medical center in New York City between March 1, 2020 and April 8, 2020. The final date of follow up was May 5, 2020.

Main outcomes and measures: Primary outcomes were hospitalization, critical illness (intensive care, mechanical ventilation, discharge to hospice and/or death) and discharge to hospice and/or death alone. Predictors included patient demographics, medical history, vital signs and laboratory results. We conducted multivariable logistic regression to identify risk factors for adverse outcomes, and competing risk survival analysis for mortality.

Results: Of 11,544 patients tested for COVID-19, 5,566 (48.2%) were positive; 5,279 were included. A total of 2,741 (51.9%) were hospitalized, of whom 1,904 (69.5%) have been discharged, and 665 (24.3%) have died or been discharged to hospice. Of 647 (23.6%) patients requiring mechanical ventilation, 391 (60.4%) have died and 170 (26.2%) have been discharged or extubated to date. The strongest risk for hospitalization was age, with odds ratio (OR)>2 for all age groups above 44 years and OR 37.9 (95% confidence interval [CI] 26.1-56.0) for age ≥75 years. Heart failure (OR 4.4, 95% CI 2.6-8.0), male sex (OR 2.8, 95% CI 2.4-3.2), chronic kidney disease (OR 2.6, 95% CI, 1.9-3.6), and any elevation in BMI (e.g., for BMI>40 OR 2.5, 95% CI, 1.8-3.4) were other risks. For development of critical illness, the strongest risks besides age were heart failure (OR 1.9, 95% CI, 1.4-2.5); BMI > 40 (OR 1.5, 95% CI 1.0-2.2); and male sex (OR 1.5, 95% CI 1.3-1.8). However, among hospitalized patients, admission oxygen saturation <88% (OR 3.7, 95% CI 2.8-4.8), troponin >1 (OR 4.8, 95% CI, 2.1-10.9), C-reactive protein (CRP) >200 (OR 5.1, 95% CI, 2.8-9.2), and d-dimer>2500 (OR 3.9, 95% CI, 2.6-6.0) were more strongly associated with critical illness than age or comorbidities. Risk of critical illness decreased significantly over the study period. Similar associations were found for mortality alone.

Conclusions: Age and comorbidities are powerful predictors of hospitalization and to a lesser extent of critical illness and mortality; however, when added, admission oxygen impairment and markers of inflammation are most strongly associated with critical illness and mortality. Outcomes appear to be improving over time.

Background

The first announcement of a cluster of novel pneumonia-like illness was made on December 31, 2019 by China. Since then, the causative organism, SARS-Cov-2, has produced a global pandemic that to date has infected over 2.2 million people and directly resulted in over 150,000 known deaths.

While several reports from China,[1,2] Italy,[3,4] and most recently the United States [5-7] have described some characteristics of patients with COVID-19, the disease caused by SARS-Cov-2, little is understood about factors associated with hospital admission and with severe disease. Studies to date have included few patients with severe outcomes,[1,8-12] or have not compared those to patients with less virulent disease,[13-15] making it difficult to assess characteristics associated with poor outcomes. No large studies have conducted multivariable regression to help identify the strongest risk factors.

New York City is now the epicenter of the COVID-19 outbreak in the United States, with over 170,000 known cases in the city and over 13,000 confirmed deaths as of May 5: more than anywhere else in the country.[17] In this report, we describe characteristics of COVID-19 patients treated at a large quaternary academic health system in New York City and Long Island, and the association of these characteristics with adverse outcomes.

Methods

Study setting

The study was conducted at NYU Langone Health, which includes over 260 outpatient office sites and four acute care hospitals (Tisch Hospital and NYU Langone Orthopedic Hospital in Manhattan, NYU Langone Hospital – Brooklyn in Brooklyn, and NYU Winthrop on Long

Island), ranging from a quaternary care hospital to a safety net institution. As the epidemic evolved, the health system added intensive care unit beds and inpatient capacity, resulting in a peak of approximately 394 ICU beds and 1,357 non-ICU beds.

Study cohort

We began with all patients tested for SARS-Cov-2 between March 1, 2020 and April 8, 2020. We then created a cohort of patients with confirmed COVID-19, defined as a positive result on real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay of nasopharyngeal or oropharyngeal swab specimens. Initial tests were conducted by the New York City Department of Health and Mental Hygiene; as of March 16, tests were conducted in our clinical laboratory using the Roche SARS-CoV2 assay in the Cobas 6800 instruments through emergency use authorization (EUA) granted by the FDA. On March 31, we added testing using the SARS-CoV2 Xpert Xpress assay in the Cepheid GeneXpert instruments also under EUA by FDA. The targets amplified by these assays are the ORF1/a and E in the Roche Cobas assay and N2 and E genes in the Cepheid XpertXpress. After March 16, only nasopharyngeal samples were collected and tested.

Testing was performed for patients presenting to the emergency department who were likely to be admitted with any complaint consistent with COVID-19, including fever, cough, shortness of breath, fatigue, gastrointestinal complaints, syncope, known exposure to a COVID-19 positive patient, or clinician concern. In addition, ambulatory testing was available by appointment with clinician's referral until March 26, 2020, when New York State recommended restricting testing of patients with mild or moderate illness. Outpatient testing of symptomatic or concerned employees remained available throughout the study period. Repeat testing of negative

specimens was conducted at clinician discretion. If testing was repeated and discordant (i.e. negative test followed by a positive test), we used the positive result.

We excluded from the COVID-19 cohort 287 patients who were not hospitalized, were missing all data besides age and sex, and had no prior visits within the health system. We obtained complete follow up on the COVID-19 cohort through May 5, 2020.

Data sources and patient and public involvement

All study data was obtained from the electronic health record (Epic Systems, Verona, WI), which is an integrated electronic health record (EHR) including all inpatient and outpatient visits in the health system. For data on tobacco use, body mass index (BMI) and comorbidities, we included any data in the EHR, including data entered during prior inpatient or outpatient visits in the problem list, medical history section or on encounter diagnoses.

Patients and the public were not a priori involved in the design and conduct of the study, in the choice of outcomes, in recruitment, or in planned dissemination. However, we incorporated many comments from the public on an earlier preprint version of the paper into the final analysis.

Main outcomes

We assessed three primary outcomes: inpatient hospitalization; critical illness, defined as a composite of care in the intensive care unit, use of mechanical ventilation, discharge to hospice, or death; and discharge to hospice or death among hospitalized patients. We assessed outcomes longitudinally over the entire study period, not just at the time of the initial testing event. For patients with multiple visits, the most severe outcome was assigned. For instance, patients who did not need hospitalization at time of initial testing but were later hospitalized

were assigned to the hospitalization group. Similarly, patients who were initially admitted and discharged and then readmitted requiring invasive ventilation were assigned to the critical illness group.

Predictors

We obtained from the electronic health record the following variables: age at time of testing, sex, race/ethnicity as reported by the patient (aggregated into non-Hispanic white, non-Hispanic African American, Asian, Hispanic, other/multiracial and unknown), and history of hypertension, hyperlipidemia, coronary artery disease, heart failure, pulmonary disease (defined by chronic obstructive pulmonary disease or asthma), malignancy (excluding non-metastatic non-melanoma skin cancer), diabetes, and obesity (defined by most recent body mass index). We also obtained vital signs and first set of laboratory results where available. For multivariable modeling, we bucketed vital sign and laboratory results into categories by degree of abnormality based on clinical judgment because of non-linear associations with outcome. We selected these predictors based on prior published literature[1,5] and our clinical experience with COVID-19 patients.

Statistical analysis

We used descriptive statistics to characterize each cohort of patients: those not hospitalized, all those hospitalized, those hospitalized without critical illness, and those with critical illness (care in intensive care unit, mechanical ventilation, discharge to hospice, or death). We then fitted multivariable logistic regression models with admission and with critical illness as the outcomes to identify factors associated with those outcomes. In analyses using hospitalization as the outcome, we included only patient demographics and comorbidities, since

77% of the patients who were not admitted were evaluated in ambulatory testing centers and did not have vitals or laboratory studies collected. For the critical illness analyses, we included the above predictors and for one of the models added temperature and oxygen saturation on presentation, as well as the first result of c-reactive protein, d-dimer, ferritin, procalcitonin, and troponin when obtained. We included all selected predictors based on *a priori* clinical significance after testing for collinearity using the variance inflation factor (VIF) and ensuring none had VIF>2.[18] We also tested for overall multicolllinearity among all variables simultaneously using the determinant of correlation matrix implemented in R's mctest library and found no significant results.[19]

For the admission model, we included all patients testing positive (excluding the 287 patients with no data besides age and sex). We constructed two models for association with critical illness. First, we constructed a model restricted to hospitalized patients including all demographic and comorbidity predictors, and a random effect for hospital to account for clustering by facility. Second, we added to that model vital signs and the first set of laboratory results, to assess clinical associations with critical illness among hospitalized patients. We excluded from the second model four patients who expired in the emergency department before vital signs or laboratory results could be collected. We obtained odds ratios from the models and profiled confidence intervals for the odds ratios using the approach of Venables & Ripley,[20] since assuming normality of the maximum likelihood estimate to estimate Wald-type confidence intervals can lead to biased estimates.[21] We also calculated average marginal effects for each predictor by using the margins library in R, which uses a discrete first-difference in predicted outcomes to obtain the AME.

Finally, we fitted a competing risk model for the mortality or hospice outcome with time from first positive test as the start point, including only hospitalized patients.[22] We considered discharge from hospital to be a competing risk, since mortality data are limited after that point unless the patient is readmitted to our system (in which case the newest hospitalization would be included). Patients still hospitalized as of May 5, 2020 were counted as censored. The model was fitted with the R library cmprisk[23] and the proportionality assumption was checked with the goffte library.[24] We fitted two competing risk models, one adjusting for demographics and comorbidities, and one adding admission vitals and laboratory studies.

All statistical analyses were conducted with R, version 3.6.3. All analyses used 2-sided statistical tests and we considered a p value < 0.05 to be statistically significant without adjustment for multiple testing.

This study was approved by the NYU Grossman School of Medicine Institutional Review Board (IRB #i20-00485), which granted both a waiver of informed consent, and a waiver of the Health Information Portability and Privacy Act.

Results

During the study period, the health system tested 11,544 patients for COVID-19, of whom 5,566 (48.2%) were positive and 287 were then excluded for lack of data. Of the remaining 5,279 patients testing positive, 2,538 (48.1%) were treated only as outpatients through the end of the study period, and 2,741 (51.9%) required admission to the hospital. Nearly all those admitted to the hospital (2,729, 99.6%) have experienced a study outcome: 1,739/2,741 (63.4%) were discharged without critical illness and 990/2,741 (36.1%) experienced critical illness, including 665/2,741 (24.3%) who have been discharged to hospice or died to date.

Among the 990 patients with critical illness, 647 (65.4%) required mechanical ventilation, 102 (10.3%) required intensive care without mechanical ventilation, and 241 (24.3%) were discharged to hospice or died without either intensive care or mechanical ventilation. Final outcomes to date for each subgroup are shown in **Figure 1**.

Characteristics of study population

The median age of the COVID-19 positive study population was 54 years (interquartile range, 38 to 66), and 2,615 (49.5%) were male. A total of 1,296 (24.6%) had diabetes, 1,865 (35.3%) obesity, and 2,752 (52.1%) any form of cardiovascular disease. Among hospitalized patients, the median length of stay was 7 days (interquartile range, 3 to 13; full range 0-52). Median length of stay for those still hospitalized with critical illness (N=160) is 36 (IQR 32-40, full range 3-52). See **Appendix Table S1** for characteristics of those testing negative. Among tests performed in the emergency department, 83.9% were for patients that were admitted and 16.1% were for patients that were discharged (**Appendix Tables S2 and S3**). Characteristics of patients seen in the ED for suspected COVID-19 but not tested are shown in **Appendix Table S4**.

Hospitalized patients were more likely to be male (61.2% vs 36.9%) and were substantially more likely to have comorbidities than non-hospitalized patients (any comorbidity, 79.7% vs 44.8%), particularly with regard to cardiovascular disease (70.6% vs. 32.2%), diabetes (37.9% vs 10.1%), and chronic kidney disease (21.2% vs. 2.6%) (**Table 1**). Differences in sex and comorbidities between hospitalized patients experiencing critical illness and those who did not were much smaller. Among these patients, differences in clinical presentation and laboratory results were more prominent. Patients with critical illness more often presented with hypoxia (initial O2 saturation 25th percentile 86% versus 92%), and had higher initial levels of c-reactive

protein (median 136.3 vs 89.1), d-dimer (median 528 vs 324), ferritin (median 925 vs 613), procalcitonin (0.27 vs 0.10) and troponin (0.07 vs 0.02) (**Table 2**).

Predictors of hospitalization

In multivariable analysis of the full COVID-19 positive cohort, the factors most strongly associated with hospitalization were age, including 75 years or older (OR 37.9, 95% CI, 26.1-56.0; average marginal effect [AME] 58%), age 65-74 (OR 8.7, 95% CI, 8.7-11.2, AME 40%), heart failure (OR 4.4, 95% CI 2.6-8.0, AME 22%), male sex (OR 2.8, 95% CI 2.4-3.2, AME 16%), chronic kidney disease (OR 2.6, 95% CI, 1.9-3.6, AME 14%), and any elevation in BMI (e.g., for BMI>40 OR 2.5, 95% CI, 1.8-3.4, AME 14%). Also significant was hypertension. Hyperlipidemia was associated with lower hospitalization risk (OR 0.6, 95% CI, 0.5-0.7, AME -7%) as was former or current smoking status; however, unknown smoking status had higher risk (OR 1.4, 95% CI 1.2-1.8, AME 5%) (**Table 1**). A sensitivity analysis adding patients seen in the ED for suspected COVID-19 but not tested produced similar results (**Appendix Table S5**).

Among hospitalized patients with COVID-19, the factors most associated with critical illness were age, including 75 years or older (OR 3.5, 95% CI 2.5-4.8) and 65-74 (OR 2.9, 95% CI, 2.1-4.0); heart failure (OR 1.9, 95% CI, 1.4-2.5); BMI > 40 (OR 1.5, 95% CI 1.0-2.2); and male sex (OR 1.5, 95% CI 1.3-1.8), with diabetes also significant (**Table 3**). Risk of critical illness declined progressively as the study period progressed, with lowest being in the last week (OR 0.4, 95% CI, 0.2-0.6).

Being self-reported Hispanic was associated with increased risk of admission but not critical illness; the increased admission risk was eliminated once ED treat-and-release patients

were included (**Appendix Table S5**). African American patients had similar admission risk as white patients and lower risk of critical illness (OR 0.7, 95% CI, 0.5-0.9).

After adding admission vitals and first set of laboratory results to the critical illness model, only age, heart failure and BMI >40 remained significant risks; in this model, the factors most associated with critical illness were admission oxygen saturation <88% (OR 3.7, 95% CI 2.8-4.8), troponin >1 (OR 4.8, 95% CI, 2.1-10.9), C-reactive protein (CRP) >200 (OR 5.1, 95% CI, 2.8-9.2), and d-dimer>2500 (OR 3.9, 95% CI, 2.6-6.0) (**Table 3**).

The competing risk mortality analysis showed similar characteristics to confer increased hazard as the critical illness model, but fewer were significant. The hazard ratio increased proportionally by age, with HR 10.3 (95% CI, 6.4-16.8) for age ≥75. Other significant factors included heart failure (HR 1.8, 95% CI 1.4-2.2), male sex (HR 1.3, 95% CI 1.1-1.5), and cancer (HR 1.3, 95% CI, 1.1-1.6). Vitals and laboratory results on presentation carried significant additional hazard, chiefly hypoxia on presentation (HR 2.0, 95% CI 1.6-2.5 for SpO2<88%), C reactive protein (all abnormal levels had HR >3.5), d-dimer (HR 2.2, 95% CI 1.6-3.0 for first result >2500) and troponin (HR 2.1, 95% CI 1.4-3.2 for first result >1) (**Table 4**). Representative cumulative incidence functions are shown in **Figure 2** (age groupings), **Figure 3** (heart failure, cancer, diabetes, male sex) and **Figure 4** (admission oxygen saturation, C-reactive protein, d-dimer, lymphocyte count).

Discussion

In this report, we describe characteristics of 5,279 adult patients with laboratory-confirmed COVID-19 disease in New York City, of whom 2,741 required hospital admission and 990 required intensive care, mechanical ventilation, were discharged to hospice and/or died.

A total of 94% of hospitalized patients have been discharged alive or to hospice or have died, providing robust final outcome results. We find particularly strong associations of older age, male sex, heart failure, chronic kidney disease and obesity with hospitalization and critical illness risk among all patients with COVID-19, with less influence of chronic pulmonary disease and other forms of heart disease. By contrast, we found comorbidities to be less strongly associated with critical illness in hospitalized patients. Among those patients, we noted the importance of hypoxia despite supplemental oxygen and early elevations in inflammatory markers (especially d-dimer and c-reactive protein) in distinguishing among patients who go on to develop critical illness and those who do not. In the hospitalized population, measures of inflammation were much more important than demographic characteristics and comorbidities.

The first detailed COVID-19 case series included 1,099 hospitalized patients with laboratory-confirmed infection in China, of whom only 25 (2.3%) underwent invasive ventilation and 15 (1.4%) died.[1] A recent report of 5700 hospitalized patients from a different health system in New York City found that at least 9.7% had already died (24.5% of mechanically ventilated patients); however, 53.8% of the patients in this study (72.2% of ventilated) were still hospitalized, with a median follow up of only 4.5 days. By contrast, 23.6% of hospitalized patients in our case series required invasive ventilation and 24.3% have died to date, with 93% of patients having completed hospitalization. If all remaining hospitalized patients died, the overall mortality would be a maximum of 30.5%. Given the very high prevalence of disease in New York City and the relative paucity of baseline hospital beds per capita (1.5-2.7 beds per 1,000 in all boroughs except Manhattan), admission thresholds may be higher in New York City than in China (4.2 beds per 1,000).[27,28] Moreover, in the series by Guan et al, only a quarter of the

hospitalized patients had any chronic comorbidity, whereas in our series 80% of hospitalized patients had at least one of eight major chronic diseases.

In fact, outcomes in the majority of reports are similar to ours. A commentary by the Chinese Center for Disease Control and Prevention described outcomes for 72,314 cases, of which 14% were severe (similar to hospitalized patients in our series) and 5% critical with respiratory or multi-organ failure (similar to those requiring ICU level care or mechanical ventilation in our series).[2] Among critical cases, mortality was 49%; we find 57% among all ICU or ventilated patients. Finally, our results are also consistent with a recent national case series reported by the US CDC that found that 457 of 1,037 (44%) hospitalized patients required ICU admission, and that three quarters had at least one chronic condition.[6] Overall, the death rate we find for critically ill patients is a bit higher than the typical mortality rate from acute respiratory distress syndrome (ARDS) of about 35-45%.[29,30]

The comorbidities we identified as associated with hospitalization in COVID-19 are largely similar to those associated with any type of severe infectious disease requiring hospitalization or ICU level care,[31] though we were surprised that chronic pulmonary disease did not feature more prominently. Others have also noted the surprising absence of asthma and COPD as risks for severity of illness in patients with Covid-19.[32] The pathophysiologic reasons for this are unknown. The demographic distribution of hospitalized patients is also similar to other acute respiratory infections. For instance, while advanced age was by far the most important predictor of hospitalization and severe outcomes (as it is for most illnesses), 53% of hospitalized adult patients were younger than 65 years. This is typical of the hospitalization pattern in viral respiratory disease. Studies of influenza hospitalizations in the United States have

found that people younger than 65 years (including children) account for 53-57% of influenza-related hospitalizations.[33,34]

Surprisingly, though some have speculated that high rates of smoking in China explained some of the morbidity in those patients, we did not find tobacco use to be associated with increased risk of hospitalization or critical illness; in fact, it even appeared protective for hospitalization. However, this may be artifactual: patients with unknown smoking status had significantly higher risks of admission and of critical illness. It is possible that data are disproportionately missing for current or former smokers who might not care to answer that question; if so that would attenuate the apparent benefit of smoking. Very few (<5%) of patients had a recorded history of vaping; separate analyses could not be conducted for those patients.

We noted striking association of inflammatory markers with mortality and critical illness among hospitalized patients; particularly, early elevations in c-reactive protein and d-dimer. Hyperinflammatory states are well described in severe sepsis;[35] however, the degree to which COVID-19 related inflammation is similar to or different than that typically found in sepsis is unknown. Some emerging case reports suggest that patients with critical COVID-19 disease are developing complications from hypercoagulability,[10] including both pulmonary emboli[36] and microscopic thrombi.[37] In this regard it is notable that one of the chronic conditions strongly associated with critical illness was obesity. Obesity is well-recognized to be a pro-inflammatory condition.[38,39] In addition, this might explain why hyperlipidemia appeared to be protective for hospitalization, though not for critical illness: statin therapy is anti-inflammatory and has been shown to reduce cytokine levels.[40] Some studies suggest that elevated LDL itself may be beneficial in reducing mortality from respiratory diseases through direct anti-infectious properties, though mean LDL levels were low in our population.[41] Finally, we noted that early

elevation in procalcitonin was an important risk for critical illness and mortality, although COVID-19 appears to be characterized by low procalcitonin levels in general. While many patients with elevated procalcitonin and critical illness were treated with antibiotics, it remains unclear whether these patients actually had bacterial disease or whether the elevation in procalcitonin was another manifestation of a general hyperinflammatory state.

Last, we were interested to note that, while risk of hospitalization was constant across the study period, risk of critical illness (and directionally, but not significantly, mortality) decreased over time. Our institution was stretched but not overwhelmed by the epidemic and did not experience significant equipment or treatment shortages. The improvement in outcomes over time (in the setting of a functioning health system) raises the possibility that familiarity with the disease, ongoing iteration of protocols and practices in response to observed outcomes, and initiation of new treatments may improve outcomes even in the absence of vaccination or regimens known to be effective.

This study includes several limitations. Most important, data on non-hospitalized patients was more limited because many did not have vital signs or blood samples collected, and may not have had as detailed a medical history taken. They are also a heterogenous group made even more heterogeneous by changing testing thresholds over time. We may therefore be overestimating the importance of chronic disease in hospitalization risk. This limitation may be further exacerbated by the fact that patients treated and released from the ED were not commonly tested and thus omitted from our analysis unless later hospitalized, yet might be more likely to have comorbidities than those tested in outpatient settings. However, a sensitivity analysis including these patients showed similar results. Our patients were all from a single geographic region, treated within a single health system; factors associated with poor outcomes

may differ elsewhere, though our patient population is very diverse. We did not have inflammatory markers available for non-hospitalized patients; it is possible that these would have been strong predictors for hospitalization risk, not just critical illness, if available. Moreover, a standardized admission laboratory protocol was only established about two weeks into the epidemic, resulting in missing laboratory data for earlier patients, especially those who were less acutely ill. Finally, our outcome assignments may be imperfect: some patients in the non-hospitalized group may have been hospitalized at other institutions, and some discharged patients may have been readmitted elsewhere with critical illness, or may have died post-discharge.

Overall, we find that age and comorbidities are powerful predictors of requiring hospitalization rather than outpatient care; however, degree of oxygen impairment and markers of inflammation are strongest predictors of poor outcomes during hospitalization. Clinicians should consider routinely obtaining inflammatory markers during hospitalizations for COVID-19.

What is already known on this topic

- Demographics and prevalence of comorbidities in patients with COVID-19, particularly hospitalized patients, have been described in several countries
- Early outcomes of patients with critical illness have been described, but usually include a substantial portion of patients still with incomplete follow up.
- It is uncertain which demographics, comorbidities and laboratory results increase risk for adverse outcomes.

What this study adds

- This comprehensive study of all patients with COVID-19 tested and treated at a health system in New York City, in which 93% of hospitalized patients have died or been discharged, indicates that the overall mortality rate for hospitalized patients was between 24-30%
- Age, heart failure, male sex, chronic kidney disease and obesity were major risk factors for hospitalization and for development of critical illness once hospitalized.
- Hypoxia and elevated inflammatory laboratory studies early in hospitalization were significant markers for adverse events.

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Figure legends

Figure 1: Flow diagram of included patients

Figure 2: Cumulative incidence function for discharge alive and death, by age group

Figure 3: Cumulative incidence function for discharge alive and death, by heart failure, cancer, diabetes and male sex.

Figure 4: Cumulative incidence function for discharge alive and death, by admission oxygenation, C-reactive protein, d-dimer and lymphocyte count

Table 1: Characteristics of Covid-19 patients, by hospitalization status, and multivariable risk of hospitalization

Characteristic	Overall, N=5,279 N (%) or median (IQR)	Not hospitalized, N=2,538 N (column %) or median (IQR)	Hospitalized, N=2,741 N (column %) or median (IQR)	Risk of hospitalization Odds ratio (95% CI)	p	Average marginal effect
Week						
10 (March 2-8)	7 (0.1)	1 (0.0)	6 (0.2)	Reference		
11 (March 9-15)	92 (1.7)	33 (1.3)	59 (2.2)			
12 (March 16-22)	996 (18.9)	637 (25.1)	359 (13.1)	0.4 (0.24-0.67)	<0.001	-14%
13 (March 23-29)	1182 (22.4)	401 (15.8)	781 (28.5)	1.42 (0.85-2.34)	0.176	5%
14 (March 30-April 5)	2115 (40.1)	1056 (41.6)	1059 (38.6)	0.78 (0.47-1.27)	0.317	-4%
15 (April 6-April 8)	887 (16.8)	410 (16.2)	477 (17.4)	0.66 (0.39-1.1)	0.111	-6%
Age, median	54 (38-66)	42 (32-55)	63 (51-74)			
Age, years						
19-44	1846 (35.0)	1409 (55.5)	437 (15.9)	Reference	<0.001	
45-54	902 (17.1)	492 (19.4)	410 (15.0)	2.14 (1.76-2.59)	<0.001	14%
55-64	1021 (19.3)	416 (16.4)	605 (22.1)	3.67 (3.01-4.48)	<0.001	24%
65-74	797 (15.1)	176 (6.9)	621 (22.7)	8.7 (6.77-11.22)	<0.001	40%
≥75	713 (13.5)	45 (1.8)	668 (24.4)	37.87 (26.1-56.03)	<0.001	58%
Male	2615 (49.5)	937 (36.9)	1678 (61.2)	2.76 (2.39-3.2)	<0.001	16%
Race/ethnicity						
Non-Hispanic white	2003 (37.9)	909 (35.8)	1094 (39.9)	Reference		
Non-Hispanic African American	835 (15.8)	443 (17.5)	392 (14.3)	0.81 (0.65-1.01)	0.057	-3%
Asian	383 (7.3)	196 (7.7)	187 (6.8)	1.29 (0.97-1.72)	0.078	4%
Hispanic	1330 (25.2)	599 (23.6)	731 (26.7)	1.63 (1.35-1.97)	<0.001	8%
Other/ Multiracial	397 (7.5)	172 (6.8)	225 (8.2)	1.6 (1.21-2.11)	<0.001	7%
Unknown	331 (6.3)	219 (8.6)	112 (4.1)	0.89 (0.65-1.23)	0.488	-2%
Tobacco use						
Never, including passive exposure	3268 (61.9)	1678 (66.1)	1590 (58.0)	Reference		
Former	902 (17.1)	337 (13.3)	565 (20.6)	0.69 (0.56-0.85)	<0.001	-6%
Current	288 (5.5)	147 (5.8)	141 (5.1)	0.59 (0.43-0.81)	0.001	-8%
Unknown	821 (15.6)	376 (14.8)	445 (16.2)	1.43 (1.16-1.75)	<0.001	5%
Obesity						
BMI <25 kg/m^2	1406 (26.6)	756 (29.8)	650 (23.7)	Reference		
BMI 25.0-29.9 kg/m^2	1769 (33.5)	830 (32.7)	939 (34.3)	1.3 (1.07-1.57)	0.007	4%
BMI 30.0-39.9 kg/m^2	1554 (29.4)	655 (25.8)	899 (32.8)	1.8 (1.47-2.2)	<0.001	9%
BMI ≥40 kg/m^2	311 (5.9)	126 (5.0)	185 (6.7)	2.45 (1.78-3.36)	<0.001	14%
Unknown	239 (4.5)	171 (6.7)	68 (2.5)	0.47 (0.31-0.69)	<0.001	-11%

Characteristic	Overall, N=5,279 N (%) or median (IQR)	Not hospitalized, N=2,538 N (column %) or median (IQR)	Hospitalized, N=2,741 N (column %) or median (IQR)	Risk of hospitalization Odds ratio (95% CI)	p	Average marginal effect
Any chronic condition*	3323 (62.9)	1138 (44.8)	2185 (79.7)			
Any cardiovascular condition*	2752 (52.1)	818 (32.2)	1934 (70.6)			
Coronary artery disease	704 (13.3)	102 (4.0)	602 (22.0)	1.08 (0.81-1.44)	0.600	1%
Heart failure	367 (7.0)	17 (0.7)	350 (12.8)	4.43 (2.59-8.04)	<0.001	22%
Hyperlipidemia	1714 (32.5)	552 (21.7)	1162 (42.4)	0.62 (0.52-0.74)	<0.001	-7%
Hypertension	2256 (42.7)	557 (21.9)	1699 (62.0)	1.78 (1.49-2.12)	<0.001	
Diabetes	1296 (24.6)	256 (10.1)	1040 (37.9)	2.24 (1.84-2.73)	<0.001	12%
Asthma or chronic obstructive pulmonary disorder	934 (17.7)	375 (14.8)	559 (20.4)	1.08 (0.88-1.33)	0.471	1%
Chronic kidney disease	647 (12.3)	66 (2.6)	581 (21.2)	2.6 (1.89-3.61)	<0.001	14%
Cancer	403 (7.6)	108 (4.3)	295 (10.8)	0.88 (0.65-1.19)	0.405	-2%
Temperature at presentation, degrees Celsius*	37.4 (36.9-38.1)	37.2 (36.8-37.7)	37.4 (36.9-38.2)			
Temperature ≥ 38^{o} C at presentation*	959 (18.2) **	109 (4.3)	850 (31.0)			
Oxygen saturation at presentation*	95 (91-97) **	97 (96-99) †	94 (90-96) ‡			
Proportion with oxygen saturation < 88% at presentation*	426 (8.1)	2 (0.1)	424 (15.5)			

*Not included in multivariable model

**Missing for 74% of non-hospitalized patients

†Measured on supplemental oxygen for 23% of patients

‡Measured on supplemental oxygen for 99% of patients

Table 2: Characteristics of admitted patients, by complication status, among those reaching study endpoint (discharge or critical illness)

Characteristic	All hospitalized with outcomes, N=2,729 N (%) or median (IQR)	Discharged, no critical illness, N=1,739 N (column %) or median (IQR)	Critical illness, N=990 N (column %) or median (IQR)
Week			
10 (March 2-8)	6 (0.2)	4 (0.2)	2 (0.2)
11 (March 9-15)	59 (2.2)	32 (1.8)	27 (2.7)
12 (March 16-22)	358 (13.1)	210 (12.1)	148 (14.9)
13 (March 23-29)	780 (28.6)	485 (27.9)	295 (29.8)
14 (March 30-April 5)	1050 (38.5)	679 (39.0)	371 (37.5)
15 (April 6-April 8)	476 (17.4)	329 (18.9)	147 (14.8)
Age, median years	63 (51-74)	60 (48-71)	68 (58-78)
Age, years			
19-44	435 (15.9)	344 (19.8)	91 (9.2)
45-54	407 (14.9)	310 (17.8)	97 (9.8)
55-64	602 (22.1)	391 (22.5)	211 (21.3)
65-74	619 (22.7)	355 (20.4)	264 (26.7)
≥75	666 (24.4)	339 (19.5)	327 (33.0)
Male sex	1672 (61.3)	1016 (58.4)	656 (66.3)
Race/ethnicity			
Non-Hispanic white	1089 (39.9)	654 (37.6)	435 (43.9)
Non-Hispanic African American	390 (14.3)	278 (16.0)	112 (11.3)
Asian	185 (6.8)	107 (6.2)	78 (7.9)
Hispanic	728 (26.7)	493 (28.3)	235 (23.7)
Other/ Multiracial	225 (8.2)	141 (8.1)	84 (8.5)
Unknown	112 (4.1)	66 (3.8)	46 (4.6)
Tobacco use			
Never, including passive exposure	1584 (58.0)	1067 (61.4)	517 (52.2)
Former	561 (20.6)	325 (18.7)	236 (23.8)
Current	141 (5.2)	97 (5.6)	44 (4.4)
Unknown	443 (16.2)	250 (14.4)	193 (19.5)
Obesity			
BMI <25 kg/m^2	648 (23.7)	382 (22.0)	266 (26.9)
BMI 25.0-29.9 kg/m^2	932 (34.2)	608 (35.0)	324 (32.7)
BMI 30.0-39.9 kg/m^2	896 (32.8)	592 (34.0)	304 (30.7)
BMI ≥40 kg/m^2	185 (6.8)	115 (6.6)	70 (7.1)
Unknown	68 (2.5)	42 (2.4)	26 (2.6)
Any chronic condition*	2176 (79.7)	1343 (77.2)	833 (84.1)
Any cardiovascular condition*	1927 (70.6)	1166 (67.1)	761 (76.9)

Characteristic	All hospitalized with outcomes, N=2,729 N (%) or median (IQR)	Discharged, no critical illness, N=1,739 N (column %) or median (IQR)	Critical illness, N=990 N (column %) or median (IQR)
Coronary artery disease	602 (22.1)	325 (18.7)	277 (28.0)
Heart failure	349 (12.8)	160 (9.2)	189 (19.1)
Hyperlipidemia	1157 (42.4)	692 (39.8)	465 (47.0)
LDL, median	64 (46-86)	71 (52-91)	56 (39-75)
Hypertension	1693 (62.0)	1013 (58.3)	680 (68.7)
Diabetes	1035 (37.9)	611 (35.1)	424 (42.8)
Asthma or chronic obstructive pulmonary disorder	556 (20.4)	345 (19.8)	211 (21.3)
Chronic kidney disease	580 (21.3)	321 (18.5)	259 (26.2)
Cancer	292 (10.7)	154 (8.9)	138 (13.9)
Temperature at presentation, degrees Celsius	37.4 (36.9-38.2)	37.4 (36.9-38.2)	37.4 (36.9-38.2)
Temperature ≥ 38^{o} C at presentation	846 (31.0)	533 (30.6)	313 (31.6)
Oxygen saturation at presentation	94 (90-96) †	95 (92-97) ‡	92 (86-95)
Oxygen saturation < 88 percent at presentation	422 (15.5)	136 (7.8)	286 (28.9)
First absolute lymphocyte count, 10^3/µl	0.8 (0.6-1.2)	0.9 (0.6-1.2)	0.8 (0.5-1.1)
Missing lymphocyte count	34 (1.2)	17 (1.0)	17 (1.7)
First creatinine, mg/dL	1.0 (0.80-1.39)	0.95 (0.79-1.23)	1.11 (0.88-1.61)
Missing creatinine	55 (2.0)	38 (2.2)	17 (1.7)
First alanine aminotransferase, units/L*	34 (23-55)	33.5 (22-55)	36 (24-57)
Missing alanine aminotransferase	115 (4.2)	89 (5.1)	26 (2.6)
First aspartate aminotransferase, units/L*	46 (32.0-69.0)	42 (29.5-62.0)	53 (36.0-82.0)
Missing aspartate aminotransferase	163 (6.0)	112 (6.4)	51 (5.2)
First C-reactive protein, mg/L	108.3 (53.3-169.0)	89.1 (41.9-148.0)	136.3 (85.8-204.2)
Missing C-reactive protein	165 (6.0)	123 (7.1)	42 (4.2)
First d-dimer, ng/mL	386.5 (237.0-713.8)	324 (208.0-545.0)	528 (319.0-1174.0)
Missing d-dimer	373 (13.7)	280 (16.1)	93 (9.4)
First ferritin, ng/mL	710.2 (348.0-1461.2)	613 (305.0-1291.5)	925 (468.2-1716.7)
Missing ferritin	218 (8.0)	164 (9.4)	54 (5.5)
First procalcitonin, ng/mL	0.14 (0.06-0.40)	0.1 (0.05-0.23)	0.27 (0.12-0.82)
Missing procalcitonin	191 (7.0)	147 (8.5)	44 (4.4)
First troponin-I, ng/mL	0.03 (0.01-0.10)	0.02 (0.01-0.10)	0.07 (0.01-0.10)
Missing troponin-I	219 (8.0)	172 (9.9)	47 (4.7)
Length of stay, days*	7 (3-13)	5 (3-9)	[Discharged or Died] 9 (5-17) [Still Hospitalized] 36 (32-40)

*Not included in multivariable model

†Measured on supplemental oxygen for 100% of patients
‡Measured on supplemental oxygen for 99% of patients

Table 3: Multivariable logistic regression results for risk of critical illness, among hospitalized patients discharged or with critical illness

Characteristic	Among hospitalized patients, excluding vitals and laboratory results (N=2,275)		Among hospitalized patients, including vitals and laboratory results (N=2,275)	
	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
Week				
10-11 (March 2-15)	Reference		Reference	
12 (March 16-22)	0.76 (0.44-1.3)	0.323	0.49 (0.25-1.0)	0.037
13 (March 23-29)	0.58 (0.35-1.0)	0.045	0.21 (0.10-0.4)	<0.001
14 (March 30-April 5)	0.55 (0.33-0.9)	0.026	0.16 (0.08-0.3)	<0.001
15 (April 6-April 8)	0.37 (0.21-0.6)	<0.001	0.08 (0.04-0.2)	<0.001
Age, years				
19-44	Reference		Reference	
45-54	1.12 (0.80-1.6)	0.495	0.78 (0.54-1.1)	0.212
55-64	2.04 (1.50-2.8)	<0.001	1.32 (0.93-1.9)	0.122
65-74	2.88 (2.09-4.0)	<0.001	1.73 (1.19-2.5)	0.004
≥75	3.46 (2.46-4.8)	<0.001	2.32 (1.57-3.4)	<0.001
Male	1.54 (1.29-1.8)	<0.001	1.06 (0.85-1.3)	0.602
Race/ethnicity				
Non-Hispanic white	Reference		Reference	
Non-Hispanic African American	0.67 (0.51-0.9)	0.004	0.57 (0.41-0.8)	0.001
Asian	1.30 (0.92-1.8)	0.134	1.24 (0.82-1.9)	0.302
Hispanic	0.93 (0.74-1.2)	0.541	0.89 (0.69-1.2)	0.375
Other/ Multiracial	1.15 (0.84-1.6)	0.392	1.24 (0.86-1.8)	0.254
Unknown	1.23 (0.80-1.9)	0.336	1.10 (0.68-1.8)	0.704
Tobacco use				
Never	Reference		Reference	
Former	1.06 (0.85-1.3)	0.589	1.05 (0.82-1.3)	0.719
Current	0.77 (0.52-1.2)	0.211	0.82 (0.53-1.3)	0.394
Unknown	1.52 (1.19-1.9)	0.001	1.42 (1.08-1.9)	0.012
Obesity				
BMI <25 kg/m^2	Reference		Reference	
BMI 25.0-29.9 kg/m^2	0.86 (0.69-1.1)	0.181	0.94 (0.73-1.2)	0.651
BMI 30.0-39.9 kg/m^2	0.98 (0.77-1.2)	0.846	1.11 (0.85-1.5)	0.440
BMI ≥40 kg/m^2	1.52 (1.04-2.2)	0.029	1.71 (1.10-2.7)	0.016
Unknown	0.80 (0.46-1.4)	0.434	1.05 (0.54-2.0)	0.891
Coronary artery disease	0.96 (0.77-1.2)	0.757	0.92 (0.71-1.2)	0.556
Heart failure	1.88 (1.43-2.5)	<0.001	1.93 (1.40-2.6)	<0.001
Hyperlipidemia	0.94 (0.77-1.1)	0.503	0.93 (0.75-1.2)	0.514
Hypertension	0.96 (0.77-1.2)	0.671	0.96 (0.75-1.2)	0.756

Characteristic	Among hospitalized patients, excluding vitals and laboratory results (N=2,275)		Among hospitalized patients, including vitals and laboratory results (N=2,275)	
	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
Diabetes	1.24 (1.03-1.5)	0.025	1.23 (0.99-1.5)	0.061
Asthma or chronic obstructive pulmonary disorder	0.89 (0.70-1.1)	0.345	0.99 (0.76-1.3)	0.932
Chronic kidney disease	1.07 (0.85-1.3)	0.542	0.73 (0.55-1.0)	0.037
Cancer	1.23 (0.95-1.6)	0.121	1.30 (0.95-1.8)	0.098
Temperature on presentation, degrees Celsius				
<38			Reference	
38-39			1.08 (0.85-1.4)	0.518
>39			1.06 (0.78-1.4)	0.707
Oxygen saturation on presentation, %				
SpO2 >92			Reference	
SpO2 88-92			1.49 (1.18-1.9)	0.001
SpO2 <88			3.67 (2.78-4.8)	<0.001
First lymphocyte count, 10^3/µl				
>1.2			Reference	
>0.8-1.2			1.09 (0.82-1.4)	0.573
0.5-0.8			1.19 (0.93-1.5)	0.172
<0.5			1.76 (1.26-2.5)	0.001
Missing			4.76 (1.02-22.2)	0.047
First creatinine, mg/dL				
0-1.1			Reference	
>1.1-2			1.52 (1.20-1.9)	0.001
>2			1.66 (1.11-2.5)	0.013
Missing			1.47 (0.33-6.7)	0.615
First C reactive protein, mg/L				
0-15			Reference	
>15-100			2.35 (1.37-4.0)	0.002
>100-200			3.86 (2.23-6.7)	<0.001
>200			5.09 (2.82-9.2)	<0.001
Missing			2.59 (1.10-6.1)	0.030
First d-dimer, ng/mL				
0-250				
>250-500			1.58 (1.21-2.1)	0.001
>500-1000			2.26 (1.66-3.1)	<0.001

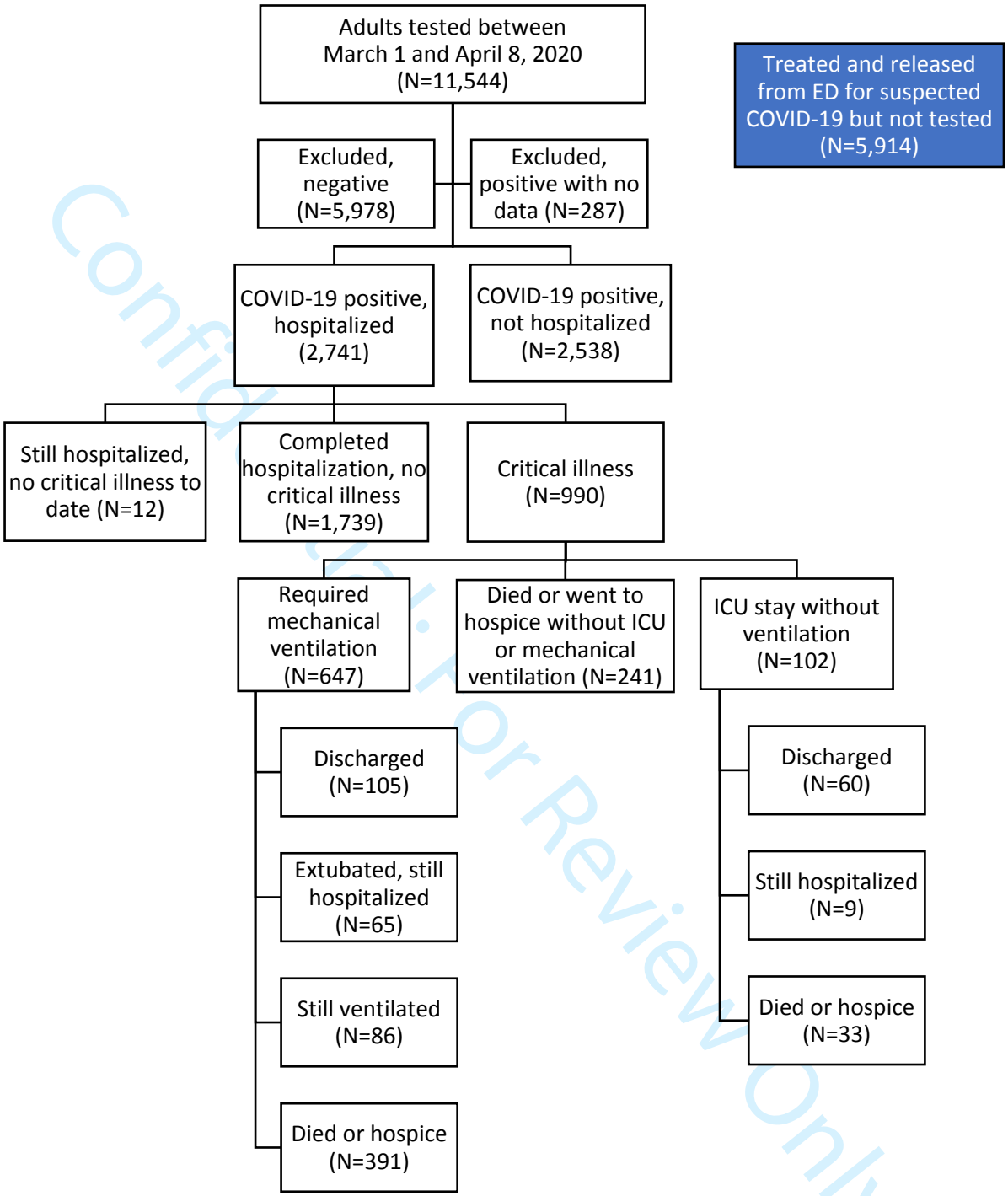
Characteristic	Among hospitalized patients, excluding vitals and laboratory results (N=2,275)		Among hospitalized patients, including vitals and laboratory results (N=2,275)	
	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
>1000-2500			2.37 (1.58-3.6)	<0.001
>2500			3.93 (2.60-6.0)	<0.001
Missing			0.75 (0.48-1.2)	0.229
First ferritin, ng/mL				
0-300				
>300-500			0.96 (0.67-1.4)	0.818
>500-1000			1.13 (0.83-1.5)	0.434
>1000-2500			1.14 (0.83-1.6)	0.409
>2500			1.40 (0.94-2.1)	0.099
Missing			0.75 (0.39-1.5)	0.401
First procalcitonin, ng/mL				
0-0.5			Reference	
>0.5			1.54 (1.18-2.0)	0.001
Missing			0.75 (0.44-1.3)	0.286
First troponin, ng/mL				
<0.1			Reference	
0.1-1			2.09 (1.51-2.9)	<0.001
>1			4.78 (2.10-10.9)	<0.001
Missing			0.84 (0.51-1.4)	0.488

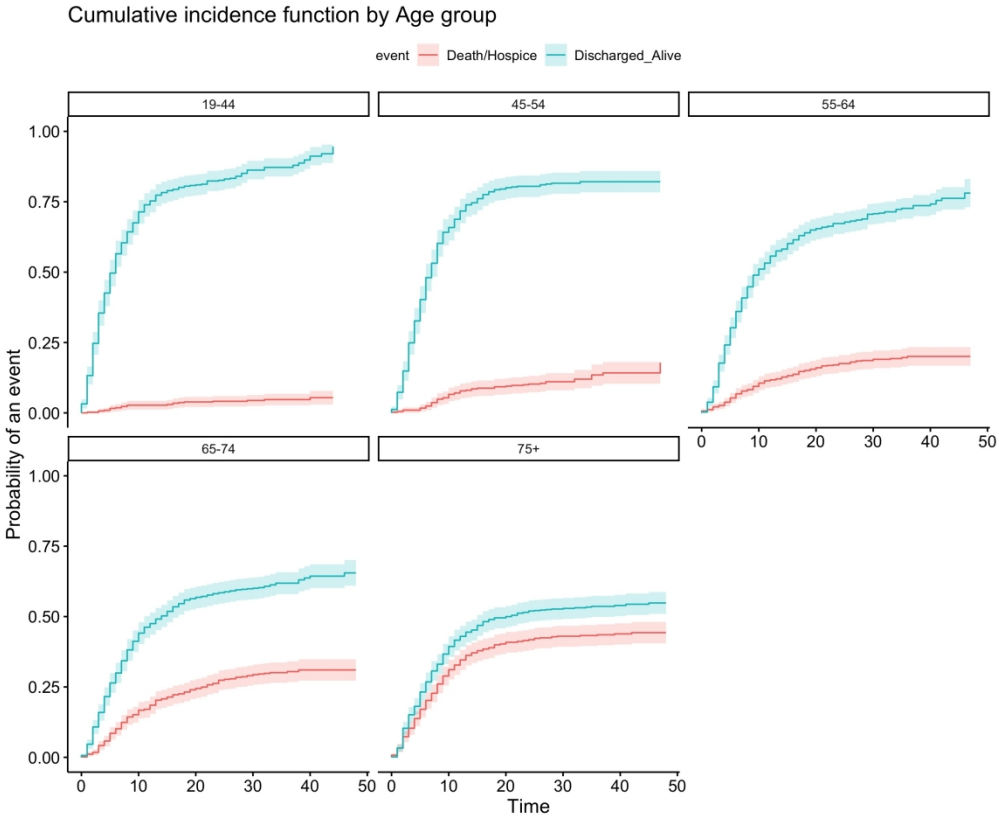
Table 4: Competing risk model for mortality, among hospitalized patients

Characteristic	Among hospitalized patients, excluding vitals and laboratory results (N=2,287) Hazard ratio (95% CI)	p	Among hospitalized patients, including vitals and laboratory results (N=2,287) Hazard ratio (95% CI)	p
Week				
10-11 (March 2-15)	Reference		Reference	
12 (March 16-22)	0.87 (0.54-1.41)	0.580	1.07 (0.62-1.84)	0.800
13 (March 23-29)	0.84 (0.53-1.32)	0.440	0.96 (0.55-1.68)	0.880
14 (March 30-April 5)	0.82 (0.52-1.30)	0.400	0.85 (0.49-1.50)	0.580
15 (April 6-April 8)	0.73 (0.44-1.19)	0.210	0.67 (0.37-1.22)	0.190
Age, years				
19-44	Reference		Reference	
45-54	2.59 (1.56-4.32)	<0.001	1.95 (1.16-3.31)	0.012
55-64	4.40 (2.73-7.11)	<0.001	3.18 (1.93-5.21)	<0.001
65-74	6.99 (4.34-11.27)	<0.001	4.83 (2.93-7.96)	<0.001
≥75	10.34 (6.37-16.79)	<0.001	7.69 (4.60-12.84)	<0.001
Male	1.27 (1.08-1.50)	0.005	0.92 (0.77-1.11)	0.390
Race/ethnicity				
Non-Hispanic white	Reference		Reference	
Non-Hispanic African American	0.78 (0.60-1.02)	0.070	0.71 (0.53-0.94)	0.019
Asian	1.29 (0.94-1.77)	0.120	1.26 (0.91-1.75)	0.160
Hispanic	1.17 (0.95-1.44)	0.130	1.21 (0.98-1.49)	0.072
Other/ Multiracial	1.07 (0.80-1.45)	0.640	1.17 (0.86-1.60)	0.310
Unknown	1.09 (0.71-1.67)	0.690	1.23 (0.82-1.83)	0.320
Tobacco use				
Never	Reference		Reference	
Former	1.13 (0.93-1.37)	0.210	1.07 (0.88-1.31)	0.490
Current	0.90 (0.61-1.31)	0.570	0.92 (0.62-1.38)	0.690
Unknown	1.56 (1.26-1.93)	<0.001	1.50 (1.21-1.86)	<0.001
Obesity				
BMI <25 kg/m^2	Reference		Reference	
BMI 25.0-29.9 kg/m^2	0.91 (0.74-1.11)	0.340	1.01 (0.82-1.25)	0.940
BMI 30.0-39.9 kg/m^2	1.02 (0.82-1.27)	0.850	1.08 (0.87-1.36)	0.480
BMI ≥40 kg/m^2	1.41 (0.98-2.01)	0.061	1.45 (0.99-2.13)	0.053
Unknown	1.85 (1.13-3.02)	0.014	1.97 (1.23-3.17)	0.005
Coronary artery disease	1.12 (0.92-1.36)	0.240	1.10 (0.90-1.35)	0.360
Heart failure	1.77 (1.43-2.20)	<0.001	1.54 (1.23-1.93)	<0.001
Hyperlipidemia	0.95 (0.79-1.13)	0.550	0.98 (0.82-1.17)	0.790
Hypertension	0.94 (0.76-1.16)	0.540	0.98 (0.78-1.23)	0.860
Diabetes	1.10 (0.93-1.31)	0.260	1.01 (0.85-1.21)	0.870

Characteristic	Among hospitalized patients, excluding vitals and laboratory results (N=2,287)		Among hospitalized patients, including vitals and laboratory results (N=2,287)	
	Hazard ratio (95% CI)	p	Hazard ratio (95% CI)	p
Asthma or chronic obstructive pulmonary disorder	0.93 (0.76-1.15)	0.510	1.03 (0.83-1.29)	0.760
Chronic kidney disease	1.18 (0.97-1.43)	0.096	0.92 (0.73-1.16)	0.490
Cancer	1.31 (1.05-1.62)	0.016	1.29 (1.03-1.62)	0.028
Temperature on presentation, degrees Celsius				
<38			Reference	
38-39			1.17 (0.96-1.43)	0.110
>39			1.04 (0.79-1.37)	0.790
Oxygen saturation on presentation, %				
SpO2 >92			Reference	
SpO2 88-92			1.46 (1.18-1.79)	<0.001
SpO2 <88			2.00 (1.61-2.48)	<0.001
Unknown			1.03 (0.62-1.71)	0.920
First lymphocyte count, 103/µl				
>1.2			Reference	
>0.8-1.2			0.89 (0.70-1.14)	0.370
0.5-0.8			1.04 (0.84-1.28)	0.720
<0.5			1.38 (1.05-1.81)	0.019
Missing			2.16 (1.09-4.27)	0.027
First creatinine, mg/dL				
0-1.1			Reference	
>1.1-2			1.36 (1.11-1.68)	0.003
>2			1.49 (1.08-2.04)	0.014
Missing			1.48 (0.56-3.90)	0.430
First C reactive protein, mg/L				
0-15			Reference	
>15-100			3.52 (1.72-7.18)	<0.001
>100-200			4.66 (2.25-9.62)	<0.001
>200			5.07 (2.41-10.67)	<0.001
Missing			3.46 (1.38-8.64)	0.008
First d-dimer, ng/mL				
0-250			Reference	
>250-500			1.50 (1.14-1.98)	0.004
>500-1000			1.70 (1.26-2.28)	<0.001
>1000-2500			1.67 (1.18-2.36)	0.004
>2500			2.16 (1.57-2.98)	<0.001
Missing			1.59 (1.04-2.44)	0.034

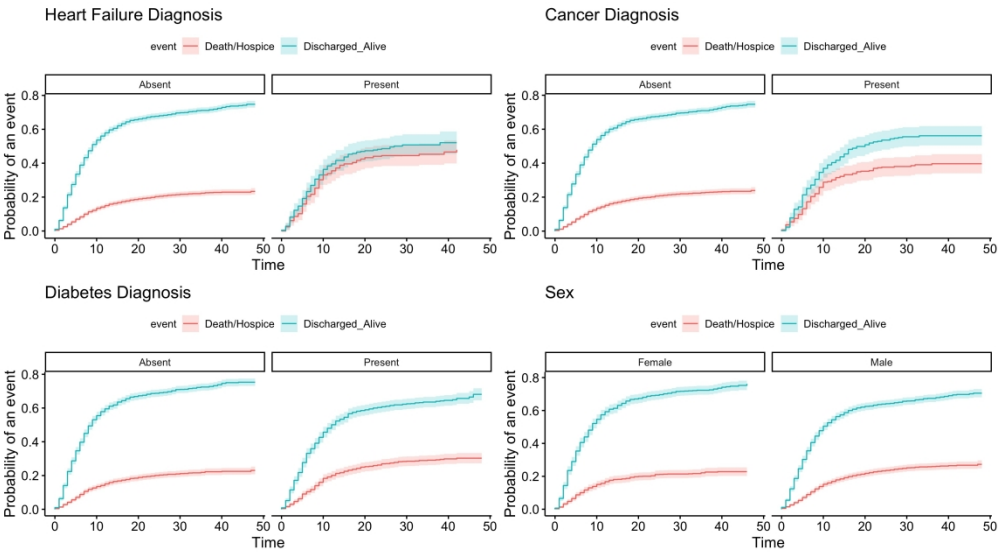
Characteristic	Among hospitalized patients, excluding vitals and laboratory results (N=2,287) Hazard ratio (95% CI)	p	Among hospitalized patients, including vitals and laboratory results (N=2,287) Hazard ratio (95% CI)	p
First ferritin, ng/mL				
0-300			Reference	
>300-500			1.08 (0.78-1.49)	0.650
>500-1000			1.19 (0.90-1.57)	0.230
>1000-2500			1.22 (0.92-1.61)	0.180
>2500			1.36 (0.97-1.90)	0.079
Missing			1.88 (1.02-3.48)	0.044
First procalcitonin, ng/mL				
0-0.5			Reference	
>0.5			1.58 (1.28-1.95)	<0.001
Missing			0.95 (0.59-1.52)	0.820
First troponin, ng/mL				
<0.1			Reference	
0.1-1			1.48 (1.19-1.84)	<0.001
>1			2.12 (1.39-3.22)	<0.001
Missing			0.58 (0.32-1.06)	0.075





Cumulative incidence function for discharge alive and death, by age group

1068x883mm (72 x 72 DPI)



Cumulative incidence function for discharge alive and death, by heart failure, cancer, diabetes and male sex

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Appendix Table S1: Characteristics of patients by test outcome*

Characteristic	All tested, N=10,620 N (column %) or median (IQR)	Tested negative, N=5,341 N (column %) or median (IQR)	Tested positive, N=5,279 N (column %) or median (IQR)
Age, years			
19-44	4606 (43.4)	2760 (51.7)	1846 (35.0)
45-54	1819 (17.1)	917 (17.2)	902 (17.1)
55-64	1893 (17.8)	872 (16.3)	1021 (19.3)
65-74	1214 (11.4)	417 (7.8)	797 (15.1)
≥75	1088 (10.2)	375 (7.0)	713 (13.5)
Male	4366 (41.1)	1751 (32.8)	2615 (49.5)
Race/ethnicity			
Non-Hispanic white	4451 (41.9)	2448 (45.8)	2003 (37.9)
Non-Hispanic African American	1492 (14.0)	657 (12.3)	835 (15.8)
Asian	927 (8.7)	544 (10.2)	383 (7.3)
Hispanic	2233 (21.0)	903 (16.9)	1330 (25.2)
Other/ Multiracial	788 (7.4)	391 (7.3)	397 (7.5)
Unknown	729 (6.9)	398 (7.5)	331 (6.3)
Tobacco use			
Current	6722 (63.3)	3454 (64.7)	3268 (61.9)
Former	1718 (16.2)	816 (15.3)	902 (17.1)
Never, including passive exposure	829 (7.8)	541 (10.1)	288 (5.5)
Unknown	1351 (12.7)	530 (9.9)	821 (15.6)
Obesity			
BMI <25 kg/m^2	3468 (32.7)	2062 (38.6)	1406 (26.6)
BMI 25.0-29.9 kg/m^2	3388 (31.9)	1619 (30.3)	1769 (33.5)
BMI 30.0-39.9 kg/m^2	2768 (26.1)	1214 (22.7)	1554 (29.4)
BMI ≥40 kg/m^2	526 (5.0)	215 (4.0)	311 (5.9)
Unknown	470 (4.4)	231 (4.3)	239 (4.5)
Any chronic condition	6105 (57.5)	2782 (52.1)	3323 (62.9)
Any cardiovascular condition	4868 (45.8)	2116 (39.6)	2752 (52.1)
Coronary artery disease	1186 (11.2)	482 (9.0)	704 (13.3)
Heart failure	694 (6.5)	327 (6.1)	367 (7.0)
Hyperlipidemia	3101 (29.2)	1387 (26.0)	1714 (32.5)
Hypertension	3769 (35.5)	1513 (28.3)	2256 (42.7)
Diabetes	1966 (18.5)	670 (12.5)	1296 (24.6)
Asthma or chronic obstructive pulmonary disorder	1970 (18.5)	1036 (19.4)	934 (17.7)
Chronic kidney disease	1083 (10.2)	436 (8.2)	647 (12.3)
Cancer	802 (7.6)	399 (7.5)	403 (7.6)

*excluding 637 patients who tested negative and 287 patients who tested positive who did not have prior visits in the health system and did not have current data on demographics or comorbidities

Appendix Table S2: Site of first positive test by admission status

Location of first positive test	Not hospitalized, N=2538 N (row %) or median (IQR)	Hospitalized, N=2741 N (row %) or median (IQR)
Outpatient	1949 (96.2)	78 (3.8)
Emergency department	505 (16.1)	2627 (83.9)
Inpatient	3 (10.0)	27 (90.0)
Missing	81 (90.0)	9 (10.0)

Appendix Table S3: Characteristics of patients by first test location

Characteristic	First tested in emergency department, N=3,132 N (column %) or median (IQR)	First tested in outpatient setting, N=2,027 N (column %) or median (IQR)
Age, years		
19-44	604 (19.3)	1201 (59.3)
45-54	498 (15.9)	377 (18.6)
55-64	680 (21.7)	323 (15.9)
65-74	669 (21.4)	106 (5.2)
≥75	681 (21.7)	20 (1.0)
Male	1911 (61.0)	648 (32.0)
Race/ethnicity		
Non-Hispanic white	1215 (38.8)	731 (36.1)
Non-Hispanic African American	470 (15.0)	350 (17.3)
Asian	206 (6.6)	173 (8.5)
Hispanic	866 (27.7)	440 (21.7)
Other/ Multiracial	241 (7.7)	150 (7.4)
Unknown	134 (4.3)	183 (9.0)
Tobacco use		
Current	159 (5.1)	119 (5.9)
Former	610 (19.5)	267 (13.2)
Never, including passive exposure	1813 (57.9)	1378 (68.0)
Unknown	550 (17.6)	263 (13.0)
Obesity		
BMI <25 kg/m^2	1072 (34.2)	648 (32.0)
BMI 25.0-29.9 kg/m^2	1004 (32.1)	527 (26.0)
BMI 30.0-39.9 kg/m^2	197 (6.3)	106 (5.2)
BMI ≥40 kg/m^2	731 (23.3)	642 (31.7)
Unknown	128 (4.1)	104 (5.1)
Any chronic condition*	2383 (76.1)	862 (42.5)
Any cardiovascular condition*	2081 (66.4)	607 (29.9)
Coronary artery disease	630 (20.1)	62 (3.1)
Heart failure	350 (11.2)	11 (0.5)
Hyperlipidemia	1262 (40.3)	407 (20.1)
Hypertension	1812 (57.9)	396 (19.5)
Diabetes	1108 (35.4)	162 (8.0)
Asthma or chronic obstructive pulmonary disorder	619 (19.8)	292 (14.4)
Chronic kidney disease	602 (19.2)	38 (1.9)
Cancer	304 (9.7)	85 (4.2)

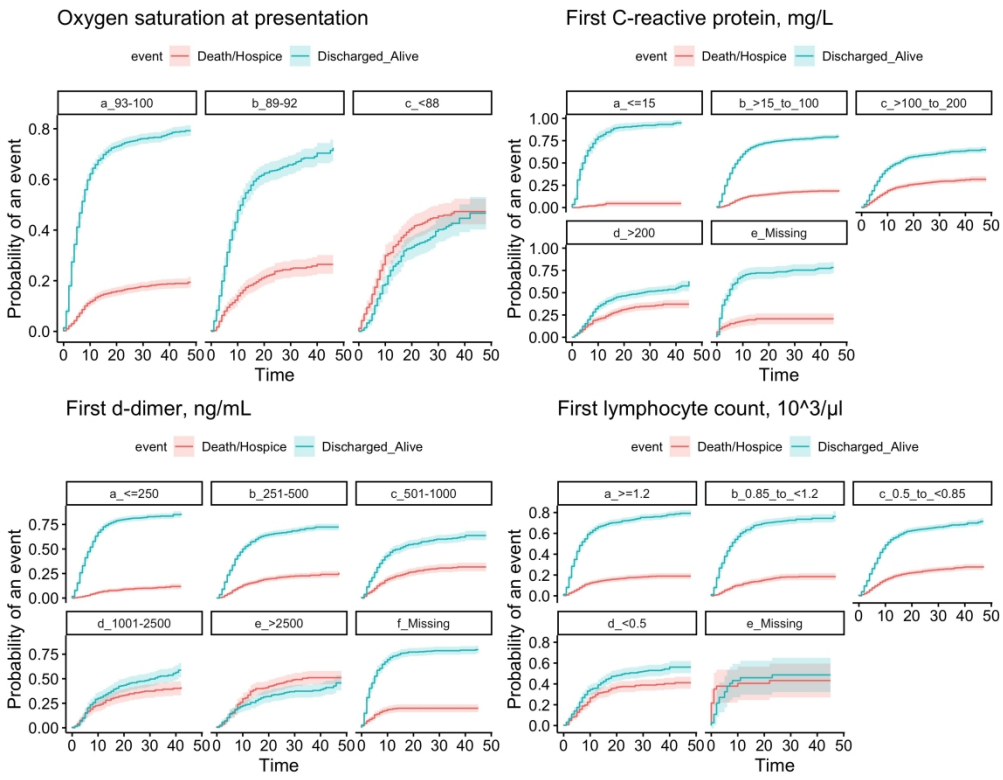
Appendix Table S4: Characteristics of patients with suspected Covid-19 in the emergency department (not tested)

Characteristic	Suspected COVID-19, N=5,914 N (%) or median (IQR)
Age, years	
19-44	3225 (54.5)
45-54	1075 (18.2)
55-64	897 (15.2)
65-74	457 (7.7)
≥75	260 (4.4)
Male	3088 (52.2)
Race/ethnicity	
Non-Hispanic white	1539 (26.0)
Non-Hispanic African American	924 (15.6)
Asian	319 (5.4)
Hispanic	2297 (38.8)
Other/ Multiracial	471 (8.0)
Unknown	364 (6.2)
Tobacco use	
Never	2984 (50.5)
Former	667 (11.3)
Current	722 (12.2)
Unknown	1541 (26.1)
Obesity	
BMI <25 kg/m^2	1256 (21.2)
BMI 25.0-29.9 kg/m^2	1506 (25.5)
BMI 30.0-39.9 kg/m^2	1246 (21.1)
BMI ≥40 kg/m^2	225 (3.8)
Unknown	1681 (28.4)
Any chronic condition*	2503 (42.3)
Any cardiovascular condition*	1780 (30.1)
Coronary artery disease	231 (3.9)
Heart failure	102 (1.7)
Hyperlipidemia	1039 (17.6)
Hypertension	1365 (23.1)
Diabetes	686 (11.6)
Asthma or chronic obstructive pulmonary disorder	887 (15.0)
Chronic kidney disease	139 (2.4)
Cancer	238 (4.0)

Appendix Table S5: Risk of hospitalization, including ED suspected cases in not hospitalized group

Characteristic	Risk of hospitalization Odds ratio (95% CI)	p	Average marginal effect
Week*			
Age, years			
19-44	Reference		
45-54	2.00 (1.70-2.35)	<0.001	8%
55-64	3.03 (2.58-3.57)	<0.001	14%
65-74	6.26 (5.17-7.59)	<0.001	26%
≥75	14.59 (11.56-18.45)	<0.001	41%
Male	2.10 (1.87-2.35)	<0.001	9%
Race/ethnicity			
Non-Hispanic white	Reference		
Non-Hispanic African American	0.65 (0.55-0.78)	<0.001	-5%
Asian	1.26 (0.99-1.59)	0.058	3%
Hispanic	0.97 (0.84-1.12)	0.694	0%
Other/ Multiracial	1.41 (1.14-1.75)	0.002	4%
Unknown	0.89 (0.68-1.15)	0.376	-1%
Tobacco use			
Never	Reference		
Former	0.73 (0.62-0.86)	<0.001	-4%
Current	0.45 (0.36-0.57)	<0.001	-9%
Unknown	1.08 (0.92-1.26)	0.332	1%
Obesity			
BMI <25 kg/m^2	Reference		
BMI 25.0-29.9 kg/m^2	1.16 (1.00-1.35)	0.058	2%
BMI 30.0-39.9 kg/m^2	1.51 (1.29-1.76)	<0.001	5%
BMI ≥40 kg/m^2	2.24 (1.74-2.88)	<0.001	11%
Unknown	0.16 (0.12-0.22)	<0.001	-16%
Coronary artery disease	1.28 (1.04-1.56)	0.018	3%
Heart failure	2.56 (1.90-3.48)	<0.001	11%
Hyperlipidemia	0.73 (0.63-0.84)	<0.001	-4%
Hypertension	1.68 (1.47-1.93)	<0.001	6%
Diabetes	1.72 (1.49-1.99)	<0.001	7%
Asthma or chronic obstructive pulmonary disorder	0.93 (0.80-1.10)	0.407	-1%
Chronic kidney disease	3.13 (2.51-3.91)	<0.001	14%
Cancer	1.09 (0.87-1.36)	0.443	1%

*included in model, but ORs too unreliable to display because of time variation in testing capability. In weeks 10-11 only 34 non-hospitalized and 65 hospitalized patients tested positive. Adding the ED non-tested population increases the non-hospitalized group to 1,782, artificially reducing the apparent hospitalization rate and skewing ORs.



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