## COVID-19 Incidence Data

County-level COVID-19 incidence data was obtained from a database developed by the *New York Times* that was based on data from public health agencies using methods defined by the Centers for Disease Control and Prevention for reporting aggregated cumulative counts of COVID-19 cases at the county level over time.<sup>1-3</sup> Data were incorporated into a choropleth map also depicting the location of participating hospitals.

## **Multiple Imputation**

For some patients, data were missing or unavailable for a subset of the prespecified candidate risk factors for mortality and/or respiratory failure. Before applying L1 (lasso) penalized regression,<sup>4-6</sup> we therefore employed multiple imputation using chained equations to avoid bias in the resulting analysis.<sup>7-9</sup> Multiple imputation ensures validity of inference if data is missing at random (missingness pattern and data values are independent conditional on observed data), the most general data-centric missing data assumption.<sup>10</sup>

## Selection of Risk Factors for Inclusion in Multivariable Models

- A team of experienced physicians, clinical researchers, and epidemiologists prespecified candidate risk factors for each outcome on the basis of reported association, plausibility, data availability (missingness<20%), and clinical utility. We maintained a ratio of >10:1 outcome events to candidate risk factors to reduce instability in variable selection and estimation.<sup>11,12</sup> Mortality and late-onset respiratory failure candidate risk factors were restricted to data available before or within 24 hours of hospital arrival (eg, highest heart rate in the first 24 hours). Candidate risk factors for early-onset respiratory failure included only data available before or at hospital arrival (eg, first-measured heart rate).
- To select lasso tuning parameters λ, multiply imputed datasets were stacked and cross-validation was performed patient-wise.<sup>13-15</sup> Analyses were based on 10 multiply imputed datasets and 10-fold cross-validation across 100 values of the tuning parameter. Each cross-validated model included a random effect for admission hospital.<sup>16</sup> For each value of the tuning parameter, the average crossvalidated area under the receiver operating characteristic curve (AUC) was calculated as the mean AUC across all iterations. The relationship between the tuning parameter and the associated models' average cross-validated AUC was smoothed via locally weighted regression (lowess) curves (Supplemental Figure 1),<sup>17</sup> the highest average cross-validated AUC tuning parameter was identified, and the most parsimonious model with an average AUC within 1 standard deviation of the maximal average AUC was selected.<sup>18</sup>

## **Patient Inclusion in Risk Factor Analyses**

For analysis of risk factors for mortality, we excluded patients (n=10) suspected to have been moribund at presentation based on survival <24 hours from hospital arrival. To avoid misclassification of the outcome, evaluation of early respiratory failure risk factors excluded patients (n=43) who were transferred to the study hospital from an inpatient unit of another hospital. Patients transferred from the emergency department of another hospital were included. Finally, analysis of late respiratory failure risk factors was restricted to patients (n=1196) who did not die or develop respiratory failure within 24 hours of arrival at the study hospital.

## References

- 1. The New York Times Github. Coronavirus (COVID-19) data in the United States. Accessed February 2, 2021. https://github.com/nytimes/covid-19-data
- Turner K, Davidson SL, Collins J, et al. Council of State and Territorial Epidemiologists. Standardized surveillance case definition and national notification for 2019 novel coronavirus disease (COVID-19). 2020. Accessed February 18, 2021. http://www.cste.org/resource/resmgr/ps/positionstatement2020/ Interim-20-ID-02\_COVID-19.pdf
- 3. Centers for Disease Control and Prevention. Cases, Data, and Surveillance: About CDC COVID-19 Data. 2020. Accessed December 17, 2020. https:// www.cdc.gov/coronavirus/2019-ncov/cases-updates/about-us-cases-deaths.html
- 4. Efron B, Hastie T, Johnstone I, et al. Least angle regression. Ann Stat. 2004;32(2):407-499.
- 5. Zou H, Hastie T. Regularization and variable selection via the elastic net. J R Stat Soc B. 2005;67(2):301-320.
- 6. Buuren SV, Groothuis-Oudshoorn K. MICE: Multivariate imputation by chained equations in R. J Stat Soft. 2011;45(3).
- 7. Rubin DB. Inference and missing data. Biometrika. 1976;63(3):581-592.
- 8. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. Stat Med. 2010;30(4):377-399.
- 9. van der Heijden GJMG, T Donders AR, Stijnen T, et al. Imputation of missing values is superior to complete case analysis and the missing-indicator method in multivariable diagnostic research: a clinical example. J Clin Epidemiol. 2006;59(10):1102-1109.
- 10. Rubin DB. Multiple imputation after 18+ years. J Am Stat Assoc. 1996;91(434):473.
- 11. Peduzzi P, Concato J, Kemper E, et al. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol. 1996;49(12):1373-1379.
- 12. Wynants L, Bouwmeester W, Moons KGM, et al. A simulation study of sample size demonstrated the importance of the number of events per variable to develop prediction models in clustered data. J Clin Epidemiol. 2015;68(12):1406-1414.
- 13.Wood AM, White IR, Royston P. How should variable selection be performed with multiply imputed data? Stat Med. 2008;27(17):3227-3246.
- 14. Du J, Boss J, Han P, et al. Variable selection with multiply-imputed datasets: choosing between stacked and grouped methods. arXiv. 2020.
  15. Kohavi R. A study of cross-validation and bootstrap for accuracy estimation and model selection. Proceedings of the International Joint Conference on Artificial Intelligence. IJCAI (U S). 1995;14(2):1137-1143. https://www.ijcai.org/Proceedings/95-2/Papers/016.pdf
- Graph Stat. 2014;23(2):460-477.
- 17. Cleveland WS, Devlin SJ. Locally weighted regression: an approach to regression analysis by local fitting. *J Am Stat Assoc*. 1988;83(403):596-610. 18. Hastie T, Tibshirani R, Friedman JH. *The Elements of Statistical Learning: Data Mining, Inference, and Prediction*. 2nd ed. Springer; 2017.

## Supplement 1 Supplementary methods.



**Supplemental Figure 1** Cross validation plots for (A) mortality, (B) early respiratory failure, and (C) late respiratory failure depict the relationship between tuning parameter (lambda) and the associated model's cross-validated area under the receiver operating characteristic curve (AUC), with lowess curves drawn to show the smoothed association.

ALIGNE Clinical Center: <u>Baystate Medical Center</u>—Lori Kozikowski, Sherell Thornton-Thompson, Leslie de Souza, Sarah Romain, Cynthia Kardos; <u>Brigham and Women's Hospital</u>—Rebecca M Baron, Mayra Pinilla Vera, Antonio Arciniegas

BOSTON Clinical Center: <u>Beth Israel Deaconess Medical Center</u>—Valerie Banner-Goodspeed, Marie McGourty, Lauren Kelly, Krystal Capers, Melisa Joseph; <u>Massachusetts General Hospital</u>—Kathryn Hibbert, Kelsey Brait, Natalie Pulido, Layla Rahimi, Anna Nicole Dartley; <u>University of Mississippi Medical Center</u>—Alan E. Jones, Rebekah Peacock, Utsav Nandi, James Galbraith, Kelsey Kunk Morgan; <u>Hennepin County Medical Center</u>—Paige DeVries, Brian Driver, Audrey Hendrickson, Michael Puskarich, Jamie Stang

CALIFORNIA Clinical Center: UCSF San Francisco–Kimberly Yee, Brian Daniel; UCLA–Nida Qadir, Steven Chang, Gregory Hendey, George Lim, Andrea Tam, Rebecca Beutler, Trisha Agarwal, Julia Vargas; <u>Stanford University Hospital</u>–Jonasel Roque, Rosemary Vojnik; <u>UC Davis</u>–Skyler J. Pearson; <u>UCSF Fresno</u>–Alyssa Hughes; <u>University of Texas</u>–Elizabeth Vidales

- **COLORADO Clinical Center**: <u>University of Colorado Hospital</u>—Marc Moss\*, Adit Ginde\*, Carrie Higgins, Jeffrey McKeehan, Lani Finck, Michelle Howell, Jennifer Friedel; <u>Denver Health Medical Center</u>—Jason S. Haukoos, Ivor Douglas, Carolynn Lyle, Stephanie Gravitz, Terra Hiller, Judy Oakes, Alicia Cupelo; <u>National Jewish Health I Saint Joseph's Hospital</u>—James Finigan, Christine Griesmer
- MICHIGAN Clinical Center: University of Michigan Medical Center—Robert C. Hyzy, Pauline K. Park, Kristine Nelson, Norman Olbrich, Kelli McDonough, Stephen Kay, Andrew Admon, Theodore J. Iwashyna; <u>Henry Ford</u>—Namita Jayaprakash, Emanuel P. Rivers, Jasreen Kaur Gill, Anja Kathrina Jaehne, Aaron Cook, Jennifer Swiderek, Jacqueline Day; <u>Wayne State University</u>—Robert Sherwin, James Wooden, Thomas Mazzocco, Jeffrey Harrison, Theodore Falcon
- MONTEFIORE-SINAI Clinical Center: <u>Montefiore Moses</u>—Michelle Ng Gong\*, Rahul Nair, Omowunmi Amosu, Hiwet Tzehaie, Ayesha Asghar, Aluko A. Hope, Jen-Ting (Tina) Chen; <u>Montefiore Weiler</u>—Brenda Lopez, Caroline Boyle, Tori Aspir, Alexandra Gordon, Bryan Musmacker; <u>University of Arizona</u>—Jarrod Mosier, Cameron Hypes, Elizabeth Salvaggio, Boris Gilson, Jonathan Blohm; <u>Mt. Sinai</u> <u>Hospital</u>—Lynne Richardson, Kusum Mathews, Maxime Centeno, Sam Acquah, Patrick Maher, Neha Goel, George Loo
- **OHIO Clinical Center**: <u>Cleveland Clinic Foundation</u>—Abhijit Duggal, Omar Mehkri, Alexander King, Stuart Houltham; <u>University of</u> <u>Cincinnati Medical Center</u>—Kristin M. Hudock, Robert Duncan Hite\*, Nicole Hummel, Jessica Anderson, Tammy Roads
- PACIFIC NORTHWEST Clinical Center: <u>Harborview Medical Center</u>—Nicholas J Johnson, Bryce RH Robinson\*, Anna Ungar, Sarah Katsandres, Stephanie Gundel; <u>University of Washington</u>—T. Eoin West, Natalie L Cobb, Lara Lovelace-Macon, Denisse Bazan Dow, Navya Garimelle, Ellen Caldwell, Engi Attia; <u>Oregon Health and Science University</u>—Catherine L Hough\*, Akram Khan, Olivia Krol, Stephanie Nonas, Nicole Fontanese, Kelly Vranas; <u>Swedish Hospital</u>—Shane O'Mahony, Julie Wallick; <u>Cedars Sinai Medical Center</u>— Tanzira Zaman, Giuliana Cerro Chiang, June Choe, Lisa Herrera, Niree Hindoyan
- PITTSBURGH Clinical Center: <u>UPMC</u>—Derek C. Angus, Donald M. Yealy, Elizabeth Gimbel, Denise Scholl, Sara DiFiore, Hunter Skroczky, Amy Magoun, Alexandra Weissman, DavidT. Huang; <u>Temple University</u>—George Souiarov, Hannah Reimer, Lillian Finlaw, Sarah Loughran
- **SOUTHEAST Clinical Center**: <u>Wake Forest Baptist Health</u>-D. Clark Files, Chadwick Miller, Lauren Koehler; <u>Virginia Commonwealth</u> <u>University Medical Center</u>-Marjolein de Wit, Jessica Mason; <u>Medical University of South Carolina</u>-Andrew J. Goodwin, Abbey Grady, Katie Kirchoff; <u>University of Virginia</u>-Jeff Sturek, Mary Marshall
- UTAH: Intermountain Medical Center–Samuel Brown\*, Ithan Peltan, Julia Bryan, Jason Jacobs, Brent Armbruster, Joseph Bledsoe\*, Rebecca Roper, Michael Lanspa; <u>University of Utah Hospital</u>–Estelle S. Harris, Lisa J. Weaver, Macy A.G. Barrios, Lindsey J. Waddoups, Ann M. Lyons, Robert Paine III, Benjamin A. Haaland
- VANDERBILT Clinical Center: <u>Duke University Medical Center</u>—John Eppensteiner, Grace Hall, Andrew Bouffler, Lauren McGowan, Sam Francis, Bria Hall; <u>Louisiana State University Health Sciences Center</u>—Bennet deBoisblanc, Paula Lauto, Connie Romaine, Marie Sandi; <u>Vanderbilt University Medical Center</u>—Todd W. Rice\*, Wesley H. Self\*, Margaret Hays, Megan Roth, Jakea Johnson
- **Clinical Coordinating Center:** <u>Massachusetts General Hospital Biostatistics Center (CCC)</u>—David A. Schoenfeld\*, B. Taylor Thompson\*, Douglas L. Hayden, Nancy Ringwood, Cathryn Oldmixon, Christine Ulysse, Richard Morse, Ariela Muzikansky, Laura Fitzgerald, Samuel Whitaker, Alexander Nagrebetsky
- Johns Hopkins Medicine: Roy G. Brower, Sarina Sahetya
- National Heart, Lung, and Blood Institute: Lora Reineck, Neil Aggarwal, Karen Bienstock, Michelle Freemer, Myron Maclawiw, Gail Weinmann
- Protocol Review Committee: Laurie J. Morrison, Mark N. Gillespie, Richard J. Kryscio, Wojciech Zareba, Anne Rompalo, Michael Boeckh
- Data and Safety Monitoring Board: Polly Parsons, Jason D. Christie, Jesse R. Hall, Nicholas J. Horton, Laurie S. Zoloth, Neal Dickert Jr, Deborah Diercks

\*Clinical Center or CCC Principal Investigator.

Supplement 2 PETAL Network investigators and collaborating personnel.

## Supplemental Table 1 COVID-19 Ordinal Outcomes Scale

Description	Score		
Home without oxygen	1		
Long-term care facility or home with oxygen <sup>a</sup>	2		
Hospitalized, not receiving oxygen	3		
Hospitalized, with nasal cannula or face mask oxygen	4		
Hospitalized, receiving noninvasive ventilation or high-flow oxygen	5		
Hospitalized, receiving mechanical ventilation	6		
Hospitalized, receiving mechanical ventilation plus other organ support <sup>b</sup>	7		
Death or discharge receiving hospice care	8		
<ul> <li><sup>a</sup> Includes patients discharged to long-term acute care hospitals, skilled nursing facilities, and rehabilitation facilities on any degree of respiratory support.</li> <li><sup>b</sup> Other eligible organ support includes vasopressor, renal replacement therapy, and extracorporeal membrane oxygenation.</li> </ul>			

## Supplemental Table 2 Additional baseline patient characteristics<sup>a</sup>

	No. (%) of patients			
		Hospital outco	me	
Characteristic	Overall (N = 1480)	Discharged alive (n = 1218)	Died (n=262)	
Comorbidities				
Myocardial infarction	74 (5.0)	57 (4.7)	17 (6.5)	
Congestive heart failure	151 (10.2)	95 (7.8)	56 (21.4)	
Hypertension	845 (57.1)	653 (53.6)	192 (73.3)	
Peripheral vascular disease	63 (4.3)	43 (3.5)	20 (7.6)	
Cerebrovascular disease	118 (8.0)	82 (6.7)	36 (13.7)	
Dementia	86 (5.8)	57 (4.7)	29 (11.1)	
Chronic pulmonary disease	351 (23.7)	279 (22.9)	72 (27.5)	
Long-term home oxygen	70 (4.7)	49 (4.0)	21 (8.0)	
Chronic obstructive pulmonary disease	123 (8.3)	91 (7.5)	32 (12.2)	
Asthma	225 (15.2)	188 (15.4)	37 (14.1)	
Interstitial lung disease	24 (1.6)	16 (1.3)	8 (3.1)	
Chronic liver disease	53 (3.6)	37 (3.0)	16 (6.1)	
Diabetes	473 (32.0)	337 (27.7)	136 (51.9)	
Obesity (body mass index <sup>D</sup> ≥30)	712/1382 (51.5)	599/1140 (52.5)	113/242 (46.7)	
Connective tissue disease	49 (3.3)	39 (3.2)	10 (3.8)	
Chronic renal failure	154 (10.4)	111 (9.1)	43 (16.4)	
Long-term dialysis	43 (2.9)	30 (2.5)	13 (5.0)	
Immunocompromised	137 (9.3)	106 (8.7)	31 (11.8)	
Cancer	133 (9.0)	91 (7.5)	42 (16.0)	
Solid tumor (no metastasis)	69 (4.7)	49 (4.0)	20 (7.6)	
Solid tumor (with metastasis)	37 (2.5)	25 (2.1)	12 (4.6)	
Lymphoma	16 (1.1)	10 (0.8)	6 (2.3)	
Leukemia	20 (1.4)	15 (1.2)	5 (1.9)	
HIV or AIDS	18 (1.2)	15 (1.2)	3 (1.1)	
Alcohol abuse	30 (2.0)	26 (2.1)	4 (1.5)	
Drug abuse	20 (1.4)	15 (1.2)	5 (1.9)	
Depression	223 (15.1)	189 (15.5)	34 (13.0)	
Home medications				
Angiotensin-converting enzyme inhibitor	266 (18.0)	200 (16.4)	66 (25.2)	
Angiotensin receptor blocker	192 (13.0)	146 (12.0)	46 (17.6)	
Other antihypertensive agent	609 (41.1)	464 (38.1)	145 (55.3)	
Statin	528 (35.7)	393 (32.3)	135 (51.5)	
Aspirin	353 (23.9)	245 (20.1)	108 (41.2)	
Systemic corticosteroids	92 (6.2)	67 (5.5)	25 (9.5)	
Inhaled corticosteroids	152 (10.3)	121 (9.9)	31 (11.8)	
Immunosuppressive medication	92 (6.2)	70 (5.7)	22 (8.4)	
[Hydroxy]chloroquine	26 (1.8)	20 (1.6)	6 (2.3)	
Long-term	6 (0.4)	4 (0.3)	2 (0.8)	
Azithromycin	109 (7.4)	95 (7.8)	14 (5.3)	
Long-term	4 (0.3)	4 (0.3)	0 (0.0)	

<sup>a</sup> Where  $\geq$ 1 patient had missing data, the number of patients with nonmissing data is shown. <sup>b</sup> Calculated as weight in kilograms divided by height in meters squared.

# Supplemental Table 3 Adults with positive SARS-CoV-2 tests admitted to study hospitals from March 1 to April 1, 2020

Characteristic	Overall (N=4927)
Age, y, median (IQR) (n=4895)	62 (50-73)
Female, No. (%) (n=4921)	2120 (43.1)
Race/ethnicity, No. (%)	
Hispanic/Latino	1081 (21.9)
Asian (non-Hispanic)	168 (3.4)
Black (non-Hispanic)	1855 (37.6)
White (non-Hispanic)	1055 (21.4)
Native Hawaiian/Pacific Islander (non-Hispanic)	10 (0.2)
American Indian/Native Alaskan (non-Hispanic)	8 (0.2)
Multiple (non-Hispanic)	11 (0.2)
Other/unknown	739 (15.0)

Supplemental Table 4 Detailed clinical characteristics of patients at the time of hospital admission<sup>a</sup>

	Overall (N=1480)	Hospital outcome	
Characteristic		Discharged alive (n=1218)	Died (n=262)
Symptom			
Fever	1237 (83.6)	1036 (85.1)	201 (76.7)
Chills	573 (38.7)	505 (41.5)	68 (26.0)
Cough	1253 (84.7)	1058 (86.9)	195 (74.4)
Productive cough	360 (24.3)	305 (25.0)	55 (21.0)
Sore throat	205 (13.9)	179 (14.7)	26 (9.9)
Rhinorrhea	178 (12.0)	161 (13.2)	17 (6.5)
Chest pain	249 (16.8)	227 (18.6)	22 (8.4)
Dyspnea	1181 (79.8)	984 (80.8)	197 (75.2)
Myalgia/arthralgia	535 (36.1)	478 (39.2)	57 (21.8)
Confusion	148 (10.0)	78 (6.4)	70 (26.7)
Anosmia or ageusia	77 (5.2)	73 (6.0)	4 (1.5)
Nausea or vomiting	362 (24.5)	318 (26.1)	44 (16.8)
Abdominal pain	148 (10.0)	126 (10.3)	22 (8.4)
Diarrhea	399 (27.0)	349 (28.7)	50 (19.1)
Initial vital signs			
Hypotension <sup>D</sup>	56/1474 (3.8)	32/1212 (2.6)	24/262 (9.2)
Heart rate >100 beats per minute	512/1474 (34.7)	428/1212 (35.3)	84/262 (32.1)
Tachypnea <sup>c</sup>	388/1478 (26.3)	297/1216 (24.4)	91/262 (34.7)
Hypoxemia (Spo <sub>2</sub> <90%)	179/1474 (12.1)	127/1213 (10.5)	52/261 (19.9)
Score on Glasgow Coma Scale (n=1462)	15 (15-15)	15 (15-15)	15 (14-15)
Spo <sub>2</sub> , % (n=1474)	95 (92-97)	95 (92-97)	94 (91-97)
Pao <sub>2</sub> /Fio <sub>2</sub> ratio			
≥300	938/1452 (64.6)	832/1195 (69.6)	106/257 (41.2)
200-299	319/1452 (22.0)	248/1195 (20.8)	71/257 (27.6)
100-199	144/1452 (9.9)	92/1195 (7.7)	52/257 (20.2)
<100	51/1452 (3.5)	23/1195 (1.9)	28/257 (10.9)
SOFA score ≥2	1203 (81.3)	949 (77.9)	254 (96.9)
Initial laboratory results			
Hemoglobin, g/dL (n=1472)	13.3 (12.0-14.6)	13.4 (12.2-14.7)	12.4 (10.8-13.8)
Platelets, 1000/µL (n=1466)	187 (146-237)	192 (150-238)	173 (132-234)
Lymphocyte count <1000/µL	680/1271 (53.5)	532/1036 (51.4)	148/235 (63.0)
Urea nitrogen, mg/dL (n=1446)	15 (11-24)	14 (10-21)	25 (16-39)
Albumin, g/dL (n=1133)	3.7 (3.3-4.0)	3.7 (3.4-4.0)	3.4 (3.0-3.8)
Lactate dehydrogenase, U/L (n=590)	335 (251-443)	321 (248-421)	443 (313-567)
C-reactive protein, mg/L (n=577)	21 (8-84)	19 (7-80)	28 (13-123)
Ferritin >1000 ng/mL	163/568 (28.7)	124/483 (25.7)	39/85 (45.9)
p-dimer >1.0 mg/L	168/438 (38.4)	122/370 (33.0)	46/68 (67.6)

Abbreviations: Fio2, fraction of inspired oxygen; SOFA, Sequential Organ Failure Assessment; Spo2, oxygen saturation as measured by pulse oximetry.

<sup>a</sup> Values reported as number (percentage) or median (IQR). Where ≥1 patient had missing data, the number of patients with nonmissing data is shown.
 <sup>b</sup> Defined as systolic blood pressure <90 mm Hg or mean arterial pressure <65 mm Hg.</li>
 <sup>c</sup> Defined as respiratory rate >22 breaths per minute.

Supplemental Table 5 Complications clinically diagnosed during hospitalization<sup>a</sup>

		Hospital outcome	
Complication	Overall (N=1480)	Discharged alive (n = 1218)	Died (n=262)
Stroke	14 (0.9)	7 (0.6)	7 (2.7)
Atrial fibrillation	145 (9.8)	80 (6.6)	65 (24.8)
Ventricular arrhythmias	43 (2.9)	17 (1.4)	26 (9.9)
Cardiac arrest	81 (5.5)	4 (0.3)	77 (29.4)
Myocardial infarction	47 (3.2)	28 (2.3)	19 (7.3)
Congestive heart failure	67 (4.5)	39 (3.2)	28 (10.7)
Acute respiratory distress syndrome	483 (32.6)	283 (23.2)	200 (76.3)
Arterial ischemic event	5 (0.3)	4 (0.3)	1 (0.4)
Venous thromboembolism	46 (3.1)	33 (2.7)	13 (5.0)
Deep vein thrombosis	28 (1.9)	21 (1.7)	7 (2.7)
Pulmonary embolism	21 (1.4)	14 (1.1)	7 (2.7)
Shock	302 (20.4)	141 (11.6)	161 (61.5)
Bacteremia	82 (5.5)	50 (4.1)	32 (12.2)
Acute renal failure <sup>b</sup>	321/1437 (22.3)	173/1188 (14.6)	148/249 (59.4)

 $^a_b$  Values reported as number (percentage). Complications were obtained from clinical documentation.  $^b_b$  Restricted to patients not requiring hemodialysis at baseline.

Supplemental Table 6 Clinical management within 24 hours of hospital admission<sup>a</sup>

		Hospital outcome	
Characteristic	Overall (N=1480)	Discharged alive (n=1218)	Died (n=262)
Highest level of care			
General care area	1032 (69.7)	930 (76.4)	102 (38.9)
Intermediate care	79 (5.3)	59 (4.8)	20 (7.6)
Intensive care	369 (24.9)	229 (18.8)	140 (53.4)
Respiratory support techniques			
Nasal cannula or face mask	773 (52.2)	648 (53.2)	125 (47.7)
High-flow nasal cannula	29 (2.0)	20 (1.6)	9 (3.4)
Noninvasive positive pressure ventilation	25 (1.7)	15 (1.2)	10 (3.8)
Mechanical ventilation	203 (13.7)	110 (9.0)	93 (35.5)
Prone positioning	30 (2.0)	20 (1.6)	10 (3.8)
Inhaled pulmonary vasodilator	19 (1.3)	10 (0.8)	9 (3.4)
Extracorporeal membrane oxygenation	5 (0.3)	4 (0.3)	1 (0.4)
Vasopressors or inotropes	131 (8.9)	62 (5.1)	69 (26.3)
Renal replacement therapy	33 (2.2)	20 (1.6)	13 (5.0)
Pharmacologic therapy administered			
Azithromycin	791 (53.4)	646 (53.0)	145 (55.3)
Other antibiotics	978 (66.1)	774 (63.5)	204 (77.9)
Therapeutic anticoagulation	166 (11.2)	113 (9.3)	53 (20.2)
Hydroxychloroquine or chloroquine	309 (20.9)	247 (20.3)	62 (23.7)
Interleukin 6 receptor antagonist	18 (1.2)	12 (1.0)	6 (2.3)
Oral or intravenous corticosteroids	135 (9.1)	102 (8.4)	33 (12.6)
Remdesivir	20 (1.4)	18 (1.5)	2 (0.8)
Lopinavir/ritonavir	12 (0.8)	8 (0.7)	4 (1.5)
<sup>a</sup> Values reported as number (percentage).			

# Supplemental Table 7 Risk factors for early respiratory failure<sup>a,b</sup>

Risk factor	Cross-validation models including variable, %	Candidate risk factor included in final model?	Odds ratio (95% Cl)
Female sex	50.4	Yes	0.71 (0.51-0.98)
Body mass index	55.1	Yes	1.03 (1.01-1.05)
Chronic cardiovascular disease	60.2	Yes	1.21 (0.86-1.69)
Cough	59.2	Yes	0.62 (0.41-0.95)
Dyspnea	73.2	Yes	2.19 (1.36-3.53)
URI symptoms	46.5	Yes	0.79 (0.54-1.16)
Gastrointestinal symptoms	85.0	Yes	0.75 (0.54-1.04)
Respiratory rate <sup>c</sup>	100	Yes	1.09 (1.06-1.12)
Glasgow Coma Scale <15 <sup>c</sup>	100	Yes	4.69 (3.07-7.16)
Serum creatinine (mg/dL) <sup>c</sup>	61.6	Yes	1.10 (1.02-1.18)
White blood count (×1000/µL) <sup>c</sup>	99.6	Yes	1.07 (1.04-1.11)
Serum AST >40 U/L <sup>c</sup>	89.7	Yes	1.77 (1.27-2.49)
Days from symptom onset	27.1	No	—
Age	28.8	No	_
Race/ethnicity	15.3	No	
Chronic respiratory disease	35.0	No	
Diabetes	39.6	No	_
Smoking and/or vaping	20.7	No	_
Chronic use of systemic steroids	19.7	No	_
Long-term care facility resident	28.1	No	_
Heart rate <sup>c</sup>	34.5	No	
Systolic blood pressure <sup>c</sup>	39.8	No	_
Temperature <sup>c</sup>	14.6	No	_

Abbreviations: AST, aspartate aminotransferase; URI, upper respiratory tract infection.

<sup>a</sup> Early respiratory failure defined as defined as treatment with ≥11 L/min oxygen by face mask, high flow oxygen device, noninvasive positive pressure ventilation, or invasive mechanical ventilation within 24 hours of hospital arrival. Death without respiratory failure within 24 hours was treated as a respiratory failure event to account for effects of patients' care goals on respiratory support interventions.
 <sup>b</sup> Analysis includes 1437 patients admitted directly to the study hospital or transferred to the study hospital from an outside emergency department.
 <sup>c</sup> First-available value after study hospital arrival.

# Supplemental Table 8 Risk factors for late respiratory failure<sup>a,b</sup>

( Risk factor	Cross-validation models including variable, %	Candidate risk factor included in final model?	Odds ratio (95% Cl)
Days from symptom onset	99.8	Yes	0.94 (0.90-0.98)
Female sex	96.7	Yes	0.55 (0.41-0.74)
Age, y <40 40-49 50-59 60-69 70-79 ≥80	89.1	Yes	Reference 1.49 (0.76-2.90) 1.91 (1.04-3.53) 2.49 (1.36-4.59) 4.11 (2.19-7.72) 4.89 (2.52-9.47)
Diabetes	94.7	Yes	1.39 (1.01-1.90)
Long-term care facility resident	82.2	Yes	0.81 (0.46-1.44)
Highest heart rate (per 10 beat per minute increase) <sup>c</sup>	77.1	Yes	1.07 (1.06-1.08)
Highest respiratory rate, <sup>c</sup>	100	Yes	1.06 (1.04-1.09)
Body temperature <sup>d</sup> Hypothermic (<36 °C) Normothermic (36-38 °C) Hyperthermic (>38 °C)	80.5	Yes	0.35 (0.13-0.91) Reference 1.50 (1.10-2.05)
First-available score on Glasgow Coma Scale <15 <sup>c</sup>	99.9	Yes	2.05 (1.19-3.53)
First-available serum creatinine level (mg/dL) <sup>c</sup>	91.0	Yes	1.06 (0.98-1.16)
First-available white blood cell count (×1000/µL) <sup>c</sup>	87.9	Yes	1.05 (1.02-1.09)
Race/ethnicity	40.8	No	—
Body mass index	27.2	No	_
Chronic respiratory disease	31.4	No	_
Chronic cardiovascular disease	33.5	No	_
Smoking and/or vaping	39.6	No	_
Chronic use of systemic steroids	21.1	No	_
Lowest systolic blood pressure <sup>c</sup>	49.3	No	_
First-available serum level of aspartate aminotransferase >4	10 U/L <sup>c</sup> 23.1	No	_

<sup>a</sup> Late respiratory failure defined as defined as treatment with ≥11 L/min oxygen by face mask, high flow oxygen device, noninvasive positive pressure ventilation, or invasive mechanical ventilation beginning >24 hours of hospital arrival. Death without respiratory failure after 24 hours was treated as a respiratory failure event to account for effects of patients' care goals on respiratory support interventions.
 <sup>b</sup> Analysis includes 1196 patients who did not die or develop respiratory failure within 24 hours of study hospital arrival.
 <sup>c</sup> Value obtained within 24 hours of hospital arrival.
 <sup>d</sup> Temperature most different from 37 °C in the first 24 hours after arrival at the study hospital.

Supplemental Table 9 Surviving patients' demographic, clinical, and management characteristics by discharge on new or increased respiratory support<sup>a</sup>

		Respiratory support at discharge		
Characteristic	All survivors (N=1218)	New or increased respiratory support (n=221)	No escalation from baseline respiratory support (n=997)	
Age	59.3 (46.9-70.2)	65.2 (52.0-73.4)	58.4 (46.1-69.0)	
Female sex	560 (46.0)	105 (47.5)	455 (45.6)	
Race/ethnicity				
Hispanic or Latino	247 (20.3)	46 (20.8)	201 (20.2)	
Non-Hispanic Black	367 (30.1)	53 (24.0)	314 (31.5)	
Non-Hispanic White	433 (35.6)	98 (44.3)	335 (33.6)	
Other/unknown	171 (14.0)	24 (10.9)	147 (14.7)	
Body mass index <sup>b</sup> (n=1140)	30.4 (26.2-35.9)	30.5 (26.0-35.3)	30.4 (26.3-36.1)	
Charlson Comorbidity Index	2 (1-4)	3 (1-5)	2 (1-4)	
Comorbidities				
Chronic pulmonary disease	279 (22.9)	58 (26.2)	221 (22.2)	
Cardiovascular disease	162 (13.3)	33 (14.9)	129 (12.9)	
Chronic renal failure	111 (9.1)	24 (10.9)	87 (8.7)	
Hypertension	653 (53.6)	132 (59.7)	521 (52.3)	
Diabetes	337 (27.7)	63 (28.5)	274 (27.5)	
Admitted from care facility	70/1214 (5.8)	11 (5.0)	59 (5.9)	
Hospital day 1 SOFA score	2 (2-4)	3 (2-4)	2 (1-3)	
Initial vital signs				
Respiratory rate, breaths per minute (n=1216)	20 (18-22)	20 (18-23)	20 (18-22)	
Glasgow Coma Scale score <15	103/1204 (8.6)	17 (7.7)	86 (8.6)	
$Pao_2/Fio_2$ ratio (n = 1195)	337 (279-431)	291 (232-337)	360 (291-431)	
Respiratory failure	345 (28.3)	106 (48.0)	239 (24.0)	
Admitted to intensive care unit	371 (30.5)	107 (48.4)	264 (26.5)	
Therapies during hospitalization				
Inpatient respiratory support (ever)				
Nasal cannula or face mask	934 (76.7)	219 (99.1)	715 (71.7)	
High-flow nasal cannula	178 (14.6)	65 (29.4)	113 (11.3)	
Noninvasive positive pressure ventilation	90 (7.4)	30 (13.6)	60 (6.0)	
Mechanical ventilation	226 (18.6)	62 (28.1)	164 (16.4)	
Vasopressors or inotropes	184 (15.1)	48 (21.7)	136 (13.6)	
Renal replacement therapy	62 (5.1)	15 (6.8)	47 (4.7)	
Pharmacologic therapy				
Therapeutic anticoagulation	240 (19.7)	51 (23.1)	189 (19.0)	
Hydroxychloroquine or chloroquine	629 (51.6)	133 (60.2)	496 (49.7)	
Interleukin 6 receptor antagonist	71 (5.8)	16 (7.2)	55 (5.5)	
Systemic corticosteroids	134 (11.0)	30 (13.6)	104 (10.4)	
Remdesivir	72 (5.9)	11 (5.0)	61 (6.1)	
Hospital length of stay, d	8 (5-15)	11 (6-19)	7 (4-13)	

Abbreviations: FIO2, fraction of inspired oxygen; SOFA, Sequential Organ Failure Assessment; SpO2, oxygen saturation as measured by pulse oximetry. <sup>a</sup> Values reported as number (percentage) or median (IQR). Where ≥1 patient had missing data, the number of patients with nonmissing data is shown. <sup>b</sup> Calculated as weight in kilograms divided by height in meters squared.

Supplemental Table 10 Demographic, clinical, and management characteristics among patients admitted from home stratified by discharge with new health care services<sup>a</sup>

		Health care services at discharge	
Characteristic	All survivors admitted from home <sup>b</sup> (N=1153)	New home- or facility-based health care services (n=259)	No new health care services (n=894)
Age	58.6 (46.4-69.3)	69.5 (59.0-78.6)	55.5 (43.8-66.0)
Female sex	531 (46.1)	119 (45.9)	412 (46.1)
Race/ethnicity			
Hispanic or Latino	239 (20.7)	43 (16.6)	196 (21.9)
Non-Hispanic Black	352 (30.5)	75 (29.0)	277 (31.0)
Non-Hispanic White	403 (35.0)	116 (44.8)	287 (32.1)
Other/unknown	159 (13.8)	25 (9.7)	134 (15.0)
Body mass index (n=1089)	30.5 (26.2-36.1)	28.7 (25.2-33.7)	30.8 (26.7-36.4)
Charlson Comorbidity Index	2 (1-4)	4 (2-5)	2 (0-3)
Comorbidities			
Chronic pulmonary disease	262 (22.7)	63 (24.3)	199 (22.3)
Cardiovascular disease	143 (12.4)	61 (23.6)	82 (9.2)
Chronic renal failure	103 (8.9)	38 (14.7)	65 (7.3)
Hypertension	612 (53.1)	164 (63.3)	448 (50.1)
Diabetes	318 (27.6)	85 (32.8)	233 (26.1)
Hospital day 1 SOFA score	2 (2-3)	4 (2-6)	2 (1-3)
Initial vital signs			
Respiratory rate breaths per minute $(n=1151)$	20 (18-22)	20 (18-24)	20 (18-22)
Glasgow Coma Scale score <15	74/1139 (6.5)	45/254 (177)	29/885 (3.3)
$Pao_2/Fio_2$ ratio (n = 1133)	337 (279-431)	319 (221-390)	360 (291-431)
Respiratory failure	330 (28.6)	166 (64.1)	164 (18.3)
Admitted to intensive care unit	355 (30.8)	160 (61.8)	195 (21.8)
Therapies during hospitalization			
Inpatient respiratory support (ever)			
Nasal cannula or face mask	880 (76.3)	231 (89.2)	649 (72.6)
High-flow nasal cannula	172 (14.9)	78 (30.1)	94 (10.5)
Noninvasive positive pressure ventilation	84 (7.3)	41 (15.8)	43 (4.8)
Mechanical ventilation	212 (18.4)	134 (517)	78 (8 7)
Vasopressors or inotropes	179 (15.5)	120 (46.3)	59 (6.6)
Renal replacement therapy	58 (5.0)	36 (13.9)	22 (2.5)
Pharmacologic therapy			(,
Therapeutic anticoagulation	222 (19.3)	108 (41.7)	114 (12.8)
Hydroxychloroquine or chloroquine	604 (52.4)	172 (66.4)	432 (48.3)
Interleukin 6 receptor antagonist	69 (6,0)	33 (12 7)	36 (4 0)
Systemic corticosteroids	129 (11 2)	55 (21.2)	74 (8 3)
Remdesivir	71 (6.2)	25 (9.7)	46 (5.1)
Hospital length of stay, d	8 (4-14)	22 (12-32)	6 (4-10)

Abbreviations: Fio<sub>2</sub>, fraction of inspired oxygen; SOFA, Sequential Organ Failure Assessment; Spo<sub>2</sub>, oxygen saturation as measured by pulse oximetry. <sup>a</sup> Values reported as number (percentage) or median (IQR). Where ≥1 patient had missing data, the number of patients with nonmissing data is shown. <sup>b</sup> Includes patients surviving to discharge who did not reside in a long-term care or rehabilitation facility or a long-term acute care hospital at baseline.





**Supplemental Figure 3** Unadjusted hospital mortality stratified by selected clinical and demographic parameters. Data shown are stratified mortality rate with binomial 95% confidence interval.