

Risk Factors for Intensive Care Unit Admission and In-hospital Mortality among Hospitalized Adults Identified through the U.S. Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization Surveillance Network (COVID-NET)

Lindsay Kim^{1,2*}, Shikha Garg^{1,2,*}, Alissa O'Halloran¹, Michael Whitaker^{1,3}, Huong Pham¹, Evan J. Anderson^{4,5,6}, Isaac Armistead⁷, Nancy M. Bennett⁸, Laurie Billing⁹, Kathryn Como-Sabetti¹⁰, Mary Hill¹¹, Sue Kim¹², Maya L. Monroe¹³, Alison Muse¹⁴, Arthur L. Reingold¹⁵, William Schaffner¹⁶, Melissa Sutton¹⁷, H. Keipp Talbot¹⁶, Salina M. Torres¹⁸, Kimberly Yousey-Hindes¹⁹, Rachel Holstein^{1,20}, Charisse Cummings^{1,21}, Lynette Brammer¹, Aron J. Hall¹, Alicia M. Fry¹, and Gayle E. Langley¹

¹CDC COVID-NET Team, Atlanta, GA, USA

²US Public Health Service, Rockville, MD, USA

³Eagle Global Scientific, Atlanta, GA, USA

⁴Departments of Medicine and Pediatrics, Emory University School of Medicine, Atlanta, GA, USA

⁵Emerging Infections Program, Georgia Department of Health, Atlanta, GA, USA

⁶Veterans Affairs Medical Center, Atlanta, GA, USA

⁷University of Colorado Anschutz Medical Campus, Aurora, CO, USA

⁸University of Rochester School of Medicine and Dentistry, Rochester, NY, USA

⁹Ohio Department of Health, Columbus, OH, USA

¹⁰Minnesota Department of Health, St. Paul, MN, USA

¹¹Salt Lake County Health Department, Salt Lake City, UT, USA

¹²Michigan Department of Health and Human Services, Lansing, MI, USA

¹³Maryland Department of Health, Baltimore, MD, USA

¹⁴New York State Department of Health, Albany, NY, USA

¹⁵University of California Berkeley, Berkeley, CA, USA

¹⁶Vanderbilt University School of Medicine, Nashville, TN, USA

¹⁷Oregon Health Authority, Portland, OR, USA

¹⁸New Mexico Department of Health, Santa Fe, NM, USA

¹⁹Connecticut Emerging Infections Program, Yale School of Public Health, New Haven, CT, USA

²⁰Oak Ridge Institute for Science and Education, Oak Ridge, TN, USA

²¹Chickasaw Nation Industries, Norman, OK, USA

*These authors contributed equally to this work.

Corresponding author:

Lindsay Kim, 1600 Clifton Road, MS H24-5, Atlanta, GA 30329, 404-639-5218, LKim@cdc.gov

Summary:

Among 2,491 adults hospitalized with laboratory-confirmed COVID-19, 32% required intensive care unit (ICU) admission, 19% required mechanical ventilation, and 17% died in-hospital. Increasing age, male sex, and underlying conditions were associated with higher risk of ICU admission and death.

Accepted Manuscript

ABSTRACT

Background: Currently, the United States has the largest number of reported coronavirus disease 2019 (COVID-19) cases and deaths globally. Using a geographically diverse surveillance network, we describe risk factors for severe outcomes among adults hospitalized with COVID-19.

Methods: We analyzed data from 2,491 adults hospitalized with laboratory-confirmed COVID-19 during March 1–May 2, 2020 identified through the Coronavirus Disease 2019-Associated Hospitalization Surveillance Network comprising 154 acute care hospitals in 74 counties in 13 states. We used multivariable analyses to assess associations between age, sex, race and ethnicity, and underlying conditions with intensive care unit (ICU) admission and in-hospital mortality.

Results: Ninety-two percent of patients had ≥ 1 underlying condition; 32% required ICU admission; 19% invasive mechanical ventilation; and 17% died. Independent factors associated with ICU admission included ages 50-64, 65-74, 75-84 and ≥ 85 years versus 18-39 years (adjusted risk ratio (aRR) 1.53, 1.65, 1.84 and 1.43, respectively); male sex (aRR 1.34); obesity (aRR 1.31); immunosuppression (aRR 1.29); and diabetes (aRR 1.13). Independent factors associated with in-hospital mortality included ages 50-64, 65-74, 75-84 and ≥ 85 years versus 18-39 years (aRR 3.11, 5.77, 7.67 and 10.98, respectively); male sex (aRR 1.30); immunosuppression (aRR 1.39); renal disease (aRR 1.33); chronic lung disease (aRR 1.31); cardiovascular disease (aRR 1.28); neurologic disorders (aRR 1.25); and diabetes (aRR 1.19).

Conclusion: In-hospital mortality increased markedly with increasing age. Aggressive implementation of prevention strategies, including social distancing and rigorous hand hygiene, may benefit the population as a whole, as well as those at highest risk for COVID-19-related complications.

Keywords: COVID-19, SARS-CoV-2, hospitalization, mortality, surveillance

Accepted Manuscript

INTRODUCTION

Since a new coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), was first identified in China in December 2019, approximately 6 million cases of coronavirus disease-2019 (COVID-19) have been reported globally [1]. As of July 7, approximately 3 million cases, including ~130,000 deaths, have been reported in the United States, and case counts continue to rise [1] with evidence of widespread community transmission [2].

Reports from China, Italy, and New York City have demonstrated that hospitalized patients are generally older and have underlying medical conditions, such as hypertension and diabetes [3-5]. These studies have also found that older patients and those with certain underlying medical conditions were at higher risk for severe outcomes [3, 6, 7]. Among cases reported to the U.S. Centers for Disease Control and Prevention (CDC) from local and state health departments, the prevalence of underlying medical conditions increased as severity of infections increased [8, 9], although findings were limited by incomplete information. Questions remain about the independent association of sex, race and ethnicity, and specific underlying conditions with severe outcomes among persons hospitalized with COVID-19, after adjusting for age and other potential confounders.

Comprehensive data on U.S. patients with severe COVID-19 infections are needed to better inform clinicians' understanding of groups at risk for poor outcomes and to inform prevention efforts and future interventions. We implemented population-based surveillance for laboratory-confirmed COVID-19-associated hospitalizations, collecting clinical data from hospitalized patients in 154 hospitals in 13 states since March 1, 2020. Using a convenience sample of patients identified through this surveillance system, we describe the characteristics of U.S. adults hospitalized with COVID-19 and assess risk factors for intensive care unit (ICU) admission and in-hospital mortality.

METHODS

Surveillance Overview

The Coronavirus Disease 2019-Associated Hospitalization Surveillance Network (COVID-NET) has been previously described [10]. Eligible COVID-19-associated hospitalizations occurred among persons who (1) resided in a pre-defined surveillance catchment area; and (2) had a positive SARS-CoV-2 test within 14 days prior to or during hospitalization.

COVID-NET surveillance occurs in acute care hospitals within 99 counties in 14 states (California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah), covering a catchment population of approximately 32 million persons (~10% of the U.S. population). COVID-NET surveillance was initiated for cases with hospital admission on or after March 1, 2020. Although COVID-NET includes all age groups, for this analysis, we excluded children <18 years of age due to small counts (n=101) and one surveillance site (Iowa) for which medical chart abstractions were not conducted. We also excluded patients who were still hospitalized at the time of this analysis and all patients for whom medical chart abstractions had not yet been completed as of May 2, 2020. Because the COVID-19 pandemic limited the ability of surveillance officers to access medical records at facilities, patients were more likely to be included in this analysis if they were hospitalized at facilities that allowed remote chart access, participated in Health Information Exchanges, or were able to mail or fax records.

Laboratory-confirmed COVID-19-associated hospitalizations were identified using laboratory and reportable condition databases, hospital infection control databases, electronic medical records, and/or review of hospital discharge records. Laboratory tests were ordered at the discretion of the treating healthcare provider.

Medical chart reviews were conducted by trained surveillance officers using a standard case report form. Underlying medical conditions were categorized into major groups (Appendix Table 1). Obesity and severe obesity were defined as a calculated body mass index (BMI) ≥ 30 kg/m² and BMI ≥ 40 kg/m², respectively. Chest radiograph results were obtained from the radiology reports and not from review of the original radiograph. We defined severe outcomes as either ICU admission or in-hospital mortality.

Statistical Analysis

After the exclusions noted above, we included adults hospitalized within 154 acute care hospitals in 74 counties in 13 states with an admission date during March 1–May 2, 2020 who had either been discharged from the hospital or died during hospitalization and had complete medical chart abstractions. We calculated proportions using the number of patients with data available on each characteristic as the denominator.

We examined the association of demographic factors, underlying medical conditions, and use of angiotensin-converting enzyme (ACE)-inhibitors and angiotensin receptor blockers (ARBs) prior to hospitalization with ICU admission and in-hospital death using chi square tests. Variables considered for inclusion in the final models included current or former smoker, hypertension, obesity, diabetes, chronic lung disease (CLD), cardiovascular disease (CVD) (excluding hypertension), neurologic disorders, renal disease, immunosuppression, gastrointestinal/liver disease, hematologic conditions, rheumatologic/autoimmune conditions, and use of ACE-inhibitors or ARBs prior to hospitalization. All multivariable models included age groups (18–39, 40–49, 50–64, 65–74, 75–84, and ≥ 85 years), sex, and race and ethnicity; models incorporated clustering by site to account for geographic differences. Other variables with p-values < 0.10 in bivariate analyses were included in the multivariable analyses. Log-linked Poisson generalized estimating equations regression with an

exchangeable correlation matrix [11, 12] was used to generate adjusted risk ratios (aRR) and 95% confidence intervals (CI) for the risk of ICU admission and in-hospital death. Additional multivariable models were used to examine the association between the number of underlying medical conditions and ICU admission or in-hospital death. Two-sided p-values <0.05 were considered statistically significant. All analyses were performed using the SAS 9.4 software (SAS Institute Inc., Cary, NC, USA).

These data were collected as part of routine public health surveillance and determined to be non-research by CDC. Participating sites obtained approval for the COVID-NET surveillance protocol from their respective state and local IRBs, as required.

RESULTS

A total of 2,491 COVID-19-associated hospitalized adults from 13 surveillance sites were included (Appendix Figure 1). Patients came from 43% (154/357) of the acute care hospitals included in COVID-NET surveillance across the 13 sites (Appendix Table 2). The median age and sex distribution of included and excluded patients were similar (Appendix Table 3).

Characteristics of hospitalized patients with COVID-19

Among the 2,491 hospitalized adults, median age was 62 years (interquartile range (IQR), 50–75), and almost 75% were ≥ 50 years (Table 1). Forty-seven percent of patients (n=1178/2490) were non-Hispanic whites, 30% non-Hispanic blacks (n=755/2490), and 12% Hispanics (n=306/2490). Nearly one-third of patients were current or former smokers.

Almost all patients (n=2278/2489, 92%) had ≥ 1 underlying medical condition, with hypertension (n=1428/2488, 57%), obesity (n=1154/2332, 50%), and chronic metabolic disease (n=1024/2486, 41%) most frequently documented. Among patients with chronic

metabolic disease, 80% (n=819/1024) had diabetes mellitus; hypertension alone was documented in only 4% (n=91/2490) of patients. The proportion of patients with any documented underlying medical condition increased with age ($p<0.05$) (Figure 1A). Prevalence of CLD, neurologic conditions, obesity, and renal disease varied between males and females ($p<0.05$, Figure 1B). CVD, CLD, and neurologic conditions were more prevalent among non-Hispanic whites, while diabetes, hypertension, obesity and renal disease were more common among non-Hispanic blacks ($p<0.05$, Figure 1C).

Cough (75%), fever or chills (74%), and shortness of breath (70%) were commonly documented symptoms at admission (Table 2 and Appendix Table 4). Gastrointestinal symptoms, including nausea, vomiting, and diarrhea, were documented in almost 30% of patients. Median length of hospitalization was 6 days (IQR, 3–11). Median values of initial vital signs were within normal range, except for elevated blood pressure (Table 2). Thirty-three individuals had a pathogen detected from positive blood cultures (Appendix Table 5). Viral co-detections from respiratory specimens were rare among those who were tested (n=38/1549, 2.5%) (Appendix Table 6). Among 1932 patients with chest radiograph performed, 92% (n=1769) were documented as abnormal (Table 2, Appendix Table 7). Ninety-five percent (n=540/566) of patients with chest computerized tomography (CT) had abnormal findings, and ground glass opacity was documented in 62% (n=350/566) (Table 2, Appendix Table 7).

Forty-five percent (n=1125/2482) of patients received investigational treatments for COVID-19 during hospitalization (Table 2). The most common treatments included hydroxychloroquine (n=1065/1125, 95%) and the combination of azithromycin and ≥ 1 other COVID-19 treatment (n=725/1125, 64%) (non-mutually exclusive categories). The most frequent discharge diagnoses recorded in hospital discharge summaries were pneumonia (n=1395/2485, 56%), acute respiratory failure (n=999/2487, 40%), acute renal failure (n=456/2,485, 18%), and sepsis (n=443/2,479, 18%).

Thirty-two percent (n=798/2490) of patients required ICU admission with median length of ICU stay of 6 days (IQR, 2–11) (Table 2). Median days from hospital admission to ICU admission was

1 day (range, 0–19; IQR, 0–2). Among 2,489 hospitalized patients, the highest respiratory support received was invasive mechanical ventilation in 19% (n=462), bilevel positive airway pressure (BIPAP) or continuous positive airway pressure (CPAP) in 3% (n=82), and high flow nasal cannula (HFNC) in 7% (n=170). Fifty-three percent (n=246/462) of patients that received invasive mechanical ventilation died in-hospital (median age, 71 years; IQR, 62–79). Vasopressors were used in 15% (n=373/2486) of patients, while renal replacement therapy was used in 5% (n=115/2487). As age increased, so did the proportion of patients who required ICU admission, invasive mechanical ventilation, and vasopressors ($p < 0.05$, Figure 2A). Males were admitted to the ICU and treated with invasive mechanical ventilation, HFNC, or vasopressors more frequently than females ($p < 0.05$) (Figure 2B). Non-Hispanic whites more frequently received BIPAP, CPAP or HFNC than other race and ethnicities ($p < 0.05$, Figure 2C).

Seventeen percent (n=420/2490) of patients died during hospitalization. Median age was 76 years (IQR, 66–85); 58% (n=244) were male; 71% (n=299) were admitted to the ICU; and 59% (n=246) received invasive mechanical ventilation (Table 2). The median length of hospitalization among patients who died was 7 days (IQR, 4–12). The proportion of patients who died increased with increasing age, ranging from 3% among 18–49 years to 10% among 50–64 years to 29% among ≥ 65 years (Figure 2A). Males died more frequently compared to females ($p < 0.05$) (Figure 2B), as did non-Hispanic whites compared to other race and ethnicities ($p < 0.05$, Figure 2C).

Risk factors for ICU admission and death

Factors independently associated with ICU admission included age 50–64 years (adjusted risk ratio (aRR) = 1.53; 95% confidence interval (CI), 1.28 to 1.83); 65–74 years (aRR = 1.65; CI, 1.34 to 2.03); 75–84 years (aRR = 1.84; CI, 1.60 to 2.11); ≥ 85 years (aRR = 1.43; CI, 1.00 to 2.04); male sex (aRR = 1.34; CI, 1.20 to 1.50); obesity (aRR = 1.31; CI, 1.16 to 1.47); immunosuppression (aRR = 1.29; CI, 1.13 to 1.47); and diabetes (aRR = 1.13; CI, 1.03 to 1.24) (Figure 3A and Appendix Table 8A).

Independent factors associated with in-hospital mortality included age 50–64 years (aRR = 3.11; CI 1.50 to 6.46); age 65–74 years (aRR = 5.77; CI, 2.64 to 12.64); age 75–84 years (aRR = 7.67; CI, 3.35 to 17.59); age ≥85 years (aRR = 10.98; CI, 5.09 to 23.69); male sex (aRR = 1.30; CI, 1.14 to 1.49); immunosuppression (aRR = 1.39; CI, 1.13 to 1.70); renal disease (aRR = 1.33; CI, 1.10 to 1.61); CLD (aRR = 1.31; CI, 1.13 to 1.52); CVD (aRR = 1.28; CI, 1.03 to 1.58); neurologic disorders (aRR = 1.25; CI, 1.04 to 1.50); and diabetes (aRR = 1.19; CI, 1.01 to 1.40) (Figure 3B and Appendix Table 8B).

Having ≥3 underlying medical conditions was significantly associated with higher risk of ICU admission and death after adjusting for age, sex, and race and ethnicity (Appendix Tables 9A and 9B).

DISCUSSION

Using a geographically diverse, multi-site, population-based U.S. surveillance system, we found that among a sample of adults hospitalized with laboratory-confirmed COVID-19, almost one-third required ICU admission, 19% received invasive mechanical ventilation, and 17% died during hospitalization. About 75% of patients were ≥50 years, and >90% had underlying medical conditions. Older age, being male, and the presence of certain underlying medical conditions were associated with a higher risk of ICU admission and in-hospital mortality.

In a published COVID-NET analysis, we found that when comparing the racial and ethnic distribution of residents of the surveillance catchment areas to the racial and ethnic distribution of COVID-19-associated hospitalizations, non-Hispanic blacks were disproportionately hospitalized with COVID-19 compared to non-Hispanic whites [10]. In this analysis, however, we found that once hospitalized, non-Hispanic blacks did not have increased risk of poorer outcomes compared to other race and ethnicities after adjusting for age and underlying conditions. Other recent U.S. studies have also found no association between black race and ICU admission or in-hospital mortality [4, 13, 14].

COVID-19-associated hospitalizations, ICU admissions, and deaths have been shown to occur more frequently with increasing age [6, 9, 15]. In our study, age ≥ 65 years was the strongest independent predictor of ICU admission and in-hospital mortality. Persons aged 75–84 years had the highest the risk of ICU admission compared to 18-49 years old, and those ≥ 85 years experienced 11 times the risk of death. These findings are similar to other studies from China, Europe, and the United States [4, 9, 15-18]. Our data provide support that older persons are particularly vulnerable to severe COVID-19 disease and should be targeted for aggressive preventive measures [8].

Being male was associated with a higher risk of ICU admission and death after adjusting for age, race and ethnicity, and underlying conditions. Other studies have similarly shown male sex to be associated with COVID-19-associated hospitalizations [4, 19], ICU admissions [20], and need for mechanical ventilation [21].

Similar to other U.S. studies, we found that nearly all hospitalized patients with COVID-19 had at least one underlying medical condition [4, 22]. In contrast, underlying medical conditions were documented in only 25–50% of hospitalized cases from China [3, 23]. Our analysis further demonstrated that a higher number of underlying medical conditions increased the risk of ICU admission (1.3 times the risk in persons with ≥ 3 vs. no underlying condition) and in-hospital mortality (1.8 times the risk in persons with ≥ 3 vs. no underlying condition).

In a retrospective case study among 1590 laboratory-confirmed hospitalized COVID-19 cases in 575 Chinese hospitals, Guan et al. found that after adjusting for age and smoking status, chronic obstructive pulmonary disease, diabetes, hypertension and malignancy were risk factors for a composite endpoint of ICU admission, invasive mechanical ventilation, and death [3]. Similarly, we found an association between underlying medical conditions and severe outcomes, with diabetes, CLD, CVD, neurologic disease, renal disease and immunosuppression associated with in-hospital death, and diabetes, obesity, and immunosuppression associated with ICU admission. While hypertension was highly prevalent in our patient population, it was not associated with ICU

admission or death. This is similar to recently published U.S. studies that did not find an association between hypertension and mortality [24, 25]. While several Chinese studies found hypertension to be associated with more severe clinical outcomes, the prevalence of hypertension was much lower than reported in U.S. studies, and management and control of hypertension might vary between China and the U.S [3, 18, 26]. Additional studies are needed to determine whether hypertension, which is highly prevalent in the U.S. population, increases the risk of COVID-19-associated hospitalizations and whether the duration of hypertension and the degree to which it is controlled impact the risk for severe COVID-19 disease. Similarly, the associations between the duration and degree of glycemic control in diabetes and severity of COVID-19 disease require further investigation. Obesity, which was also highly prevalent in our study, imparted increased risk for ICU admission, but not death. This finding may, in part, be explained by a trend of decreasing obesity prevalence with increasing age, which was a strong risk factor for mortality. Healthcare providers should be aware of these findings to appropriately triage and manage patients with high-risk conditions that may either increase risk for hospitalization or poorer outcomes once hospitalized [27, 28].

In our study, which was limited to patients that had either been discharged or died in-hospital, 15% of patients received vasopressor support, and 19% received invasive mechanical ventilation. Other U.S. studies have found that up to 32% of hospitalized patients have received vasopressors and 17–33% have received invasive mechanical ventilation [20-22, 29], though some of these studies included patients who were still hospitalized at the time of analysis. In our study, 53% of patients requiring mechanical ventilation died, which is slightly lower than the 60% published in a recent study from New York City [4], which reported a similar age distribution and prevalence of underlying medical conditions among hospitalized cases as our data. These proportions of severe outcomes among U.S. patients are also generally higher than those found in U.S. adults hospitalized with seasonal influenza [30, 31]. Our findings may help to inform resource planning and allocation in healthcare facilities during the COVID-19 pandemic.

There are limitations to our analysis. COVID-NET is an ongoing surveillance system, and a convenience sample of COVID-19 hospitalized patients was included, representing those who were discharged or died in-hospital during March 1–May 2, 2020 and for whom medical records were available and chart abstractions were completed. The hospitals that contributed cases to this analysis represented 43% of all the hospitals under surveillance; therefore, our findings may not be representative of the entire COVID-NET population or all adults hospitalized with COVID-19 in the United States. Nevertheless, COVID-NET encompasses a large geographic area with multiple hospitals and likely offers a more racially and ethnically diverse patient population compared to other single-center or state-based studies. Additionally, it is likely that not all COVID-19-associated hospitalizations were captured because of the lack of widespread testing capability during the study period and because identification of COVID-19 patients was largely reliant on clinician-directed testing.

Based on findings from this multi-site, geographically diverse study, a high proportion of patients hospitalized with COVID-19 received aggressive interventions and had poor outcomes. Increasing age was the strongest predictor of in-hospital mortality. These findings alert healthcare providers to patient populations at highest risk for severe COVID-19-associated outcomes. Aggressive implementation of prevention strategies, including social distancing and rigorous hand hygiene, may benefit the population as a whole, as well as those at highest risk for COVID-19-related complications.

NOTES

ACKNOWLEDGMENTS

Ashley Coates, Pam Daily Kirley, Gretchen Rothrock, California Emerging Infections Program; Nisha Alden, Rachel Herlihy, Breanna Kawasaki, Colorado Department of Public Health and Environment; Paula Clogher, Hazal Kayalioglu, Amber Maslar, Adam Misiorski, Danyel Olson, Christina Parisi, Connecticut Emerging Infections Program; Kyle Openo, Emily Fawcett, Jeremiah Williams, Katelyn Lengacher, Georgia Emerging Infections Program; Andrew Weigel, Iowa Department of Health; Brian Bachaus, Timothy Blood, David Blythe, Alicia Brooks, Judie Hyun, Elisabeth Vaeth, Cindy Zerlout, Maryland Department of Health; Jim Collins, Kimberly Fox, Sam Hawkins, Justin Henderson, Shannon Johnson, Libby Reeg, Michigan Department of Health and Human Services; Austin Bell, Kayla Bilski, Erica Bye, Emma Contestabile, Richard Danila, Kristen Ehresmann, Hannah Friedlander, Claire Henrichsen, Emily Holodnick, Ruth Lynfield, Katherine Schliess, Samantha Siebman, Kirk Smith, Maureen Sullivan, Minnesota Department of Health; Cory Cline, New Mexico Department of Health; Kathy Angeles, Lisa Butler, Emily Hancock, Sarah Khanlian, Meaghan Novi, Sarah Shrum, New Mexico Emerging Infections Program Albuquerque; Nancy Spina, Grant Barney, Suzanne McGuire, New York State Health Department; Sophrena Bushey, Christina Felsen, Maria Gaitan, Anita Gellert, RaeAnne Kurtz, Christine Long, Shantel Peters, Marissa Tracy, University of Rochester School of Medicine and Dentistry; Laurie Billing, Maya Scullin, Jessica Shiltz, Ohio Department of Health; Nicole West, Oregon Health Authority; Kathy Billings, Katie Dyer, Anise Elie, Karen Leib, Tiffanie Markus, Terri McMinn, Danielle Ndi, Manideepthi Pemmaraju, Vanderbilt University Medical Center; Keegan McCaffrey, Utah Department of Health; Clarissa Aquino, Ryan Chatelain, Andrea George, Jacob Ortega, Andrea Price, Ilene Risk, Melanie Spencer, Ashley Swain, Salt Lake County Health Department; Mimi Huynh, Monica Schroeder, Council of State and Territorial Epidemiologists; Shua J. Chai, Field Services Branch, Division of State and Local Readiness, Center for Preparedness and Response, Centers for Disease Control and Prevention; Sharad Aggarwal, Lanson Broecker, Aaron

Curns, Rebecca M. Dahl, Alexandra Ganim, Rainy Henry, Sang Kang, Sonja Nti-Berko, Robert Pinner, Mila Prill, Scott Santibanez, Alvin Shultz, Sheng-Te Tsai, Henry Walke, Venkata Akesh R. Vundi, CDC.

Disclaimer: The conclusions, findings, and opinions expressed by the authors do not necessarily reflect the official position of the United States Department of Health and Human Services, the United States Public Health Service, the CDC, or the authors' affiliated institutions.

FUNDING

This work was supported by the Centers of Disease Control and Prevention through an Emerging Infections Program cooperative agreement (grant CK17-1701) and through a Council of State and Territorial Epidemiologists cooperative agreement (grant NU38OT000297-02-00).

POTENTIAL CONFLICTS OF INTEREST

E.J.A. reports personal fees from Abbvie, grants and personal fees from Pfizer, grants from Medimmune, Regeneron, PaxVax, Merck, Novavax, Sanofi-Pasteur, and Micron. L.B., M.H., and S.K. reports grants from the Council of State and Territorial Epidemiologists. L.B. is a recipient of Epidemiology and Laboratory Capacity (ELC) and Immunizations and Vaccines for Children (VFC) grant funding from CDC to support vaccine preventable disease epidemiology staffing, outside the submitted work. H.K.T reports personal fees from Seqirus and grants from Sanofi. W.S. reports personal fees from Pfizer and Roche Diagnostics. All other authors have no potential conflicts to disclose.

REFERENCES

1. Johns Hopkins University & Medicine. COVID-19 Map Johns Hopkins University & Medicine. Available at: <https://coronavirus.jhu.edu/map.html>. Accessed 4/2/2020.
2. Centers for Disease Control & Prevention. COVIDView. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html#outpatient>. Accessed 4/13/20220.
3. Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis. *The European respiratory journal* **2020**.
4. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ* **2020**; 369: m1966.
5. COVID-19 Surveillance Group. Characteristics of COVID-19 patients dying in Italy: report based on available data on March 20th, 2020. Rome, Italy: Istituto Superiore Di Sanita, **2020**.
6. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* **2020**.
7. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the Seattle Region - Case Series. *N Engl J Med* **2020**.
8. Team CC-R. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 - United States, February 12- March 28, 2020. *MMWR Morb Mortal Wkly Rep* **2020**; 69(13): 382-6.
9. Team CC-R. Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) - United States, February 12-March 16, 2020. *MMWR Morb Mortal Wkly Rep* **2020**; 69(12): 343-6.
10. Garg S, Kim L, Whitaker M, et al. Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019 - COVID-NET, 14 States, March 1-30, 2020. *MMWR Morb Mortal Wkly Rep* **2020**; 69(15): 458-64.
11. Liang K-Y, Zeger SL. Longitudinal Data Analysis Using Generalized Linear Models.
12. Hoogendoorn WE, Bongers PM, de Vet HC, Twisk JW, van Mechelen W, Bouter LM. Comparison of two different approaches for the analysis of data from a prospective cohort study: an application to work related risk factors for low back pain. *Occupational and environmental medicine* **2002**; 59(7): 459-65.
13. Rentsch C, Kidwai-Khan F, Tate J, et al. Covid-19 Testing, Hospital Admission, and Intensive Care Among 2,026,227 United States Veterans Aged 54-75 Years. **2020**.
14. Price-Haywood EG, Burton J, Fort D, Seoane L. Hospitalization and Mortality among Black Patients and White Patients with Covid-19. **2020**.
15. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ* **2020**; 368: m1091.
16. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* **2020**; 395(10229): 1054-62.
17. Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA* **2020**.
18. Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Internal Medicine* **2020**.
19. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA* **2020**.
20. Myers LC, Parodi SM, Escobar GJ, Liu VX. Characteristics of Hospitalized Adults With COVID-19 in an Integrated Health Care System in California. *JAMA* **2020**.

21. Goyal P, Choi JJ, Pinheiro LC, et al. Clinical Characteristics of Covid-19 in New York City. *N Engl J Med* **2020**.
22. Buckner FS, McCulloch DJ, Atluri V, et al. Clinical Features and Outcomes of 105 Hospitalized patients with COVID-19 in Seattle, Washington. *Clinical Infectious Diseases* **2020**.
23. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* **2020**; 395(10223): 507-13.
24. Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *The Lancet* **2020**; 395(10239): 1763-70.
25. Killerby ME, Link-Gelles R, Haight SC, et al. Characteristics Associated with Hospitalization Among Patients with COVID-19 - Metropolitan Atlanta, Georgia, March-April 2020. *MMWR Morb Mortal Wkly Rep* **2020**; 69(25): 790-4.
26. Wang K, Zuo P, Liu Y, et al. Clinical and laboratory predictors of in-hospital mortality in patients with COVID-19: a cohort study in Wuhan, China. *Clinical Infectious Diseases* **2020**.
27. Centers for Disease Control & Prevention. Information for Healthcare Professionals: COVID-19 and Underlying Conditions. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/underlying-conditions.html>.
28. Centers for Disease Control & Prevention. Groups at Higher Risk for Severe Illness. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/groups-at-higher-risk.html>.
29. Ziehr DR, Alladina J, Petri CR, et al. Respiratory Pathophysiology of Mechanically Ventilated Patients with COVID-19: A Cohort Study. **2020**; 201(12): 1560-4.
30. Centers for Disease Control & Prevention. Laboratory-Confirmed Influenza Hospitalizations: Characteristics. Available at: <https://gis.cdc.gov/grasp/fluview/FluHospChars.html>.
31. Arriola C, Garg S, Anderson EJ, et al. Influenza Vaccination Modifies Disease Severity Among Community-dwelling Adults Hospitalized With Influenza. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* **2017**; 65(8): 1289-97.

Table 1. Demographic and clinical characteristics of adults hospitalized with COVID-19 — COVID-NET, 13 sites (N=2,491)

	n, %
Age in years (median, IQR)	62, 50–75
Age category	
18–39	302 (12.1)
40–49	319 (12.8)
50–64	744 (29.9)
65–74	478 (19.2)
75–84	397 (15.9)
85+	251 (10.1)
Male	1,326 (53.2)
Race/ethnicity (n=2,490)	
Non-Hispanic White	1,178 (47.3)
Non-Hispanic Black	755 (30.3)
Hispanic	306 (12.3)
Non-Hispanic Other ^a	158 (6.3)
Unknown	93 (3.7)
Residence at time of hospitalization (n=2,482)	
Private residence	1,899 (76.5)
Facility ^b	495 (19.9)
Homeless/Shelter	40 (1.6)
Other ^c	45 (1.8)
Unknown	3 (0.1)
Smoker (n=2,489)	

Current	150 (6.0)
Former	642(25.8)
No or Unknown	1,697 (68.2)
Any underlying condition^d (n=2,489)	2,278 (91.5)
Hypertension (n=2,488)	1,428 (57.4)
Obesity ^e (n=2,322)	1154 (49.7)
Severe obesity ^e (n=2,322)	325 (14.0)
Chronic metabolic disease (n=2,486) ^f	1,024 (41.2)
Diabetes mellitus (n=2,486)	819 (32.9)
Chronic lung disease (n=2,484)	747 (30.1)
Asthma (n=2,484)	314 (12.6)
Chronic Obstructive Pulmonary Disease (n=2,484)	266 (10.7)
Cardiovascular disease (n=2,486)	859 (34.6)
Coronary artery disease (n=2,486) ^g	352 (14.2)
Congestive heart failure (n=2,486)	284 (11.4)
Neurologic disease (n=2,484)	548 (22.1)
Renal disease (n=2,488)	386 (15.5)
Immunosuppressive condition (n=2,487) ^h	263 (10.6)
Gastrointestinal or Liver disease (n=2,486)	118 (4.7)
Hematologic condition (n=2,483)	80 (3.2)
Rheumatologic or autoimmune disease (n=2,486)	77 (3.1)
Pregnancy (n=279) ⁱ	36 (12.9)
Number of underlying medical conditions (by major category) (n=2,490)	
0	212 (8.5)

1	480 (19.3)
2	510 (20.5)
3+	1,288 (51.7)
Medication use prior to hospitalization	
ACE-inhibitor (n=1,892)	316 (16.7)
Angiotensin receptor blockers (ARBs) (n=1,895)	257 (13.6)

Abbreviations: IQR, interquartile range; ACE, angiotensin-converting enzyme inhibitors

^aNon-Hispanic Other includes: Non-Hispanic American Indian or Alaskan Native (n=24), Non-Hispanic Asian (n=128), and Non-Hispanic multiracial (n=6)

^bFacility includes rehabilitation facilities, assisted living/residential care, group homes, nursing homes, skilled nursing facilities, long-term care facilities, long-term acute care hospitals, alcohol/drug treatment centers, and psychiatric facilities.

^cOther includes home with services (n=43), correctional facility (n=1), and hospice (n=1).

^dSee Supplementary Table 1 for definitions of underlying medical conditions.

^eObesity is defined as body mass index (BMI) ≥ 30 kg/m², and severe obesity is defined as BMI ≥ 40 kg/m².

^fChronic metabolic disease includes thyroid dysfunction (n=191), parathyroid dysfunction (n=11), adrenal disorder (n=4), metabolic syndrome (n=2), hyper/hypo-function of the pituitary gland (n=1) and inborn errors of metabolism (n=1).

^gIncludes coronary artery disease, history of coronary artery bypass grafting, and history of myocardial infarction

^hImmunosuppressive condition includes steroid therapy within 2 weeks prior to hospital admission (n=106), immunosuppressive therapy within the 12 months previous to hospital admission (n=83), solid organ malignancy (n=58), solid organ transplant (n=28), HIV infection (n=23), metastatic cancer (n=21), leukemia (n=11), multiple myeloma (n=6), lymphoma/Hodgkin's/Non-Hodgkin's (n=5), immunoglobulin deficiency/immunodeficiency (n=4), hematopoietic stem cell transplant (n=3, and graft vs. host disease (n=1).

ⁱDenominator includes women aged 15–49 years.

Table 2. Clinical course, interventions, and outcomes of adults hospitalized with COVID-19 — COVID-NET, 13 sites (N=2,491)

	%
Symptoms on admission^a (n=2,482)	
Cough	1,855 (74.7)
Fever or chills	1,835 (73.9)
Shortness of breath	1,740 (70.1)
Muscle aches/myalgias	722 (29.1)
Diarrhea	676 (27.2)
Nausea or vomiting	621 (25.0)

Hospitalization length of stay in days, median (IQR) (n=2,487)	6 (3–11)
Days from symptom onset to hospitalization (median, IQR) (n=1,937)	6 (3–8)
Initial vital signs	
Temperature (°Celsius, median, IQR) (n=2,469)	37.4 (36.9–38.1)
Heart rate (median, IQR) (n=2,479)	95 (83–108)
Systolic blood pressure (median, IQR) (n=2,483)	132 (118–147)
Respiratory rate (median, IQR) (n=2,461)	20 (18–23)
Oxygen saturation (among those on room air) (median, IQR) (n=1,969)	94 (92–97)
Initial laboratory values	
White blood cell count (median, IQR) – per mm ³ (n=2,458)	6.3 (4.7–8.5)
Hematocrit (median, IQR) - % (n=2,461)	40.6 (36.9–43.9)
Platelet count (median, IQR) – per mm ³ (n=2,461)	195.0 (156.0–249.0)
Sodium (median, IQR) – mmol/L (n=2,460)	137.0 (134.0–139.0)
Blood Urea Nitrogen (median, IQR) – mg/dl (n=2,443)	16.0 (11.0–25.0)
Creatinine (median, IQR) – mg/dl (n=2,462)	1.0 (0.8–1.4)
Glucose (median, IQR) – mg/dl (n=2,459)	117.0 (102.0–149.0)

Aspartate transaminase (median, IQR) – U/L (n=2,149)	40.0 (28.0–61.0)
Alanine aminotransferase (median, IQR) – U/L (n=2,164)	31.0 (20.0–50.0)
Arterial pH (median, IQR) (n=487)	7.35 (7.40–7.45)
Abnormal chest X-ray during hospitalization (n=1,932)	1,769 (91.6)
Abnormal chest CT during hospitalization (n=566)	540 (95.4)
Ground glass opacities (n=566)	350 (61.8)
Investigational medication regimens for COVID-19^b (n=2,482)	1,125 (45.3)
Hydroxychloroquine ^c	1,065 (94.7)
Azithromycin + ≥ 1 other COVID-19 treatment	725 (64.4)
Tocilizumab	103 (9.2)
Atazanavir ^d	94 (8.4)
Remdesivir ^c	53 (4.7)
Lopinavir/ritonavir ^d	27 (2.4)
Convalescent plasma	9 (0.8)
Chloroquine	7 (0.6)
Sarilumab ^c	6 (0.5)
Zinc	6 (0.5)
Investigational drug (not specified) RCT	1 (0.1)

ICU Admission (n=2,490)	798 (32.0)
ICU length of stay (days, median, IQR) (n=771)	6 (2–11)
Highest level of respiratory support required (n=2,489)	
Invasive mechanical ventilation	462 (18.6)
BIPAP or CPAP	82 (3.3)
High flow nasal cannula	170 (6.8)
ECMO (n=2,487)	9 (0.4)
Vasopressor use (n=2,486)	373 (15.0)
Systemic steroids (n=2,489)	321 (12.9)
Renal replacement therapy (n=2,487)	115 (4.6)
Discharge Diagnoses^e	
Pneumonia (n=2,485)	1,395 (56.1)
Acute respiratory failure (n=2,487)	999 (40.2)
Acute renal failure (n=2,485)	456 (18.4)
Sepsis (n=2,479)	443 (17.9)
Acute respiratory distress syndrome (n=2,485)	255 (10.3)
Encephalitis (n=2,482)	151 (6.1)
Congestive heart failure (n=2,485)	51 (2.1)

Asthma exacerbation (n=2,486)	43 (1.7)
COPD exacerbation (n=2,486)	39 (1.6)
Acute myocardial infarction (n=2,485)	38 (1.5)
In-hospital death (n=2,490)	420 (16.9)

Abbreviations: IQR, interquartile range; CT, computed tomography; ICU, intensive care unit; BIPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; ECMO, extracorporeal membrane oxygenation; COPD, chronic obstructive pulmonary disease

^aSee Supplementary Table 2 for additional symptom data.

^bNot mutually exclusive categories

^cIncludes randomized controlled trials where it cannot be determined whether the case received treatment vs. placebo (remdesivir, 24; hydroxychloroquine, 15; and sarilumab, 5).

^dPersons with HIV/AIDS were excluded.

^eDischarge diagnoses recorded from the hospital discharge summary and not based on ICD-10 discharge codes.

Accepted Manuscript

FIGURE LEGENDS

Figure 1. Select underlying medical conditions^a of adults hospitalized with COVID-19, by age, sex, and race and ethnicity — COVID-NET, 13 sites (N=2,491)

- A. Age (n=2,489)
- B. Sex (n=2,489)
- C. Race and Ethnicity (n=2,488)

Abbreviations: CVD, cardiovascular disease (excluding hypertension); HTN, hypertension; CLD, chronic lung disease.

^aThe underlying medical condition categories are not mutually exclusive. Patients can have more than one underlying medical condition.

*p-value <0.05

Figure 2. Interventions^a and outcomes of adults hospitalized with COVID-19, by age, sex, and race and ethnicity — COVID-NET, 13 sites (N=2,491)

- A. Age (n=2,490)
- B. Sex (n=2,490)
- C. Race and Ethnicity (n=2,490)

Abbreviations: ICU, intensive care unit; BIPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; HFNC, high flow nasal cannula; RRT, renal replacement therapy

^aFor mechanical ventilation, BIPAP/CPAP, and HFNC, patients are assigned based on the highest level of respiratory support required during hospitalization (i.e. invasive mechanical ventilation followed by BIPAP or CPAP, followed by high flow nasal cannula).

*p-value <0.05

Figure 3. Risk factors for ICU admission and in-hospital mortality — COVID-NET, 13 sites (N=2,491)

A. ICU Admission (N=2,490)^a

B. In-hospital Mortality (N=2,490)^b

^aFinal model included age, sex, race/ethnicity, smoking status, hypertension, obesity, diabetes, chronic lung disease, cardiovascular disease, neurologic disease, renal disease, immunosuppression, and outpatient use of an angiotensin receptor blocker.

^bFinal model adjusted for age, sex, race/ethnicity, smoker, hypertension, obesity, diabetes, chronic lung disease, cardiovascular disease, neurologic disease, renal disease, immunosuppression, hematologic disorders, and rheumatologic or autoimmune disease.

Figure 1A

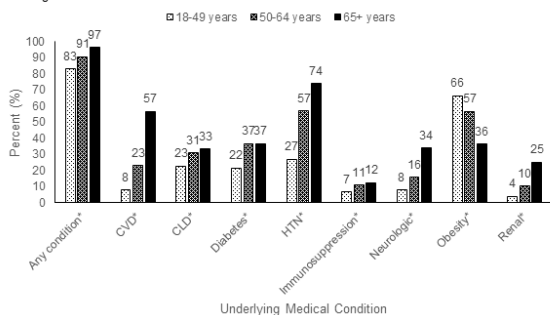


Figure 1B

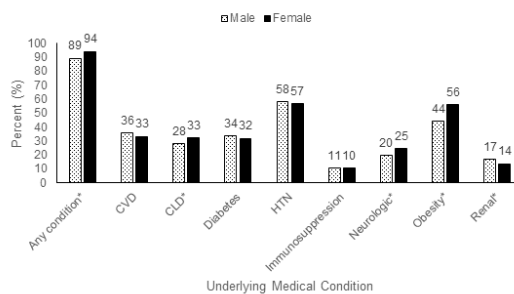
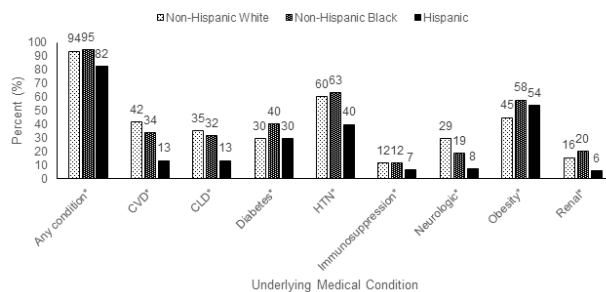


Figure 1C



Accepted

Figure 2A

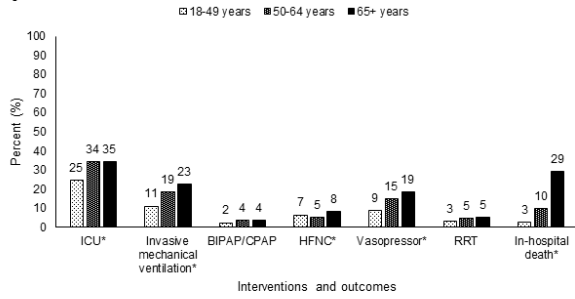


Figure 2B

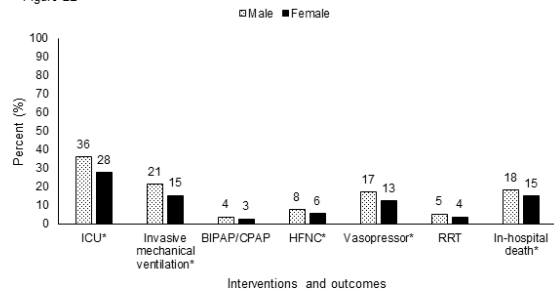
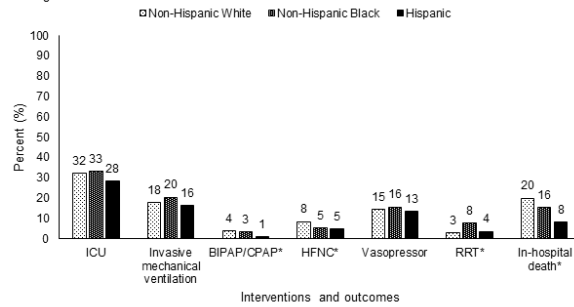


Figure 2C



Accepted Manuscript

Figure 3A*

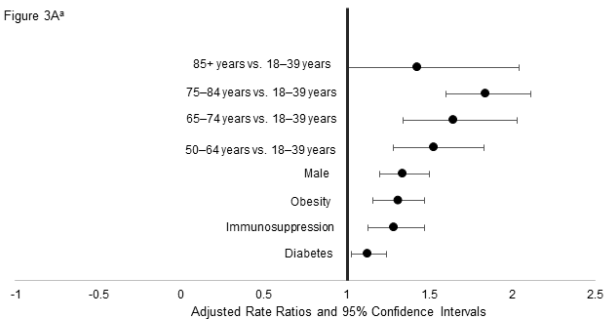
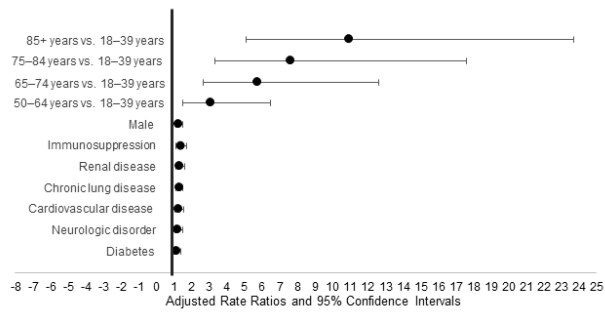


Figure 3B*



Accepted Manuscript