Title: Early initiation of corticosteroids in patients hospitalized with COVID-19 not requiring intensive respiratory support

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Data sharing: Owing to US Department of Veterans Affairs (VA) regulations and our ethics agreements, the analytic data sets used for this study are not permitted to leave the VA firewall without a data use agreement. This limitation is consistent with other studies based on VA data. However, VA data are made freely available to researchers with an approved VA study protocol. For more information, please visit https://www.virec.research.va.gov or contact the VA Information Resource Center at *VIReC@va.gov*.

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ABSTRACT

Background: Corticosteroids decrease mortality in COVID-19 patients on intensive respiratory support (IRS) but are of uncertain benefit if less severely ill. In a large, national US cohort, we examined associations between early corticosteroids and 90-day mortality in hospitalized COVID-19 patients not on IRS within 48 hours of admission.

Methods: We conducted an observational study of patients admitted to a Veterans Affairs Medical Center between June 7, 2020-December 5, 2020 within 14-days after SARS-CoV-2 positive test, excluding those receiving prior systemic corticosteroids. Amongst patients on only low-flow nasal cannula (NC) or no oxygen support (i.e., not on IRS) during initial 48 hours of admission, we compared 90-day all-cause mortality between those receiving and not receiving oral/parenteral corticosteroids within 48 hours with inverse probability weighted Cox proportional hazards models.

Findings: Of 9,058 total patients (95% men, median age 71 years, 27% black), 6,825 (75%) were not on IRS within 48 hours. Among 3,025 patients without oxygen, 598 (20%) received corticosteroids and 283 (9%) died; of 3,800 patients on NC, 2,808 (74%) received corticosteroids and 514 (13%) died. In stratified models comparing those who did and did not receive corticosteroids, patients not on oxygen experienced an 89% increased risk for 90-day mortality (hazard ratio [HR] 1.89, 95% confidence interval [CI] 1.33-2.68); there was weak evidence of increased mortality among patients on NC (HR 1.21, 95% CI 0.94-1.57).

Interpretation: In hospitalized COVID-19 patients on only NC or no oxygen support in first 48 hours, corticosteroids showed no mortality benefit at 90-days.

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Research in Context

Evidence before this study We searched PubMed for all studies published between January 1, 2020-June 1, 2021 using search terms COVID-19, corticosteroids and mortality, limiting articles to clinical trials and meta-analyses. The most robust prior evidence is from the RECOVERY trial, the largest randomized clinical trial demonstrating 28-day mortality benefit of dexamethasone in hospitalized patients with COVID-19 related respiratory failure, particularly in patients requiring intensive respiratory support; dexamethasone was not associated with mortality benefit in patients not on oxygen. However, the 90-day mortality benefit of corticosteroids in patients with COVID-19 who require less intensive respiratory support remains uncertain.

Added value of this study We found that early corticosteroid use within initial 48 hours for hospitalized COVID-19 patients is common among patients, including those not on intensive respiratory support within the initial 48 hours after admission. We found that corticosteroids were associated with increased 90-day mortality in patients on no oxygen and were not associated with mortality benefit in patients on nasal cannula within 48 hours of admission.

Implications of all the available evidence This study demonstrates that corticosteroids are used frequently in hospitalized COVID-19 patients who are on less intensive respiratory support. The lack of mortality benefit in patients on low-flow nasal cannula and increased risk of mortality in patients on no oxygen suggest that the harms of corticosteroids may outweigh benefits in this population.

INTRODUCTION

Corticosteroids have emerged as an effective therapy for critically ill patients with COVID-19. The United Kingdom RECOVERY trial demonstrated an overall 2.8% absolute decrease in mortality for patients treated with dexamethasone compared to usual care.[1] When stratified by degree of respiratory support at randomization, the magnitude of benefit associated with dexamethasone was greater amongst those on invasive mechanical ventilation (IMV) versus supplemental oxygen (inclusive of non-invasive mechanical ventilation [NIV]); dexamethasone was not associated with significant mortality benefit amongst those not on oxygen.

Dissemination of these and other results led to nearly universal use of corticosteroids for COVID-19 patients receiving respiratory support, particularly more intensive respiratory support (IRS) such as high-flow nasal cannula (HFNC), NIV and IMV.[2-5] Corticosteroids are also commonly used in patients not on IRS, despite being potentially less beneficial. Some studies investigating the association between corticosteroids and outcomes among a wider group of patients with COVID-19 – including a larger proportion not on IRS than in the RECOVERY trial – have found mixed results.[6-10] Variability may be due to host factors including immune response to infection, heterogeneity in severity of illness and level of respiratory support, duration of infection, and use of different formulations of corticosteroids[8] as well as residual confounding in observational studies. However, the findings may also suggest that certain subgroups of patients with COVID-19 benefit less from corticosteroids.

We sought to determine the association between corticosteroids and mortality using real-world clinical data from the Department of Veterans Affairs (VA), the largest integrated healthcare system in the United States. In a large, racially and geographically diverse, national cohort of hospitalized COVID-19 patients, we first assessed patterns of corticosteroid receipt. As nearly all patients on IRS received

corticosteroids, we limited analysis of associations with 90-day mortality to those not on IRS. Because sicker patients are more likely to receive corticosteroids and more likely to die, we used propensity score weighting to account for confounding by indication.

METHODS

Study Design and Population: We conducted an observational cohort study using VA electronic health record (EHR) data. We identified an initial cohort of 12,455 patients with COVID-19 admitted to a VA hospital within 14 days after a positive polymerase chain reaction (PCR) or antigen test for SARS-CoV-2 between June 7, 2020 and December 5, 2020.[11,12] Prior to June there was little use of corticosteroids in the first 48 hours. Index date was defined as date of presentation, including emergency room and any time spent under observation status prior to hospital admission if patients were not admitted directly. We determined hospital length of stay by concatenating consecutive episodes of care separated by less than 24 hours, with first episode of care on the index date identified as day one. Due to changes in COVID-19 incidence and treatment protocols over time, we divided the observation period into four phases: June 7-July 11; July 12-August 15; August 16-October 17; and October 18-December 5, 2020.

Exclusions: From the initial 12,455 patients, we excluded 3,397. The most common reason was length of stay less than 48-hours (n=1,619; 40 deaths), as these patients had insufficient time to receive corticosteroids (Figure 1), followed by systemic corticosteroid exposure prior to index date. This was defined as any duration of corticosteroids within 14 days, or receipt of corticosteroids for ≥14 days within preceding 45 days (n=879). Within each phase, we restricted to facilities with at least 10 cases of COVID-19 and at least one corticosteroid prescription (N = 107 facilities) to have sufficient variation and number of events at each site. We excluded patients who were transferred from another acute care hospital (VA or non-VA) and who were likely incidentally-detected through screening prior to or at

admission; this included patients who were not admitted to an acute medical care service or had no International Classification of Diseases, 10th Revision (ICD-10) codes for COVID-19. We also excluded 101 patients prescribed hydroxychloroquine yielding a cohort of 9,058 patients.

Respiratory Support: Next, we stratified patients by highest level of respiratory support during the initial 48 hours of hospitalization: 1) no oxygen support; 2) supplemental low-flow oxygen via nasal cannula (NC) that was not identified as a high-flow delivery device; 3) other supplemental oxygen/non-invasive ventilation (NIV), inclusive of oxygen by face mask, non-rebreather mask, NIV, or other forms of oxygen delivery not identifiable as low-flow NC or high-flow; 4) high-flow oxygen (abbreviated as high flow nasal cannula [HFNC]); and 5) invasive mechanical ventilation (IMV). When no evidence of oxygen supplementation was found, patients were classified as without oxygen (category 1). IMV was identified by structured data sources (ICD-10 procedure and Current Procedural Terminology [CPT] codes). Categories 2-4 were assessed from unstructured text notes using natural language processing (NLP) to identify key terms indicative of respiratory support. Schemas were developed iteratively with clinician review, including appropriate negation terms, based on snippets and note context. Patients on positive airway pressure (PAP) for sleep apnea without supplemental oxygen were classified as no oxygen. The NLP system was validated on 100 complete patient admissions, comprising 1,093 days reviewed. Fifty admissions were double annotated and adjudicated demonstrating Cohen's kappa of 0.89. At the admission-level, receipt of any supplemental oxygen in categories 2-4 (NC, other/NIV and HFNC) was identified by the NLP system with a sensitivity, specificity, and positive predictive value of 100%, 77% and 94% respectively. When limited to the first 48 hours of admission, the system distinguished patients not on oxygen or on NC only from all other categories with 92% accuracy.

Corticosteroid exposure: Corticosteroid administration (inclusive of dexamethasone, prednisone, prednisolone, methylprednisolone and/or hydrocortisone) was determined from bar code medication administration (BCMA) data (including intravenous). Patients who received at least one dose of an oral or parenteral corticosteroid within 48 hours after index date were considered exposed. We also determined the number of days during hospitalization that corticosteroids were administered. In each phase, we defined corticosteroid administration by site as low (<25th percentile), medium (between 25-75% percentile), or high (>75th percentile) based on the proportion in the sample receiving corticosteroids.

Outcomes: The primary outcome was 90-day all-cause mortality, ascertained using inpatient records and VA death registry data to capture deaths outside of hospitalization. All hospitalizations occurred at least 90 days prior to the most recent mortality data. We also determined the proportion who initiated IMV or were administered vasopressors after the first 48 hours. Given low numbers of events, we did not conduct multivariable analyses for these outcomes.

Covariates: We used EHR data to obtain demographics (age, race, ethnicity, sex), comorbidities, additional medications, and lab results, as well as to calculate the Charlson Comorbidity Index (CCI)[13] and the Veterans Health Administration COVID-19 (VACO) Index.[14] We focused on routinely collected laboratory tests that have been associated with increased mortality in COVID-19[15] including albumin, liver function, lactate, white blood cell count, and creatinine (Table 2 and Supplemental Table 1). We selected the worst laboratory and vital signs values within the initial 48 hours. To account for potential effects of co-prescribed medications on COVID-19 outcomes, we also included use of remdesivir and prophylactic anticoagulants within the initial 48 hours.[12] Intensive care unit (ICU) admission was determined using VA bedsection codes.[12,16]

Statistical analysis: We initially compared COVID-19 patients by the five respiratory support categories using summary statistics (Table 1). Because nearly all patients on IMV or HFNC received corticosteroids; there was insufficient variability to allow generation of propensity score weights as discussed below. Category 3, "Other/NIV" respiratory support, was heterogenous with respect to support used and illness severity. For these reasons, as well as the greater clinical equipoise, we restricted our analysis to patients not on IRS (i.e., those on only NC or no oxygen support); from these, we further excluded 28 patients administered vasopressors in the first 48 hours from subsequent mortality analyses as they could have had an alternative indication for corticosteroids.

In those not on IRS, we compared mortality by exposure to corticosteroids stratified by NC and overall. To account for confounding by indication, we generated propensity scores for the probability of receiving corticosteroids in the first 48 hours using logistic regression. Models included covariates thought to be associated with corticosteroid exposure and mortality: comorbidities, laboratory results, vital signs, site utilization patterns, co-medications and the 4 phases (Table 2 and Supplemental Table 1). We constructed inverse probability of treatment weights (IPTW) from propensity scores for each patient to create pseudo-populations with balanced distributions of covariates.[17] There was generally very little missing data (<5%) so an explicit level for missingness was used for selected covariates. In our primary analysis, we used the average treatment effect (ATE) weights, reflecting the overall population from which the sample was taken. Stabilized weights were used and the ten patients with the most extreme high and low weights were trimmed from the analysis.[18] We calculated standardized mean differences (SMD) between treatment groups and considered 0.2 or less as balanced. To compare differences in survival we generated IPTW Kaplan-Meier (KM) plots[19] and Cox proportional hazards models estimating the ATE with days since index date as the time scale to provide formal hazard ratio (HR) risk estimates

with confidence limits using a robust variance estimator. We included the VACO Index in outcome models to further account for residual confounding.[14]

Subgroup and sensitivity analyses: In primary analyses, we included all corticosteroid formulations; in subgroup analyses, we restricted to only dexamethasone. We also excluded patients admitted to the ICU within the first 48 hours, and restricted to patients age 70 and older. In sensitivity analyses, we evaluated the average treatment effect among the treated (ATT) population that received corticosteroids in weighted Cox proportional hazards models, and constructed unweighted, but multivariable adjusted models for all primary and subgroup analyses (Supplemental Tables 2 and 3).

Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, North Carolina, USA) and R version 4.0.4. Statistical significance was defined as $p < 0.05$. Our study was approved by the Institutional Review Boards of VA Puget Sound Health Care System, VA Connecticut Healthcare System and Yale University, all of whom granted waivers of consent. Study findings are reported as per the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Supplemental Table 4).

RESULTS

Patient characteristics, corticosteroid exposure and respiratory support

Patients hospitalized during the four phases (1,328; 1,564; 1,857; 4,121) were mostly male (95%). Median age was 71 years (interquartile range [IQR] 62-77); 55% were non-Hispanic white, 27% non-Hispanic black, and 9% Hispanic (Table 1). Most patients (81%) were admitted within one day after positive SARS-CoV-2 test. More than half (56%) received corticosteroids (95% dexamethasone) within the first 48 hours of admission, increasing from 38% in phase 1 to 64% in phase 4. Concurrent remdesivir

and prophylactic anticoagulants were more common in those who received corticosteroids (remdesivir 39% vs. 13%; anticoagulants 33% vs. 21%) than in those who did not.

When stratified by highest level of respiratory support provided in the first 48 hours of admission, most (77%) patients were on either no oxygen (34%) or NC only (43%) (Table 1). Corticosteroids were administered to 20% without oxygen, 74% of patients on NC, 58% on other supplemental oxygen/NIV, 91% on HFNC, and 92% on IMV. Use of corticosteroids increased over time, particularly in patients on NC (Figure 2). Overall, unadjusted 90-day mortality was 17%, and varied by level of respiratory support ranging from 9% in those without oxygen, 13% in patients on NC, and 56% in patients receiving IMV (Figure 2).

Corticosteroids and mortality in patients not on IRS

Amongst patients not on IRS, the median duration of inpatient corticosteroids was 5 days (IQR 3-7) in patients without oxygen, and 6 days (IQR 4-9) in patients on NC. These were similar to hospital length of stay (Table 1). Only 80 (2.6%) and 79 (2.1%) patients, respectively, received one day of inpatient corticosteroids.

After propensity score weighting, our samples (pseudopopulations) were well-balanced, with covariates showing SMD generally <0.1; both overall and when split by no oxygen vs NC (Table 2 and Supplemental Table 1). Among patients without oxygen, weighted KM curves (Figure 3) show that those who received corticosteroids had higher mortality over 90-days than those who did not, with differences beginning to appear at 20-days after index date. In ATE estimates (Table 3), patients without oxygen who received corticosteroids had an 89% increased hazard of 90-day mortality (HR 1.89, 95% CI 1.33-2.68). Results were consistent in sensitivity analyses using ATT estimates as well as unweighted, multivariable adjusted Cox regression models (Supplemental Table 2).

Similarly, patients on NC who received corticosteroids had higher 90-day mortality than those who did not, with weighted KM curves again diverging at 20-days (Figure 3). ATE estimates showed 21% increased mortality risk (HR 1.21, 05% CI 0.94-1.57) in patients who were on NC and received corticosteroids. HRs were similar in ATT estimates and multivariable Cox models (Supplemental Table 3). When combining patients on no oxygen or NC, corticosteroids were associated with an approximately 60% or more increased mortality risk.

Subgroup analyses

Results were similar in subgroup analyses restricting corticosteroids to dexamethasone and excluding patients who were admitted to the ICU within the first 48 hours (Table 3). Limiting the sample to patients age 70 and older, mortality estimates associated with corticosteroids were slightly higher in the older population in those on NC. All findings were again consistent using ATT or multivariable Cox models (Supplemental Tables 2 and 3).

DISCUSSION

In this analysis of a national cohort of hospitalized patients with COVID-19, receipt of corticosteroids was nearly universal among those on IRS and increasingly common among those not requiring it. Because corticosteroid receipt was nearly universal among those on IRS, we could not determine whether there was evidence of benefit. However, among patients not on oxygen in the first 48 hours of admission, corticosteroids initiated in this window were associated with increased 90-day mortality. Among those only on NC in the first 48 hours, corticosteroids were not associated with mortality benefit. Overall, when considering those not on IRS together, patients who received corticosteroids had on average a 60% or greater increase in mortality compared to those who did not receive corticosteroids.

Our findings were robust when assessed using several different approaches. Results were consistent using the ATE, reflecting the overall population from which the sample was taken, and using the ATT, reflecting the population of patients who received corticosteroids. They were also consistent controlling for potential confounders such as demographics, phase of the pandemic, site prescribing patterns, comorbidities, and laboratory values.[14] Furthermore, amongst patients age 70 and older, the mortality associated with corticosteroids appeared slightly greater in those on NC. Taken together, our findings suggest that the harms of corticosteroids – which become more apparent approximately 20 days after admission (Figure 3) – may outweigh benefits in hospitalized patients with COVID-19, particularly those who require no oxygen within 48 hours of admission. These findings may be under-estimated in studies where outcomes were assessed at 30-days and did not extend follow-up to 90-days.

While we cannot rule out residual confounding, results are consistent with the RECOVERY trial where the benefit of dexamethasone also diminished for patients not on IMV, and may have suggested possible harm in those not requiring oxygen.[1] Recent meta-analyses and observational studies have also reported greater benefit of corticosteroids in severe compared to more mild acute respiratory distress syndrome (ARDS).[7,9] However, these studies did not stratify patients further by level of respiratory support during the initial 48 hours of hospitalization, separating those who did and did not require IRS. Instead, clinical guidelines such as those issued by the National Institutes of Health recommend initiation of corticosteroids in hospitalized COVID-19 patients on oxygen, without further distinguishing between low-flow NC and forms of IRS.[20] Our findings raise a note of caution when considering potential "indication creep" in the real world for use of corticosteroids in patients who do not have moderate-severe COVID-19 requiring IRS. Further randomized controlled trials of corticosteroids in patients with COVID-19 who are not on IRS may be warranted.

From an implementation perspective, we found that uptake of corticosteroids for hospitalized COVID-19 patients was rapid. By mid-July 2020 most facilities had increased the proportion of patients administered corticosteroids to over 90% of those who were on HFNC or IMV within 48 hours of admission. Initiation of corticosteroids later during hospitalization was infrequent and decreased over time. Sites also increased use of corticosteroids for patients with less severe COVID-19, including those not on oxygen at the time of initiation (Figure 2). Patients not on IRS in the initial 48 hours represent the majority of COVID-19 admissions in the cohort; thus, our findings have important clinical implications on the potential unintended consequences of widespread corticosteroid adoption for COVID-19.

Even prior to COVID-19, the role of corticosteroids in lung infection has been uncertain. The impact of corticosteroids on patient outcomes has been inconsistent In other causes of ARDS including influenza and community-acquired pneumonia (CAP). In several viral pneumonias, corticosteroids were associated with greater risk of harm,[21-23] although they appeared beneficial in the original severe acute respiratory syndrome.[7,24] The net balance between benefit and harm of corticosteroids for pneumonia is not well understood and likely depends on multiple factors, including patient characteristics, heterogeneity in host response to infection, etiology of pneumonia, and time since onset of infection and ARDS.[25-28] While corticosteroids may decrease host inflammatory response with potential modulating effects to lung injury, they may also have harmful side effects or unintended consequences on adaptive immune responses that may be important to resolution of infection. We saw potentially an increased risk of mortality associated with corticosteroids in patients on NC who were over age 70. Whether this is due to differences in immune responses in older individuals and/or greater risk of unintended consequences from corticosteroids, such as secondary infections, requires further study.

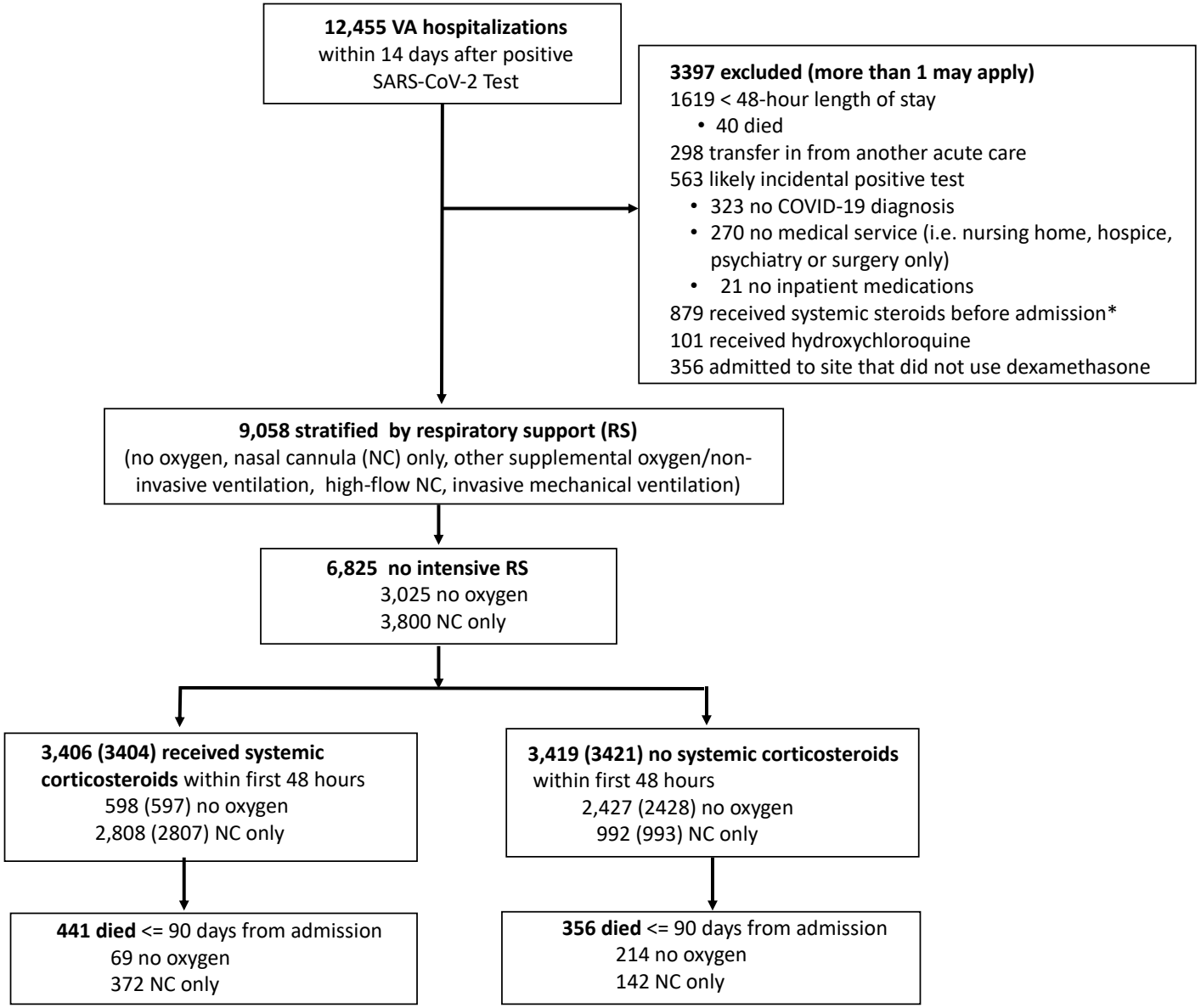
There remain additional unanswered questions regarding the timing of corticosteroids for patients hospitalized with COVID-19, particularly those not on IRS. When corticosteroids are initiated during the course of infection is likely important. For some patients, initiation within 48 hours of hospitalization may be too early in the course of disease and could impair viral clearance.[29] While the majority of patients had positive SARS-CoV-2 testing within one day prior to hospitalization in our cohort, we do not know how long symptoms preceded a patient seeking medical attention and receiving SARS-CoV-2 testing. The optimal formulation, dose and duration of corticosteroids also remain unclear, and if these should vary depending on severity of COVID-19.[2-4,29]

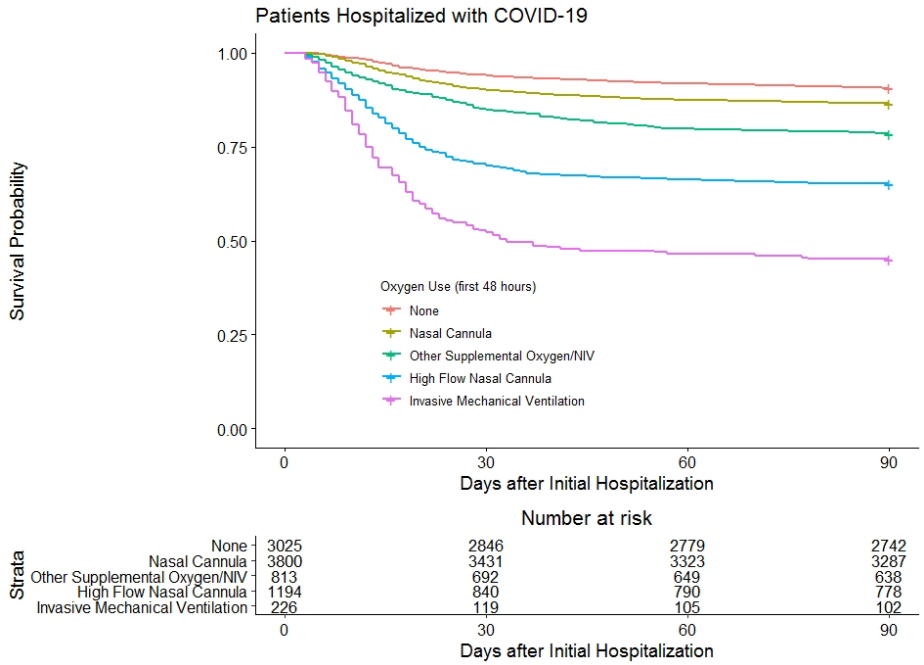
There are several limitations to our study. First, the study was observational. While we used detailed clinical data that included measures reflecting illness severity in a large population that demonstrated excellent balance in propensity for treatment, residual confounding for severity of illness could have contributed to greater mortality in those exposed to corticosteroids. In addition, the effects associated with initial corticosteroids are difficult to disentangle from other therapies that may have been concomitantly received. Some laboratory results used as covariates could have occurred after corticosteroid exposure, as both were ascertained within 48 hours. However, this approach allowed an equal time window to detect worst results in patients exposed and unexposed to corticosteroids and the impact of corticosteroids on acute laboratory results was likely limited. Although respiratory support algorithms were manually reviewed and validated, some misclassification may have occurred. Nonetheless, the substantial separation in Kaplan-Meier mortality curves with increasing mortality with greater respiratory support supports the validity of this variable. We also cannot rule out that clinicians were aware of another indication for corticosteroids beyond COVID-19 in patients who were not on oxygen or were on NC, such as airway inflammation from obstructive lung disease. However, we excluded those on steroids prior to admission and patients on vasopressors within the initial 48 hours,

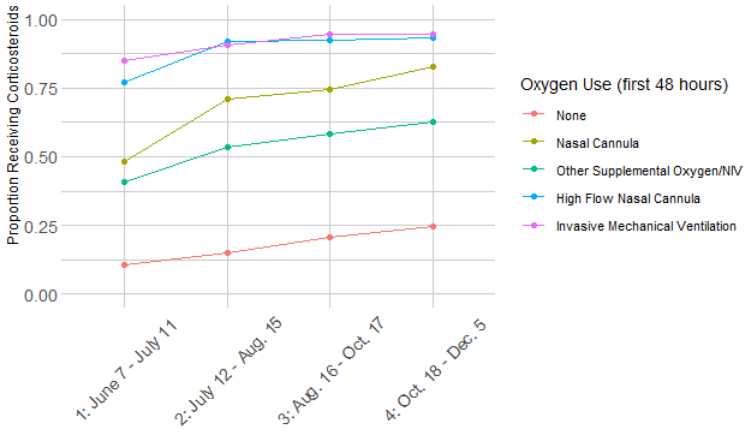
as these patients were more likely have an alternative indication for steroids. Further, we did not assess dose of corticosteroids or calculate total duration of exposure by including discharge medications after index hospitalization. Most patients had an average length of inpatient corticosteroid treatment that matched their hospital length of stay, and very few received only one dose of a corticosteroid (<3%). Finally, our cohort consisted predominantly of male Veterans, but had excellent racial and geographic variability.

In summary, we found that in patients with COVID-19 not on IRS in the first 48 hours of hospitalization, early corticosteroids were associated with increased 90-day mortality. Further, we failed to confirm a benefit of early corticosteroids to 90-day mortality in those on NC oxygen. These results were consistent in different analytic approaches that used real-world evidence with detailed clinical data in a large population to control for confounding, and remained robust in a variety of subgroup and sensitivity analyses. Our findings raise the possibility that harms of corticosteroids initiated within 48 hours of hospitalization may outweigh benefits in some patients with COVID-19 and less severe respiratory compromise, particularly in those who not on oxygen within 48 hours of hospital admission.

Figure 1. Derivation of Study Population







A. **B.**

Figure 2. Unadjusted Kaplan Meier survival curves for 90-day mortality (A) and proportion exposed to corticosteroids by respiratory support level over time (B). RECOVERY Trial corticosteroid results issued in press release on 16 June 2020.

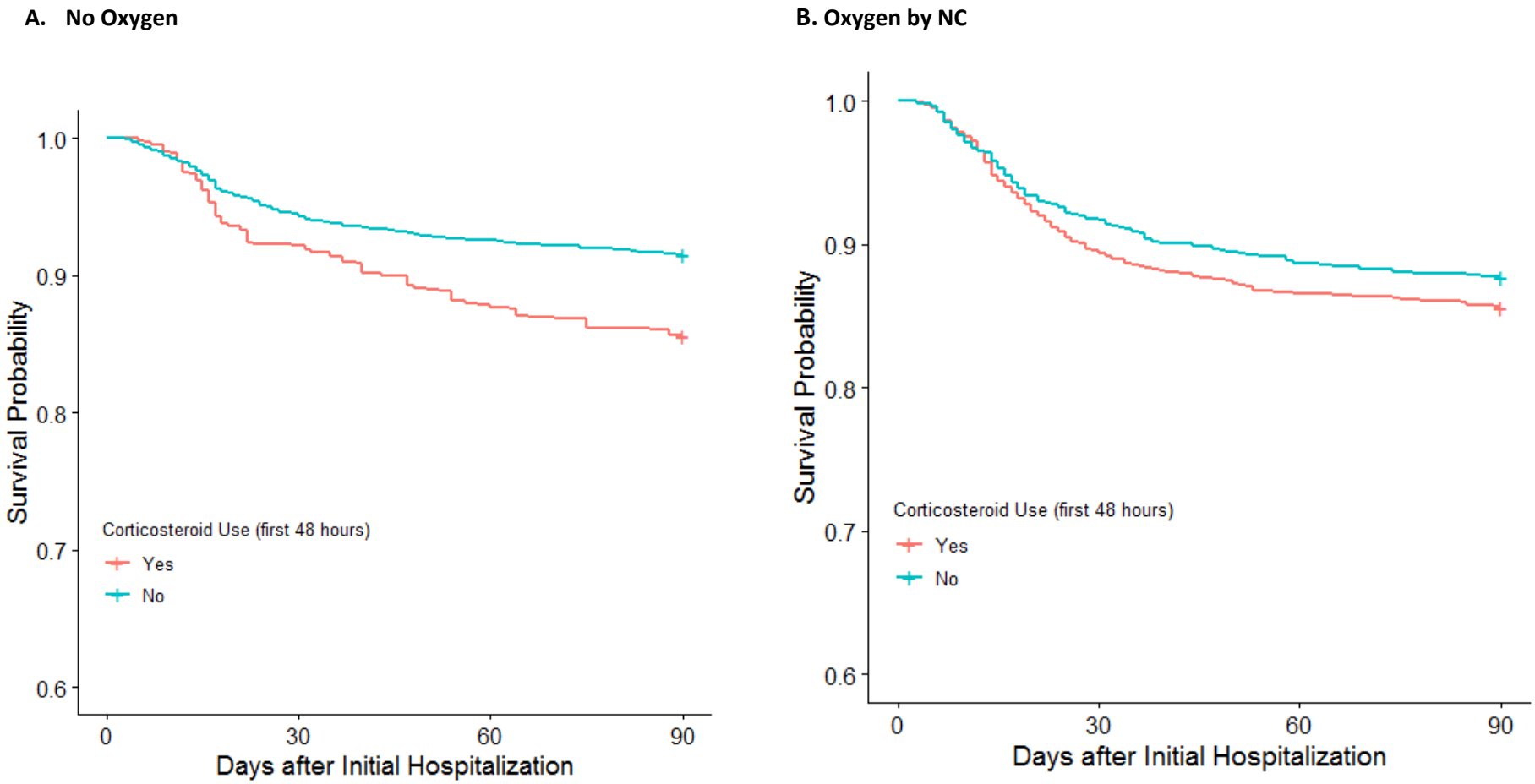


Figure 3. IPTW Kaplan Meier survival curves for 90-day mortality by corticosteroid use among those on no oxygen or NC.

IPTW = Inverse probability of treatment weighting

NC = nasal cannula

TABLE 1: Characteristics of patients stratified by highest oxygen support during first 48 hours of hospitalization for COVID-19

		Oxygen Support first 48 hours				
	Overall	None	Nasal Cannula	Other Supplemental Oxygen/NIV	High Flow Nasal Cannula	Invasive Mechanical Ventilation
Overall Cohort, n	9,058	3,025	3,800	813	1,194	226
Demographics						
Age, n (%)						
<50	806 (9%)	332 (11%)	331 (9%)	52 (6%)	73 (6%)	18 (8%)
50-59	1,081 (12%)	389 (13%)	470 (12%)	79 (10%)	121 (10%)	22 (10%)
60-69	2,134 (24%)	692 (23%)	874 (23%)	202 (25%)	300 (25%)	66 (29%)
70-79	3,259 (36%)	970 (32%)	1,397 (37%)	320 (39%)	479 (40%)	93 (41%)
80+	1,778 (20%)	642 (21%)	728 (19%)	160 (20%)	221 (19%)	27 (12%)
Sex: Male, n (%)	8,606 (95%)	2,858 (94%)	3,594 (95%)	775 (95%)	1,163 (97%)	216 (96%)
Race, n (%)						
White, non-Hispanic	4,989 (55%)	1,563 (52%)	2,121 (56%)	480 (59%)	704 (59%)	121 (54%)
Black, non-Hispanic	2,426 (27%)	928 (31%)	985 (26%)	211 (26%)	258 (22%)	44 (19%)
Hispanic	864 (10%)	276 (9%)	371 (10%)	57 (7%)	125 (10%)	35 (15%)
Other	491 (5%)	152 (5%)	208 (5%)	46 (6%)	70 (6%)	15 (7%)
Unknown	288 (3%)	106 (4%)	115 (3%)	19 (2%)	37 (3%)	11 (5%)
Phase (Admission Date, 2020), n (%)						
1: June 7 - July 11	1,365 (15%)	483 (16%)	563 (15%)	103 (13%)	169 (14%)	47 (21%)
2: July 12 - Aug. 15	1,590 (18%)	537 (18%)	695 (18%)	140 (17%)	186 (16%)	32 (14%)
3: Aug. 16 - Oct. 17	1,908 (21%)	668 (22%)	792 (21%)	163 (20%)	229 (19%)	56 (25%)
4: Oct. 18 - Dec. 5	4,195 (46%)	1,337 (44%)	1,750 (46%)	407 (50%)	610 (51%)	91 (40%)
Selected Conditions						
Dementia, n (%)	1,193 (13%)	527 (17%)	429 (11%)	123 (15%)	99 (8%)	15 (7%)
CHF, n (%)	1,886 (21%)	571 (19%)	810 (21%)	233 (29%)	233 (20%)	39 (17%)
COPD/Asthma, n (%)	2,715 (30%)	729 (24%)	1,251 (33%)	296 (36%)	377 (32%)	62 (27%)
Charlson Comorbidity Index, n (%)						
0	1,706 (19%)	634 (21%)	698 (18%)	98 (12%)	233 (20%)	43 (19%)
1-2	2,868 (32%)	940 (31%)	1,216 (32%)	219 (27%)	409 (34%)	84 (37%)
3-4	2,145 (24%)	660 (22%)	940 (25%)	224 (28%)	274 (23%)	47 (21%)
5+	2,339 (26%)	791 (26%)	946 (25%)	272 (33%)	278 (23%)	52 (23%)
Medication Use						
Steroid, Any Systemic, n (%)						
First 48 Hours	5,165 (57%)	598 (20%)	2,808 (74%)	468 (58%)	1,083 (91%)	208 (92%)
Later than 48 Hours	870 (10%)	363 (12%)	337 (9%)	115 (14%)	43 (4%)	12 (5%)
None	3,023 (33%)	2,064 (68%)	655 (17%)	230 (28%)	68 (6%)	6 (3%)
Dexamethasone, n (%)						

		Oxygen Support first 48 hours				
	Overall	None	Nasal Cannula	Other Supplemental Oxygen/NIV	High Flow Nasal Cannula	Invasive Mechanical Ventilation
First 48 Hours	4,911 (54%)	511 (17%)	2,712 (71%)	430 (53%)	1,057 (89%)	201 (89%)
Later than 48 Hours	875 (10%)	354 (12%)	344 (9%)	117 (14%)	45 (4%)	15 (7%)
None	3,272 (36%)	2,160 (71%)	744 (20%)	266 (33%)	92 (8%)	10 (4%)
Remdesivir, n (%)						
First 48 Hours	4,078 (45%)	434 (14%)	2,222 (58%)	340 (42%)	928 (78%)	154 (68%)
Later than 48 Hours	911 (10%)	314 (10%)	398 (10%)	106 (13%)	72 (6%)	21 (9%)
None	4,069 (45%)	2,277 (75%)	1,180 (31%)	367 (45%)	194 (16%)	51 (23%)
Prophylactic Anticoagulant, n (%)						
First 48 Hours	5,020 (55%)	1,606 (53%)	2,180 (57%)	438 (54%)	666 (56%)	130 (58%)
Later than 48 Hours	549 (6%)	175 (6%)	210 (6%)	53 (7%)	94 (8%)	17 (8%)
None	3,489 (39%)	1,244 (41%)	1,410 (37%)	322 (40%)	434 (36%)	79 (35%)
Intensive Care, n (%)						
First 48 Hours	2,006 (22%)	278 (9%)	583 (15%)	203 (25%)	735 (62%)	207 (92%)
Later than 48 Hours	676 (7%)	124 (4%)	352 (9%)	76 (9%)	113 (9%)	11 (5%)
None	6,376 (70%)	2,623 (87%)	2,865 (75%)	534 (66%)	346 (29%)	8 (4%)
Vasopressors, n (%)						
First 48 Hours	188 (2.1%)	9 (0.3%)	19 (0.5%)	11 (1.4%)	27 (2.3%)	122 (54.0%)
Later than 48 Hours	539 (6.0%)	47 (1.6%)	169 (4.4%)	44 (5.4%)	217 (18.2%)	62 (27.4%)
None	8331 (92.0%)	2,969 (98.1%)	3612 (95.1%)	758 (93.2%)	950 (79.6%)	42 (18.6%)
Intubation, n (%)						
First 48 Hours	226 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	226 (100%)
Later than 48 Hours	492 (5%)	49 (2%)	161 (4%)	46 (6%)	236 (20%)	0 (0%)
None	8,340 (92%)	2,976 (98%)	3,639 (96%)	767 (94%)	958 (80%)	0 (0%)
Hospital Length of Stay, days, median (interquartile range)	6 (4 – 12)	5 (3 – 11)	6 (4 – 10)	6 (4 – 12)	10 (6 – 17)	16 (10 – 30)
Mortality (unadjusted, cumulative incidence)						
30 Days, n (%)	1,151 (13%)	184 (6%)	375 (10%)	124 (15%)	360 (30%)	108 (48%)
60 Days, n (%)	1,413 (16%)	247 (8%)	477 (13%)	164 (20%)	404 (34%)	121 (54%)
90 Days, n (%)	1,512 (17%)	283 (9%)	514 (14%)	175 (22%)	416 (35%)	124 (55%)

Table 2. Characteristics of patients without oxygen or on NC after inverse probability of treatment weighting (IPTW) for estimating the average treatment effect in the total population (ATE models)

	Combined Cohort of patients without oxygen or on NC only		
Corticosteroids	No	Yes	SMD
Cohort, n	5796.7	6144.2	
Age, (%)			
<50	514.4 (8.9)	572.8 (9.3)	0.004
50-59	683.7 (11.8)	761.0 (12.4)	0.006
60-69	1329.2 (22.9)	1390.5 (22.6)	-0.003
70-79	2055.2 (35.5)	2247.7 (36.6)	0.011
80+	1214.1 (20.9)	1172.2 (19.1)	-0.019
Sex: Male, (%)	5458.7 (94.2)	5808.7 (94.5)	0.004
Race, (%)			
White, non-Hispanic	3011.8 (52.0)	3301.2 (53.7)	0.018
Black, non-Hispanic	1759.4 (30.4)	1731.6 (28.2)	-0.022
Hispanic	516.5 (8.9)	577.9 (9.4)	0.005
Other	317.7 (5.5)	330.8 (5.4)	-0.001
Unknown	191.4 (3.3)	202.9 (3.3)	0.000
Phase (Admission Date) , (%)			
1: June 7 - July 11	1077.2 (18.6)	850.2 (13.8)	-0.047
2: July 12 - Aug. 15	1049.2 (18.1)	1165.3 (19.0)	0.009
3: Aug. 16 - Oct. 17	1260.0 (21.7)	1290.7 (21.0)	-0.007
4: Oct. 18 - Dec. 5	2410.3 (41.6)	2838.0 (46.2)	0.046
Site Dexamethasone Prescribing, (%)			
Low	1477.9 (25.5)	1227.7 (20.0)	-0.055
Medium	3565.1 (61.5)	3705.7 (60.3)	-0.012
High	753.7 (13.0)	1210.9 (19.7)	0.067
Smoking Status, (%)			
Never Smoked	2008.6 (34.7)	2061.8 (33.6)	-0.011
Former Smoker	2382.6 (41.1)	2686.1 (43.7)	0.026
Current Smoker	1315.7 (22.7)	1275.6 (20.8)	-0.019
Unknown	89.8 (1.5)	120.6 (2.0)	0.004
AUDIT-C Score (%)			
0	3677.0 (63.4)	3870.0 (63.0)	-0.004
1 – 3	1236.9 (21.3)	1393.5 (22.7)	0.013
4 – 7	351.7 (6.1)	348.8 (5.7)	-0.004
8 +	130.9 (2.3)	118.7 (1.9)	-0.003
Unknown	400.2 (6.9)	413.2 (6.7)	-0.002
Comorbidities			
Myocardial Infarction (%)	491.5 (8.5)	468.9 (7.6)	-0.008
Congestive Heart Failure (%)	1257.0 (21.7)	1256.7 (20.5)	-0.012
Cerebrovascular Disease (%)	1005.1 (17.3)	988.3 (16.1)	-0.013
Dementia (%)	904.3 (15.6)	721.8 (11.7)	-0.039
Chronic Obstructive Pulmonary Disease (%)	1517.3 (26.2)	1889.6 (30.8)	0.046
Rheumatoid Arthritis (%)	79.5 (1.4)	87.7 (1.4)	0.001
Peptic ulcer (%)	133.3 (2.3)	135.0 (2.2)	-0.001
Liver disease, mild (%)	637.9 (11.0)	624.3 (10.2)	-0.008
Diabetes, Uncomplicated (%)	2707.6 (46.7)	2862.2 (46.6)	-0.001
Diabetes, Complicated (%)	1810.1 (31.2)	1773.0 (28.9)	-0.024
Hemi or paraplegia (%)	168.6 (2.9)	148.6 (2.4)	-0.005
Liver disease, moderate-severe (%)	95.4 (1.6)	98.0 (1.6)	-0.001
Metastatic cancer (%)	121.9 (2.1)	115.1 (1.9)	-0.002
HIV (%)	70.3 (1.2)	57.5 (0.9)	-0.003
Renal disease (%)	1567.4 (27.0)	1560.7 (25.4)	-0.016
Charlson Comorbidities Count (%)			
0	1122.3 (19.4)	1207.4 (19.7)	0.003
1 - 2	1767.9 (30.5)	1953.9 (31.8)	0.013
3 - 4	1327.6 (22.9)	1481.3 (24.1)	0.012

	Combined Cohort of patients without oxygen or on NC only		
Corticosteroids	No	Yes	SMD
5 +	1578.9 (27.2)	1501.7 (24.4)	-0.028
Number of Doctors (prior year) (%)			
0	2330.1 (40.2)	2475.4 (40.3)	0.001
1	1588.7 (27.4)	1685.4 (27.4)	0.000
2 - 4	1717.9 (29.6)	1835.7 (29.9)	0.002
5 +	160.0 (2.8)	147.6 (2.4)	-0.004
Specialty clinics attended			
Cardiology **(%)**	1512.0 (26.1)	1661.1 (27.0)	0.010
Coagulation (%)	88.0 (1.5)	93.8 (1.5)	0.000
Pacemaker (%)	232.5 (4.0)	220.8 (3.6)	-0.004
Dialysis (%)	98.7 (1.7)	99.8 (1.6)	-0.001
Gastoenterology (%)	508.1 (8.8)	586.5 (9.5)	0.008
Hepatology (%)	183.2 (3.2)	146.2 (2.4)	-0.008
Homeless (%)	376.3 (6.5)	304.9 (5.0)	-0.015
Co-Medications			
Prophylactic Anticoagulants 1st 48 hours (%)	3164.0 (54.6)	3444.3 (56.1)	0.015
Remdesivir, 1st 48 hours (%)	1714.5 (29.6)	2630.2 (42.8)	0.132
Laboratory values			
Albumin, g/dL (%)			
3.5 +	2125.2 (36.7)	2040.4 (33.2)	-0.035
3 - 3.49	1871.1 (32.3)	2103.8 (34.2)	0.020
< 3	1527.9 (26.4)	1775.3 (28.9)	0.025
Missing	272.5 (4.7)	224.8 (3.7)	-0.010
Alanine aminotransferase, IU/L (%)			
< 20	1678.7 (29.0)	1532.1 (24.9)	-0.040
20 - 39	2415.7 (41.7)	2621.7 (42.7)	0.010
40 +	1494.2 (25.8)	1839.4 (29.9)	0.042
Missing	208.1 (3.6)	151.1 (2.5)	-0.011
Asparate aminostransferase, IU/L (%)			
< 20	1054.7 (18.2)	829.8 (13.5)	-0.047
20 - 39	2670.2 (46.1)	2816.1 (45.8)	-0.002
40 +	2071.8 (35.7)	2498.3 (40.7)	0.049
Creatinine, mg/dL (%)			
< 1.2	2671.7 (46.1)	2857.0 (46.5)	0.004
1.2 – 1.99	2141.5 (36.9)	2265.1 (36.9)	-0.001
2 +	983.5 (17.0)	1022.1 (16.6)	-0.003
Missing	0.0 (0.0)	0.0 (0.0)	
Fibrosis-4 Index (%)			
< 1.45	1065.6 (18.4)	1062.8 (17.3)	-0.011
1.45 – 3.25	2393.0 (41.3)	2597.0 (42.3)	0.010
3.25 +	2101.8 (36.3)	2325.3 (37.8)	0.016
Missing	236.3 (4.1)	159.1 (2.6)	-0.015
Lactate, mmol/L (%)			
<1.2	1003.8 (17.3)	1075.5 (17.5)	0.002
1.2 - <2.0	1510.3 (26.1)	1816.4 (29.6)	0.035
2.0+	737.4 (12.7)	880.6 (14.3)	0.016
Missing	2545.2 (43.9)	2371.8 (38.6)	-0.053
Platelet count per microL (%)			
150 or higher	3822.5 (65.9)	4050.8 (65.9)	0.000
< 150	1964.6 (33.9)	2081.7 (33.9)	0.000
Missing	9.6 (0.2)	11.7 (0.2)	0.000
Total bilirubin, mg/dL (%)			
< 1	4395.1 (75.8)	4646.6 (75.6)	-0.002
1 - 1.2	489.1 (8.4)	558.8 (9.1)	0.007
1.2 +	730.4 (12.6)	808.8 (13.2)	0.006
Missing	182.1 (3.1)	130.1 (2.1)	-0.010
White Blood Count per microL (%)			

	Combined Cohort of patients without oxygen or on NC only		
Corticosteroids	No	Yes	SMD
4-10	3243.2 (55.9)	3097.6 (50.4)	-0.055
<4	1622.3 (28.0)	1776.7 (28.9)	0.009
>10	931.2 (16.1)	1269.8 (20.7)	0.046
C-reactive protein measured (%)	3428.1 (59.1)	3883.6 (63.2)	0.041
D-dimer measured (%)	4512.3 (77.8)	4998.2 (81.3)	0.035
Vital Signs			
Highest Temperature (F) (%)			
< 99	1968.5 (34.0)	2001.3 (32.6)	-0.014
99 - 100	1389.2 (24.0)	1452.8 (23.6)	-0.003
100 - 102	1601.0 (27.6)	1769.6 (28.8)	0.012
102 +	818.1 (14.1)	893.9 (14.5)	0.004
Missing	19.9 (0.3)	26.7 (0.4)	0.001
Mean Arterial Pressure, mmHg (%)			
< 60	141.0 (2.4)	118.5 (1.9)	-0.005
60 – 69	784.4 (13.5)	751.0 (12.2)	-0.013
70 – 89	3812.6 (65.8)	4141.8 (67.4)	0.016
90 +	1049.4 (18.1)	1112.1 (18.1)	0.000
Missing	9.3 (0.2)	20.8 (0.3)	0.002
Lowest Oxygen Saturation (%)			
< 88	312.7 (5.4)	468.1 (7.6)	0.022
88 - 92	2438.6 (42.1)	3022.9 (49.2)	0.071
93 - 95	2191.5 (37.8)	2006.9 (32.7)	-0.051
96 +	733.5 (12.7)	513.5 (8.4)	-0.043
Missing	120.3 (2.1)	132.9 (2.2)	0.001

IPTW = inverse probability of treatment weighting

Table 3. IPTW Cox Proportional Hazards Models for 90-day mortality associated with early corticosteroid exposure in patients hospitalized for COVID-19 among those not on IRS

	No oxygen supplementation	**Nasal cannula**	**Combined group: no oxygen plus NC**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**
Primary analysis	1.89 (1.33-2.68)	1.21 (0.94-1.57)	1.61 (1.33-1.94)
Subgroup analyses			
Restricted to dexamethasone	2.03 (1.35-3.07)	1.23 (0.89-1.71)	1.57 (1.22-2.03)
Excluding patients admitted to ICU in initial 48 hours	1.86 (1.22-2.83)	1.30 (0.95-1.78)	1.62 (1.28-2.06)
Restricted to patients age 70 and older	1.91 (1.28-2.85)	1.40 (1.03-1.92)	1.65 (1.30-2.08)

Models present the ATE (average treatment effect in entire population).
CI = confidence interval
HR = hazard ratio
IPTW = inverse probability of treatment weighting
IRS = intensive respiratory support

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Supplemental Table 1. Propensity weighted pseudo populations and unweighted sample

ATT

Characteristics	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	No	Yes	SMD	Yes	No
Cohort, n	2979.1	2108.3		2585.7	3755.7		5796.7	6144.2	
Age, (%)									
<50	324.5 (10.9)	192.7 (9.1)	-0.018	205.9 (8.0)	339.7 (9.0)	0.011	514.4 (8.9)	572.8 (9.3)	0.004
50-59	368.8 (12.4)	263.4 (12.5)	0.001	314.0 (12.1)	473.6 (12.6)	0.005	683.7 (11.8)	761.0 (12.4)	0.006
60-69	686.9 (23.1)	536.7 (25.5)	0.024	569.7 (22.0)	842.4 (22.4)	0.004	1329.2 (22.9)	1390.5 (22.6)	-0.003
70-79	964.0 (32.4)	719.7 (34.1)	0.018	938.2 (36.3)	1384.5 (36.9)	0.006	2055.2 (35.5)	2247.7 (36.6)	0.011
80+	634.9 (21.3)	395.7 (18.8)	-0.025	557.9 (21.6)	715.4 (19.0)	-0.025	1214.1 (20.9)	1172.2 (19.1)	-0.019
Sex: Male, (%)	2811.8 (94.4)	2014.8 (95.6)	0.012	2438.8 (94.3)	3558.1 (94.7)	0.004	5458.7 (94.2)	5808.7 (94.5)	0.004
Race, (%)									
White, non-Hispanic	1528.8 (51.3)	1028.0 (48.8)	-0.026	1362.1 (52.7)	2078.5 (55.3)	0.027	3011.8 (52.0)	3301.2 (53.7)	0.018
Black, non-Hispanic	943.3 (31.7)	686.9 (32.6)	0.009	728.0 (28.2)	984.7 (26.2)	-0.019	1759.4 (30.4)	1731.6 (28.2)	-0.022
Hispanic	259.7 (8.7)	212.2 (10.1)	0.013	252.8 (9.8)	355.2 (9.5)	-0.003	516.5 (8.9)	577.9 (9.4)	0.005
Other	149.9 (5.0)	121.5 (5.8)	0.007	159.1 (6.2)	218.3 (5.8)	-0.003	317.7 (5.5)	330.8 (5.4)	-0.001
Unknown	97.4 (3.3)	59.7 (2.8)	-0.004	83.8 (3.2)	119.0 (3.2)	-0.001	191.4 (3.3)	202.9 (3.3)	0.000
Phase (Admission Date) , (%)									
1: June 7 - July 11	474.3 (15.9)	273.5 (13.0)	-0.029	581.1 (22.5)	602.7 (16.0)	-0.064	1077.2 (18.6)	850.2 (13.8)	-0.047
2: July 12 - Aug. 15	515.4 (17.3)	325.9 (15.5)	-0.018	538.5 (20.8)	676.8 (18.0)	-0.028	1049.2 (18.1)	1165.3 (19.0)	0.009
3: Aug. 16 - Oct. 17	659.4 (22.1)	483.1 (22.9)	0.008	564.4 (21.8)	772.6 (20.6)	-0.013	1260.0 (21.7)	1290.7 (21.0)	-0.007
4: Oct. 18 - Dec. 5	1330.1 (44.6)	1025.7 (48.6)	0.040	901.7 (34.9)	1703.6 (45.4)	0.105	2410.3 (41.6)	2838.0 (46.2)	0.046
Site Dexamethasone Prescribing, (%)									
Low	768.0 (25.8)	365.1 (17.3)	-0.085	684.2 (26.5)	719.1 (19.1)	-0.073	1477.9 (25.5)	1227.7 (20.0)	-0.055
Medium	1811.7 (60.8)	1379.7 (65.4)	0.046	1510.0 (58.4)	2236.0 (59.5)	0.011	3565.1 (61.5)	3705.7 (60.3)	-0.012
High	399.5 (13.4)	363.5 (17.2)	0.038	391.5 (15.1)	800.5 (21.3)	0.062	753.7 (13.0)	1210.9 (19.7)	0.067
Smoking Status, (%)									
Never Smoked	1042.9 (35.0)	761.9 (36.1)	0.011	907.6 (35.1)	1264.8 (33.7)	-0.014	2008.6 (34.7)	2061.8 (33.6)	-0.011
Former Smoker	1149.4 (38.6)	867.1 (41.1)	0.025	1108.8 (42.9)	1705.5 (45.4)	0.025	2382.6 (41.1)	2686.1 (43.7)	0.026
Current Smoker	718.6 (24.1)	452.5 (21.5)	-0.027	527.7 (20.4)	721.5 (19.2)	-0.012	1315.7 (22.7)	1275.6 (20.8)	-0.019
Unknown	68.3 (2.3)	26.7 (1.3)	-0.010	41.6 (1.6)	63.9 (1.7)	0.001	89.8 (1.5)	120.6 (2.0)	0.004
AUDIT-C Score (%)									
0	1836.1 (61.6)	1303.7 (61.8)	0.002	1690.4 (65.4)	2422.7 (64.5)	-0.009	3677.0 (63.4)	3870.0 (63.0)	-0.004
1 – 3	599.9 (20.1)	435.8 (20.7)	0.005	579.4 (22.4)	872.6 (23.2)	0.008	1236.9 (21.3)	1393.5 (22.7)	0.013
4 – 7	211.4 (7.1)	161.7 (7.7)	0.006	118.1 (4.6)	180.5 (4.8)	0.002	351.7 (6.1)	348.8 (5.7)	-0.004
8 +	92.9 (3.1)	53.8 (2.6)	-0.006	44.7 (1.7)	59.2 (1.6)	-0.002	130.9 (2.3)	118.7 (1.9)	-0.003
Unknown	238.9 (8.0)	153.3 (7.3)	-0.007	153.1 (5.9)	220.8 (5.9)	0.000	400.2 (6.9)	413.2 (6.7)	-0.002
Comorbidities									
Myocardial Infarction (%)	247.1 (8.3)	138.3 (6.6)	-0.017	230.3 (8.9)	310.2 (8.3)	-0.006	491.5 (8.5)	468.9 (7.6)	-0.008
Congestive Heart Failure (%)	558.7 (18.8)	411.2 (19.5)	0.008	642.6 (24.9)	806.2 (21.5)	-0.034	1257.0 (21.7)	1256.7 (20.5)	-0.012

Characteristics	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	No	Yes	SMD	Yes	No
Cerebrovascular Disease (%)	534.4 (17.9)	332.8 (15.8)	-0.022	451.3 (17.5)	626.0 (16.7)	-0.008	1005.1 (17.3)	988.3 (16.1)	-0.013
Dementia (%)	517.0 (17.4)	270.8 (12.8)	-0.045	375.2 (14.5)	439.1 (11.7)	-0.028	904.3 (15.6)	721.8 (11.7)	-0.039
Chronic Obstructive Pulmonary Disease (%)	706.3 (23.7)	570.9 (27.1)	0.034	824.1 (31.9)	1226.3 (32.7)	0.008	1517.3 (26.2)	1889.6 (30.8)	0.046
Rheumatoid Arthritis (%)	50.9 (1.7)	22.5 (1.1)	-0.006	54.0 (2.1)	70.8 (1.9)	-0.002	79.5 (1.4)	87.7 (1.4)	0.001
Peptic ulcer (%)	78.9 (2.6)	46.9 (2.2)	-0.004	50.8 (2.0)	87.9 (2.3)	0.004	133.3 (2.3)	135.0 (2.2)	-0.001
Liver disease, mild (%)	397.6 (13.3)	272.8 (12.9)	-0.004	239.1 (9.2)	350.7 (9.3)	0.001	637.9 (11.0)	624.3 (10.2)	-0.008
Diabetes, Uncomplicated (%)	1327.3 (44.6)	972.6 (46.1)	0.016	1264.4 (48.9)	1834.9 (48.9)	0.000	2707.6 (46.7)	2862.2 (46.6)	-0.001
Diabetes, Complicated (%)	862.3 (28.9)	578.4 (27.4)	-0.015	837.4 (32.4)	1128.6 (30.0)	-0.023	1810.1 (31.2)	1773.0 (28.9)	-0.024
Hemi or para plegia (%)	94.4 (3.2)	49.0 (2.3)	-0.008	74.6 (2.9)	85.3 (2.3)	-0.006	168.6 (2.9)	148.6 (2.4)	-0.005
Liver disease, moderate-severe (%)	73.8 (2.5)	63.9 (3.0)	0.006	27.1 (1.0)	42.5 (1.1)	0.001	95.4 (1.6)	98.0 (1.6)	-0.001
Metastatic cancer (%)	62.3 (2.1)	23.3 (1.1)	-0.010	32.3 (1.3)	63.3 (1.7)	0.004	121.9 (2.1)	115.1 (1.9)	-0.002
HIV (%)	39.4 (1.3)	29.1 (1.4)	0.001	39.0 (1.5)	51.2 (1.4)	-0.001	70.3 (1.2)	57.5 (0.9)	-0.003
Renal disease (%)	735.1 (24.7)	537.2 (25.5)	0.008	729.4 (28.2)	964.6 (25.7)	-0.025	1567.4 (27.0)	1560.7 (25.4)	-0.016
Charlson Comorbidities Count (%)									
0	621.0 (20.8)	448.5 (21.3)	0.004	485.5 (18.8)	689.1 (18.3)	-0.004	1122.3 (19.4)	1207.4 (19.7)	0.003
1 - 2	920.5 (30.9)	688.0 (32.6)	0.017	733.7 (28.4)	1184.0 (31.5)	0.032	1767.9 (30.5)	1953.9 (31.8)	0.013
3 - 4	654.1 (22.0)	456.2 (21.6)	-0.003	617.4 (23.9)	913.0 (24.3)	0.004	1327.6 (22.9)	1481.3 (24.1)	0.012
5 +	783.5 (26.3)	515.6 (24.5)	-0.018	749.1 (29.0)	969.6 (25.8)	-0.032	1578.9 (27.2)	1501.7 (24.4)	-0.028
Number of Doctors (prior year) (%)									
0	1276.8 (42.9)	885.2 (42.0)	-0.009	985.6 (38.1)	1430.6 (38.1)	0.000	2330.1 (40.2)	2475.4 (40.3)	0.001
1	816.9 (27.4)	627.3 (29.8)	0.023	674.8 (26.1)	1043.7 (27.8)	0.017	1588.7 (27.4)	1685.4 (27.4)	0.000
2 - 4	812.5 (27.3)	555.7 (26.4)	-0.009	850.5 (32.9)	1196.5 (31.9)	-0.010	1717.9 (29.6)	1835.7 (29.9)	0.002
5 +	72.9 (2.4)	40.1 (1.9)	-0.005	74.8 (2.9)	84.9 (2.3)	-0.006	160.0 (2.8)	147.6 (2.4)	-0.004
Specialty clinics attended									
Cardiology **(%)**	732.6 (24.6)	531.3 (25.2)	0.006	741.9 (28.7)	1059.3 (28.2)	-0.005	1512.0 (26.1)	1661.1 (27.0)	0.010
Coagulation (%)	47.5 (1.6)	46.8 (2.2)	0.006	40.3 (1.6)	49.8 (1.3)	-0.002	88.0 (1.5)	93.8 (1.5)	0.000
Pacemaker (%)	112.6 (3.8)	115.5 (5.5)	0.017	92.3 (3.6)	115.7 (3.1)	-0.005	232.5 (4.0)	220.8 (3.6)	-0.004
Dialysis (%)	34.9 (1.2)	21.2 (1.0)	-0.002	70.4 (2.7)	66.6 (1.8)	-0.010	98.7 (1.7)	99.8 (1.6)	-0.001
Gastoenterology (%)	256.1 (8.6)	175.1 (8.3)	-0.003	234.8 (9.1)	368.2 (9.8)	0.007	508.1 (8.8)	586.5 (9.5)	0.008
Hepatology (%)	105.7 (3.5)	67.7 (3.2)	-0.003	77.4 (3.0)	94.7 (2.5)	-0.005	183.2 (3.2)	146.2 (2.4)	-0.008
Homeless (%)	231.8 (7.8)	148.3 (7.0)	-0.007	127.0 (4.9)	141.8 (3.8)	-0.011	376.3 (6.5)	304.9 (5.0)	-0.015
Co-medications									
Prophylactic Anticoagulants	1597.7 (53.6)	1127.2 (53.5)	-0.002	1488.4 (57.6)	2171.8 (57.8)	0.003	3164.0 (54.6)	3444.3 (56.1)	0.015
Remdesivir, 1st 48 hours (%)	433.7 (14.6)	439.7 (20.9)	0.063	999.8 (38.7)	2174.3 (57.9)	0.192	1714.5 (29.6)	2630.2 (42.8)	0.132
Laboratory Results									
Albumin, g/dL (%)									
3.5 +	1267.1 (42.5)	770.3 (36.5)	-0.060	795.3 (30.8)	1084.5 (28.9)	-0.019	2125.2 (36.7)	2040.4 (33.2)	-0.035
3 - 3.49	924.4 (31.0)	728.9 (34.6)	0.035	878.8 (34.0)	1348.7 (35.9)	0.019	1871.1 (32.3)	2103.8 (34.2)	0.020
< 3	622.6 (20.9)	529.5 (25.1)	0.042	811.5 (31.4)	1199.6 (31.9)	0.006	1527.9 (26.4)	1775.3 (28.9)	0.025
Missing	165.0 (5.5)	79.6 (3.8)	-0.018	100.1 (3.9)	122.9 (3.3)	-0.006	272.5 (4.7)	224.8 (3.7)	-0.010
Alanine aminotransferase, IU/L (%)									
< 20	949.8 (31.9)	596.0 (28.3)	-0.036	656.3 (25.4)	853.0 (22.7)	-0.027	1678.7 (29.0)	1532.1 (24.9)	-0.040
20 - 39	1155.8 (38.8)	865.1 (41.0)	0.022	1137.9 (44.0)	1638.7 (43.6)	-0.004	2415.7 (41.7)	2621.7 (42.7)	0.010
40 +	731.2 (24.5)	613.5 (29.1)	0.046	714.2 (27.6)	1184.6 (31.5)	0.039	1494.2 (25.8)	1839.4 (29.9)	0.042

Characteristics	No Oxygen			Nasal Canula				Combined Cohort	
	No	Yes	SMD	No	No	Yes	SMD	Yes	No
Missing	142.3 (4.8)	33.6 (1.6)	-0.032	77.2 (3.0)	79.4 (2.1)	-0.009	208.1 (3.6)	151.1 (2.5)	-0.011
Asparate aminostransferase, IU/L (%)									
< 20	699.1 (23.5)	272.4 (12.9)	-0.105	331.1 (12.8)	399.0 (10.6)	-0.022	1054.7 (18.2)	829.8 (13.5)	-0.047
20 - 39	1372.6 (46.1)	1075.9 (51.0)	0.050	1166.3 (45.1)	1679.2 (44.7)	-0.004	2670.2 (46.1)	2816.1 (45.8)	-0.002
40 +	907.4 (30.5)	760.0 (36.0)	0.056	1088.4 (42.1)	1677.6 (44.7)	0.026	2071.8 (35.7)	2498.3 (40.7)	0.049
Creatinine, mg/dL (%)									
< 1.2	1499.4 (50.3)	967.2 (45.9)	-0.045	1108.0 (42.9)	1704.5 (45.4)	0.025	2671.7 (46.1)	2857.0 (46.5)	0.004
1.2 – 1.99	1035.8 (34.8)	811.3 (38.5)	0.037	992.1 (38.4)	1432.2 (38.1)	-0.002	2141.5 (36.9)	2265.1 (36.9)	-0.001
2 +	432.9 (14.5)	329.8 (15.6)	0.011	485.6 (18.8)	619.0 (16.5)	-0.023	983.5 (17.0)	1022.1 (16.6)	-0.003
Missing	11.0 (0.4)	0.0 (0.0)	-0.004	0.0 (0.0)	0.0 (0.0)		0.0 (0.0)	0.0 (0.0)	
Fibrosis-4 Index (%)									
< 1.45	686.8 (23.1)	439.5 (20.8)	-0.022	353.2 (13.7)	569.2 (15.2)	0.015	1065.6 (18.4)	1062.8 (17.3)	-0.011
1.45 – 3.25	1204.6 (40.4)	837.1 (39.7)	-0.007	1067.9 (41.3)	1644.5 (43.8)	0.025	2393.0 (41.3)	2597.0 (42.3)	0.010
3.25 +	928.5 (31.2)	798.1 (37.9)	0.067	1083.7 (41.9)	1456.9 (38.8)	-0.031	2101.8 (36.3)	2325.3 (37.8)	0.016
Missing	159.2 (5.3)	33.6 (1.6)	-0.038	81.0 (3.1)	85.1 (2.3)	-0.009	236.3 (4.1)	159.1 (2.6)	-0.015
Lactate, mmol/L (%)									
1_1.2	493.0 (16.5)	441.7 (21.0)	0.044	455.4 (17.6)	695.1 (18.5)	0.009	1003.8 (17.3)	1075.5 (17.5)	0.002
2_1.2LT2	682.6 (22.9)	558.3 (26.5)	0.036	713.6 (27.6)	1170.2 (31.2)	0.036	1510.3 (26.1)	1816.4 (29.6)	0.035
3_GE2	348.1 (11.7)	312.3 (14.8)	0.031	385.0 (14.9)	559.1 (14.9)	0.000	737.4 (12.7)	880.6 (14.3)	0.016
Missing	1455.5 (48.9)	796.0 (37.8)	-0.111	1031.7 (39.9)	1331.3 (35.4)	-0.045	2545.2 (43.9)	2371.8 (38.6)	-0.053
Platelet count per microL (%)									
150 or higher	2019.9 (67.8)	1370.8 (65.0)	-0.028	1636.0 (63.3)	2488.6 (66.3)	0.030	3822.5 (65.9)	4050.8 (65.9)	0.000
< 150	943.2 (31.7)	737.4 (35.0)	0.033	946.9 (36.6)	1262.6 (33.6)	-0.030	1964.6 (33.9)	2081.7 (33.9)	0.000
Missing	16.0 (0.5)	0.0 (0.0)	-0.005	2.9 (0.1)	4.5 (0.1)	0.000	9.6 (0.2)	11.7 (0.2)	0.000
Total bilirubin, mg/dL (%)									
< 1	2268.0 (76.1)	1624.2 (77.0)	0.009	1978.0 (76.5)	2841.7 (75.7)	-0.008	4395.1 (75.8)	4646.6 (75.6)	-0.002
1 - 1.2	218.7 (7.3)	180.6 (8.6)	0.012	228.2 (8.8)	354.7 (9.4)	0.006	489.1 (8.4)	558.8 (9.1)	0.007
1.2 +	368.0 (12.4)	281.1 (13.3)	0.010	307.6 (11.9)	487.2 (13.0)	0.011	730.4 (12.6)	808.8 (13.2)	0.006
Missing	124.4 (4.2)	22.3 (1.1)	-0.031	71.9 (2.8)	72.2 (1.9)	-0.009	182.1 (3.1)	130.1 (2.1)	-0.010
White Blood Count per microL (%)									
4-10	1746.6 (58.6)	1082.6 (51.3)	-0.073	1378.3 (53.3)	1818.5 (48.4)	-0.049	3243.2 (55.9)	3097.6 (50.4)	-0.055
<4	803.4 (27.0)	653.7 (31.0)	0.040	769.2 (29.7)	1095.3 (29.2)	-0.006	1622.3 (28.0)	1776.7 (28.9)	0.009
>10	429.1 (14.4)	372.0 (17.6)	0.032	438.2 (16.9)	841.9 (22.4)	0.055	931.2 (16.1)	1269.8 (20.7)	0.046
C-reactive protein measured (%)	1689.4 (56.7)	1364.5 (64.7)	0.080	1550.1 (59.9)	2386.3 (63.5)	0.036	3428.1 (59.1)	3883.6 (63.2)	0.041
D-dimer measured (%)	2184.7 (73.3)	1657.5 (78.6)	0.053	2106.3 (81.5)	3153.8 (84.0)	0.025	4512.3 (77.8)	4998.2 (81.3)	0.035
Vital Signs									
Highest Temperature (F) (%)									
< 99	1226.6 (41.2)	832.8 (39.5)	-0.017	684.9 (26.5)	1071.6 (28.5)	0.020	1968.5 (34.0)	2001.3 (32.6)	-0.014
99 - 100	735.0 (24.7)	479.8 (22.8)	-0.019	542.6 (21.0)	846.3 (22.5)	0.015	1389.2 (24.0)	1452.8 (23.6)	-0.003
100 - 102	693.4 (23.3)	522.8 (24.8)	0.015	869.7 (33.6)	1231.0 (32.8)	-0.009	1601.0 (27.6)	1769.6 (28.8)	0.012
102 +	314.2 (10.5)	267.2 (12.7)	0.021	478.5 (18.5)	591.4 (15.7)	-0.028	818.1 (14.1)	893.9 (14.5)	0.004
Missing	9.8 (0.3)	5.8 (0.3)	-0.001	9.9 (0.4)	15.4 (0.4)	0.000	19.9 (0.3)	26.7 (0.4)	0.001

Characteristics	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	No	Yes	SMD	Yes	No
Mean Arterial Pressure, mmHg (%)									
< 60	70.8 (2.4)	53.4 (2.5)	0.002	61.1 (2.4)	72.9 (1.9)	-0.004	141.0 (2.4)	118.5 (1.9)	-0.005
60 – 69	365.0 (12.3)	205.2 (9.7)	-0.025	387.6 (15.0)	509.2 (13.6)	-0.014	784.4 (13.5)	751.0 (12.2)	-0.013
70 – 89	1954.5 (65.6)	1416.8 (67.2)	0.016	1721.5 (66.6)	2531.4 (67.4)	0.008	3812.6 (65.8)	4141.8 (67.4)	0.016
90 +	582.2 (19.5)	431.2 (20.5)	0.009	407.1 (15.7)	630.2 (16.8)	0.010	1049.4 (18.1)	1112.1 (18.1)	0.000
Missing	6.6 (0.2)	1.7 (0.1)	-0.001	8.5 (0.3)	12.1 (0.3)	0.000	9.3 (0.2)	20.8 (0.3)	0.002
Lowest Oxygen Saturation (%)									
< 88	43.0 (1.4)	25.2 (1.2)	-0.002	245.8 (9.5)	415.6 (11.1)	0.016	312.7 (5.4)	468.1 (7.6)	0.022
88 - 92	887.9 (29.8)	707.3 (33.6)	0.037	1410.9 (54.6)	2170.9 (57.8)	0.032	2438.6 (42.1)	3022.9 (49.2)	0.071
93 - 95	1415.5 (47.5)	997.6 (47.3)	-0.002	727.3 (28.1)	896.6 (23.9)	-0.043	2191.5 (37.8)	2006.9 (32.7)	-0.051
96 +	564.1 (18.9)	307.0 (14.6)	-0.044	156.6 (6.1)	193.7 (5.2)	-0.009	733.5 (12.7)	513.5 (8.4)	-0.043
Missing	68.6 (2.3)	71.2 (3.4)	0.011	45.1 (1.7)	78.9 (2.1)	0.004	120.3 (2.1)	132.9 (2.2)	0.001

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Characteristics	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	No	Yes	SMD	Yes	No
Cohort, n	452.7	595.0		1638.9	2793.0		2200.7	3388.0	
Age, (%)									
<50	39.7 (8.8)	59.0 (9.9)	0.011	138.8 (8.5)	261.0 (9.3)	0.009	177.4 (8.1)	320.0 (9.4)	0.014
50-59	60.0 (13.3)	90.0 (15.1)	0.019	192.7 (11.8)	344.0 (12.3)	0.006	262.4 (11.9)	434.0 (12.8)	0.009
60-69	113.7 (25.1)	138.0 (23.2)	-0.019	360.3 (22.0)	647.0 (23.2)	0.012	496.8 (22.6)	785.0 (23.2)	0.006
70-79	150.3 (33.2)	195.0 (32.8)	-0.004	611.7 (37.3)	1048.0 (37.5)	0.002	802.7 (36.5)	1243.0 (36.7)	0.002
80+	88.9 (19.6)	113.0 (19.0)	-0.007	335.5 (20.5)	493.0 (17.7)	-0.028	461.4 (21.0)	606.0 (17.9)	-0.031
Sex: Male, (%)	430.0 (95.0)	562.0 (94.5)	-0.005	1545.1 (94.3)	2644.0 (94.7)	0.004	2069.5 (94.0)	3206.0 (94.6)	0.006
Race, (%)									
White, non-Hispanic	241.0 (53.2)	321.0 (53.9)	0.007	865.2 (52.8)	1589.0 (56.9)	0.041	1174.2 (53.4)	1910.0 (56.4)	0.030
Black, non-Hispanic	134.0 (29.6)	159.0 (26.7)	-0.029	438.4 (26.7)	678.0 (24.3)	-0.025	612.6 (27.8)	837.0 (24.7)	-0.031
Hispanic	41.5 (9.2)	61.0 (10.3)	0.011	175.6 (10.7)	290.0 (10.4)	-0.003	209.1 (9.5)	351.0 (10.4)	0.009
Other	22.8 (5.0)	28.0 (4.7)	-0.003	104.0 (6.3)	152.0 (5.4)	-0.009	140.7 (6.4)	180.0 (5.3)	-0.011
Unknown	13.3 (2.9)	26.0 (4.4)	0.014	55.8 (3.4)	84.0 (3.0)	-0.004	64.1 (2.9)	110.0 (3.2)	0.003
Phase (Admission Date) , (%)									
1: June 7 - July 11	52.3 (11.6)	51.0 (8.6)	-0.030	294.7 (18.0)	270.0 (9.7)	-0.083	361.2 (16.4)	321.0 (9.5)	-0.069
2: July 12 - Aug. 15	63.6 (14.1)	79.0 (13.3)	-0.008	343.2 (20.9)	490.0 (17.5)	-0.034	380.2 (17.3)	569.0 (16.8)	-0.005
3: Aug. 16 - Oct. 17	100.9 (22.3)	139.0 (23.4)	0.011	368.3 (22.5)	587.0 (21.0)	-0.015	457.7 (20.8)	726.0 (21.4)	0.006
4: Oct. 18 - Dec. 5	235.9 (52.1)	326.0 (54.8)	0.027	632.7 (38.6)	1446.0 (51.8)	0.132	1001.6 (45.5)	1772.0 (52.3)	0.068
Site Dexamethasone Prescribing, (%)									
Low	79.3 (17.5)	84.0 (14.1)	-0.034	392.3 (23.9)	421.0 (15.1)	-0.089	481.9 (21.9)	505.0 (14.9)	-0.070
Medium	290.3 (64.1)	358.0 (60.2)	-0.040	964.2 (58.8)	1665.0 (59.6)	0.008	1353.7 (61.5)	2023.0 (59.7)	-0.018
High	83.0 (18.3)	153.0 (25.7)	0.074	282.4 (17.2)	707.0 (25.3)	0.081	365.1 (16.6)	860.0 (25.4)	0.088
Smoking Status, (%)									

Characteristics	No Oxygen			Nasal Canula				Combined Cohort	
	No	Yes	SMD	No	No	Yes	SMD	Yes	No
Never Smoked	157.4 (34.8)	203.0 (34.1)	-0.007	581.8 (35.5)	939.0 (33.6)	-0.019	782.8 (35.6)	1142.0 (33.7)	-0.019
Former Smoker	188.9 (41.7)	269.0 (45.2)	0.035	720.5 (44.0)	1305.0 (46.7)	0.028	979.9 (44.5)	1574.0 (46.5)	0.019
Current Smoker	99.6 (22.0)	112.0 (18.8)	-0.032	323.2 (19.7)	506.0 (18.1)	-0.016	415.3 (18.9)	618.0 (18.2)	-0.006
Unknown	6.8 (1.5)	11.0 (1.8)	0.004	13.5 (0.8)	43.0 (1.5)	0.007	22.8 (1.0)	54.0 (1.6)	0.006
AUDIT-C Score (%)									
0	280.2 (61.9)	369.0 (62.0)	0.001	1068.2 (65.2)	1767.0 (63.3)	-0.019	1413.4 (64.2)	2136.0 (63.0)	-0.012
1 – 3	94.0 (20.8)	132.0 (22.2)	0.014	389.1 (23.7)	674.0 (24.1)	0.004	501.8 (22.8)	806.0 (23.8)	0.010
4 – 7	29.7 (6.6)	34.0 (5.7)	-0.009	82.1 (5.0)	147.0 (5.3)	0.003	132.4 (6.0)	181.0 (5.3)	-0.007
8 +	11.9 (2.6)	15.0 (2.5)	-0.001	24.6 (1.5)	43.0 (1.5)	0.000	29.9 (1.4)	58.0 (1.7)	0.004
Unknown	36.9 (8.1)	45.0 (7.6)	-0.006	74.9 (4.6)	162.0 (5.8)	0.012	123.2 (5.6)	207.0 (6.1)	0.005
Comorbidities									
Myocardial Infarction (%)	30.4 (6.7)	36.0 (6.1)	-0.007	144.2 (8.8)	216.0 (7.7)	-0.011	183.4 (8.3)	252.0 (7.4)	-0.009
Congestive Heart Failure (%)	83.8 (18.5)	102.0 (17.1)	-0.014	381.8 (23.3)	534.0 (19.1)	-0.042	495.4 (22.5)	636.0 (18.8)	-0.037
Cerebrovascular Disease (%)	66.4 (14.7)	79.0 (13.3)	-0.014	271.0 (16.5)	418.0 (15.0)	-0.016	344.9 (15.7)	497.0 (14.7)	-0.010
Dementia (%)	47.8 (10.6)	59.0 (9.9)	-0.007	207.7 (12.7)	252.0 (9.0)	-0.036	268.3 (12.2)	311.0 (9.2)	-0.030
Chronic Obstructive Pulmonary Disease (%)	118.9 (26.3)	168.0 (28.2)	0.020	530.1 (32.3)	923.0 (33.0)	0.007	615.9 (28.0)	1091.0 (32.2)	0.042
Rheumatoid Arthritis (%)	5.8 (1.3)	9.0 (1.5)	0.002	40.0 (2.4)	49.0 (1.8)	-0.007	34.5 (1.6)	58.0 (1.7)	0.001
Peptic ulcer (%)	7.9 (1.7)	9.0 (1.5)	-0.002	27.8 (1.7)	55.0 (2.0)	0.003	39.2 (1.8)	64.0 (1.9)	0.001
Liver disease, mild (%)	53.6 (11.8)	66.0 (11.1)	-0.008	141.9 (8.7)	265.0 (9.5)	0.008	206.1 (9.4)	331.0 (9.8)	0.004
Diabetes, Uncomplicated (%)	207.8 (45.9)	278.0 (46.7)	0.008	806.5 (49.2)	1369.0 (49.0)	-0.002	1072.6 (48.7)	1647.0 (48.6)	-0.001
Diabetes, Complicated (%)	132.1 (29.2)	168.0 (28.2)	-0.010	530.6 (32.4)	819.0 (29.3)	-0.031	679.9 (30.9)	987.0 (29.1)	-0.018
Hemi or paraplegia (%)	11.4 (2.5)	10.0 (1.7)	-0.008	38.6 (2.4)	52.0 (1.9)	-0.005	50.5 (2.3)	62.0 (1.8)	-0.005
Liver disease, moderate-severe (%)	8.6 (1.9)	9.0 (1.5)	-0.004	14.1 (0.9)	32.0 (1.1)	0.003	28.4 (1.3)	41.0 (1.2)	-0.001
Metastatic cancer (%)	6.3 (1.4)	6.0 (1.0)	-0.004	18.3 (1.1)	46.0 (1.6)	0.005	49.9 (2.3)	52.0 (1.5)	-0.007
HIV (%)	7.4 (1.6)	10.0 (1.7)	0.000	26.9 (1.6)	20.0 (0.7)	-0.009	27.3 (1.2)	30.0 (0.9)	-0.004
Renal disease (%)	113.0 (25.0)	140.0 (23.5)	-0.014	456.8 (27.9)	656.0 (23.5)	-0.044	599.0 (27.2)	796.0 (23.5)	-0.037
Charlson Comorbidities Count (%)									
0	92.5 (20.4)	134.0 (22.5)	0.021	314.0 (19.2)	518.0 (18.5)	-0.006	426.0 (19.4)	652.0 (19.2)	-0.001
1 - 2	150.2 (33.2)	200.0 (33.6)	0.004	469.4 (28.6)	934.0 (33.4)	0.048	692.5 (31.5)	1134.0 (33.5)	0.020
3 - 4	106.0 (23.4)	131.0 (22.0)	-0.014	392.1 (23.9)	702.0 (25.1)	0.012	484.5 (22.0)	833.0 (24.6)	0.026
5 +	104.1 (23.0)	130.0 (21.8)	-0.011	463.4 (28.3)	639.0 (22.9)	-0.054	597.7 (27.2)	769.0 (22.7)	-0.045
Number of Doctors (prior year) (%)									
0	185.8 (41.1)	250.0 (42.0)	0.010	604.6 (36.9)	1075.0 (38.5)	0.016	842.3 (38.3)	1325.0 (39.1)	0.008
1	138.4 (30.6)	182.0 (30.6)	0.000	440.5 (26.9)	780.0 (27.9)	0.010	610.1 (27.7)	962.0 (28.4)	0.007
2 - 4	121.6 (26.9)	155.0 (26.1)	-0.008	549.1 (33.5)	879.0 (31.5)	-0.020	683.3 (31.0)	1034.0 (30.5)	-0.005
5 +	6.9 (1.5)	8.0 (1.3)	-0.002	44.7 (2.7)	59.0 (2.1)	-0.006	65.0 (3.0)	67.0 (2.0)	-0.010
Specialty clinics attended Cardiology **(%)**	109.1 (24.1)	147.0 (24.7)	0.006	461.5 (28.2)	759.0 (27.2)	-0.010	599.5 (27.2)	906.0 (26.7)	-0.005
Coagulation (%)	9.5 (2.1)	13.0 (2.2)	0.001	20.2 (1.2)	31.0 (1.1)	-0.001	30.0 (1.4)	44.0 (1.3)	-0.001
Pacemaker (%)	15.2 (3.4)	20.0 (3.4)	0.000	45.2 (2.8)	70.0 (2.5)	-0.002	81.6 (3.7)	90.0 (2.7)	-0.011
Dialysis (%)	3.9 (0.9)	5.0 (0.8)	0.000	38.2 (2.3)	33.0 (1.2)	-0.012	35.7 (1.6)	38.0 (1.1)	-0.005
Gastoenterology (%)	41.7 (9.2)	61.0 (10.3)	0.010	150.7 (9.2)	292.0 (10.5)	0.013	216.0 (9.8)	353.0 (10.4)	0.006
Hepatology (%)	9.7 (2.2)	10.0 (1.7)	-0.005	47.3 (2.9)	64.0 (2.3)	-0.006	59.2 (2.7)	74.0 (2.2)	-0.005
Homeless (%)	27.1 (6.0)	30.0 (5.0)	-0.009	70.7 (4.3)	93.0 (3.3)	-0.010	112.4 (5.1)	123.0 (3.6)	-0.015
Co-medications									

Characteristics	No Oxygen			Nasal Canula				Combined Cohort	
	No	Yes	SMD	No	No	Yes	SMD	Yes	No
Prophylactic Anticoagulants	248.2 (54.8)	332.0 (55.8)	0.010	983.7 (60.0)	1643.0 (58.8)	-0.012	1231.8 (56.0)	1975.0 (58.3)	0.023
Remdesivir, 1st 48 hours (%)	124.3 (27.5)	257.0 (43.2)	0.157	826.8 (50.4)	2001.0 (71.6)	0.212	1087.6 (49.4)	2258.0 (66.6)	0.172
Laboratory Results									
Albumin, g/dL (%)									
3.5 +	174.5 (38.6)	218.0 (36.6)	-0.019	498.7 (30.4)	781.0 (28.0)	-0.025	677.5 (30.8)	999.0 (29.5)	-0.013
3 - 3.49	151.9 (33.5)	203.0 (34.1)	0.006	551.1 (33.6)	1005.0 (36.0)	0.024	773.8 (35.2)	1208.0 (35.7)	0.005
< 3	107.9 (23.8)	151.0 (25.4)	0.015	537.1 (32.8)	928.0 (33.2)	0.005	680.4 (30.9)	1079.0 (31.8)	0.009
Missing	18.4 (4.1)	23.0 (3.9)	-0.002	51.9 (3.2)	79.0 (2.8)	-0.003	69.0 (3.1)	102.0 (3.0)	-0.001
Alanine aminotransferase, IU/L (%)									
< 20	129.5 (28.6)	148.0 (24.9)	-0.037	370.4 (22.6)	578.0 (20.7)	-0.019	540.9 (24.6)	726.0 (21.4)	-0.031
20 - 39	187.3 (41.4)	242.0 (40.7)	-0.007	737.3 (45.0)	1201.0 (43.0)	-0.020	936.1 (42.5)	1443.0 (42.6)	0.001
40 +	129.6 (28.6)	199.0 (33.4)	0.048	502.2 (30.6)	977.0 (35.0)	0.043	686.6 (31.2)	1176.0 (34.7)	0.035
Missing	6.3 (1.4)	6.0 (1.0)	-0.004	29.1 (1.8)	37.0 (1.3)	-0.004	37.1 (1.7)	43.0 (1.3)	-0.004
Asparate aminostransferase, IU/L (%)									
< 20	61.7 (13.6)	65.0 (10.9)	-0.027	139.2 (8.5)	218.0 (7.8)	-0.007	225.0 (10.2)	283.0 (8.4)	-0.019
20 - 39	218.0 (48.2)	279.0 (46.9)	-0.013	741.6 (45.3)	1218.0 (43.6)	-0.016	1025.4 (46.6)	1497.0 (44.2)	-0.024
40 +	172.9 (38.2)	251.0 (42.2)	0.040	758.1 (46.3)	1357.0 (48.6)	0.023	950.4 (43.2)	1608.0 (47.5)	0.043
Creatinine, mg/dL (%)									
< 1.2	206.5 (45.6)	277.0 (46.6)	0.009	700.3 (42.7)	1324.0 (47.4)	0.047	965.0 (43.9)	1601.0 (47.3)	0.034
1.2 – 1.99	179.4 (39.6)	244.0 (41.0)	0.014	632.4 (38.6)	1048.0 (37.5)	-0.011	861.5 (39.1)	1292.0 (38.1)	-0.010
2 +	66.8 (14.8)	74.0 (12.4)	-0.023	306.2 (18.7)	421.0 (15.1)	-0.036	374.1 (17.0)	495.0 (14.6)	-0.024
Missing	0.0 (0.0)	0.0 (0.0)	0.000	0.0 (0.0)	0.0 (0.0)		0.0 (0.0)	0.0 (0.0)	
Fibrosis-4 Index (%)									
< 1.45	96.4 (21.3)	129.0 (21.7)	0.004	197.6 (12.1)	411.0 (14.7)	0.027	335.2 (15.2)	540.0 (15.9)	0.007
1.45 – 3.25	178.7 (39.5)	239.0 (40.2)	0.007	692.4 (42.2)	1260.0 (45.1)	0.029	878.7 (39.9)	1499.0 (44.2)	0.043
3.25 +	171.1 (37.8)	220.0 (37.0)	-0.008	718.1 (43.8)	1081.0 (38.7)	-0.051	948.1 (43.1)	1301.0 (38.4)	-0.047
Missing	6.6 (1.5)	7.0 (1.2)	-0.003	30.8 (1.9)	41.0 (1.5)	-0.004	38.7 (1.8)	48.0 (1.4)	-0.003
Lactate, mmol/L (%)									
1_1.2	86.8 (19.2)	118.0 (19.8)	0.007	292.2 (17.8)	496.0 (17.8)	-0.001	376.5 (17.1)	614.0 (18.1)	0.010
2_1.2LT2	121.9 (26.9)	172.0 (28.9)	0.020	476.3 (29.1)	930.0 (33.3)	0.042	667.0 (30.3)	1102.0 (32.5)	0.022
3_GE2	64.8 (14.3)	96.0 (16.1)	0.018	239.8 (14.6)	413.0 (14.8)	0.002	327.2 (14.9)	509.0 (15.0)	0.002
Missing	179.2 (39.6)	209.0 (35.1)	-0.044	630.7 (38.5)	954.0 (34.2)	-0.043	830.0 (37.7)	1163.0 (34.3)	-0.034
Platelet count per microL (%)									
150 or higher	302.6 (66.8)	401.0 (67.4)	0.006	1046.9 (63.9)	1893.0 (67.8)	0.039	1391.4 (63.2)	2294.0 (67.7)	0.045
< 150	150.1 (33.2)	194.0 (32.6)	-0.006	590.1 (36.0)	897.0 (32.1)	-0.039	807.6 (36.7)	1091.0 (32.2)	-0.045
Missing	0.0 (0.0)	0.0 (0.0)	0.000	1.9 (0.1)	3.0 (0.1)	0.000	1.6 (0.1)	3.0 (0.1)	0.000
Total bilirubin, mg/dL (%)									
< 1	347.4 (76.7)	456.0 (76.6)	-0.001	1272.7 (77.7)	2089.0 (74.8)	-0.029	1653.3 (75.1)	2545.0 (75.1)	0.000
1 - 1.2	36.7 (8.1)	49.0 (8.2)	0.001	136.0 (8.3)	278.0 (10.0)	0.017	203.9 (9.3)	327.0 (9.7)	0.004
1.2 +	64.2 (14.2)	86.0 (14.5)	0.003	202.5 (12.4)	393.0 (14.1)	0.017	311.5 (14.2)	479.0 (14.1)	0.000
Missing	4.4 (1.0)	4.0 (0.7)	-0.003	27.7 (1.7)	33.0 (1.2)	-0.005	32.1 (1.5)	37.0 (1.1)	-0.004

Characteristics	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	No	Yes	SMD	Yes	No
White Blood Count per microL (%)									
4-10	228.8 (50.5)	274.0 (46.1)	-0.045	835.1 (51.0)	1261.0 (45.1)	-0.058	1089.7 (49.5)	1535.0 (45.3)	-0.042
<4	136.0 (30.0)	202.0 (33.9)	0.039	508.8 (31.0)	821.0 (29.4)	-0.016	692.9 (31.5)	1023.0 (30.2)	-0.013
>10	87.9 (19.4)	119.0 (20.0)	0.006	295.1 (18.0)	711.0 (25.5)	0.075	418.1 (19.0)	830.0 (24.5)	0.055
C-reactive protein measured (%)	313.0 (69.1)	415.0 (69.7)	0.006	1016.3 (62.0)	1828.0 (65.4)	0.034	1404.8 (63.8)	2243.0 (66.2)	0.024
D-dimer measured (%)	365.9 (80.8)	486.0 (81.7)	0.009	1366.2 (83.4)	2354.0 (84.3)	0.009	1817.9 (82.6)	2840.0 (83.8)	0.012
Vital Signs									
Highest Temperature (F) (%)									
< 99	156.4 (34.6)	198.0 (33.3)	-0.013	416.6 (25.4)	816.0 (29.2)	0.038	633.9 (28.8)	1014.0 (29.9)	0.011
99 - 100	114.2 (25.2)	140.0 (23.5)	-0.017	325.2 (19.8)	644.0 (23.1)	0.032	491.0 (22.3)	784.0 (23.1)	0.008
100 - 102	126.3 (27.9)	183.0 (30.8)	0.029	562.0 (34.3)	878.0 (31.4)	-0.029	695.5 (31.6)	1061.0 (31.3)	-0.003
102 +	52.9 (11.7)	71.0 (11.9)	0.002	327.2 (20.0)	438.0 (15.7)	-0.043	368.4 (16.7)	509.0 (15.0)	-0.017
Missing	2.8 (0.6)	3.0 (0.5)	-0.001	7.9 (0.5)	17.0 (0.6)	0.001	11.9 (0.5)	20.0 (0.6)	0.001
Mean Arterial Pressure, mmHg (%)									
< 60	9.8 (2.2)	9.0 (1.5)	-0.006	24.9 (1.5)	46.0 (1.6)	0.001	44.0 (2.0)	55.0 (1.6)	-0.004
60 – 69	50.0 (11.1)	51.0 (8.6)	-0.025	245.4 (15.0)	341.0 (12.2)	-0.028	289.4 (13.2)	392.0 (11.6)	-0.016
70 – 89	300.5 (66.4)	401.0 (67.4)	0.010	1106.5 (67.5)	1906.0 (68.2)	0.007	1477.4 (67.1)	2307.0 (68.1)	0.010
90 +	91.8 (20.3)	133.0 (22.4)	0.021	254.6 (15.5)	486.0 (17.4)	0.019	386.6 (17.6)	619.0 (18.3)	0.007
Missing	0.6 (0.1)	1.0 (0.2)	0.000	7.5 (0.5)	14.0 (0.5)	0.000	3.3 (0.1)	15.0 (0.4)	0.003
Lowest Oxygen Saturation (%)									
< 88	6.7 (1.5)	11.0 (1.8)	0.004	175.8 (10.7)	338.0 (12.1)	0.014	179.7 (8.2)	349.0 (10.3)	0.021
88 - 92	170.9 (37.7)	263.0 (44.2)	0.065	950.6 (58.0)	1686.0 (60.4)	0.024	1157.8 (52.6)	1949.0 (57.5)	0.049
93 - 95	202.5 (44.7)	238.0 (40.0)	-0.047	419.4 (25.6)	580.0 (20.8)	-0.048	674.2 (30.6)	818.0 (24.1)	-0.065
96 +	59.1 (13.1)	70.0 (11.8)	-0.013	65.2 (4.0)	119.0 (4.3)	0.003	148.4 (6.7)	189.0 (5.6)	-0.012
Missing	13.6 (3.0)	13.0 (2.2)	-0.008	28.0 (1.7)	70.0 (2.5)	0.008	40.6 (1.8)	83.0 (2.4)	0.006

Unweighted Population

Corticosteroids	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
Cohort, n	2421	595		988	2793		3409	3388	
Age, (%)									
<50	273 (11.3)	59 (9.9)	-0.014	70 (7.1)	261 (9.3)	0.023	343 (10.1)	320 (9.4)	-0.006
50-59	296 (12.2)	90 (15.1)	0.029	125 (12.7)	344 (12.3)	-0.003	421 (12.3)	434 (12.8)	0.005
60-69	551 (22.8)	138 (23.2)	0.004	222 (22.5)	647 (23.2)	0.007	773 (22.7)	785 (23.2)	0.005
70-79	772 (31.9)	195 (32.8)	0.009	341 (34.5)	1048 (37.5)	0.030	1113 (32.6)	1243 (36.7)	0.040
80+	529 (21.9)	113 (19.0)	-0.029	230 (23.3)	493 (17.7)	-0.056	759 (22.3)	606 (17.9)	-0.044
Sex: Male, (%)	2287 (94.5)	562 (94.5)	0.000	931 (94.2)	2644 (94.7)	0.004	3218 (94.4)	3206 (94.6)	0.002
Race, (%)									
White, non-Hispanic	1240 (51.2)	321 (53.9)	0.027	526 (53.2)	1589 (56.9)	0.037	1766 (51.8)	1910 (56.4)	0.046
Black, non-Hispanic	765 (31.6)	159 (26.7)	-0.049	299 (30.3)	678 (24.3)	-0.060	1064 (31.2)	837 (24.7)	-0.065
Hispanic	213 (8.8)	61 (10.3)	0.015	78 (7.9)	290 (10.4)	0.025	291 (8.5)	351 (10.4)	0.018
Other	123 (5.1)	28 (4.7)	-0.004	55 (5.6)	152 (5.4)	-0.001	178 (5.2)	180 (5.3)	0.001
Unknown	80 (3.3)	26 (4.4)	0.011	30 (3.0)	84 (3.0)	0.000	110 (3.2)	110 (3.2)	0.000
Phase (Admission Date) , (%)									
1: June 7 - July 11	430 (17.8)	51 (8.6)	-0.092	289 (29.3)	270 (9.7)	-0.196	719 (21.1)	321 (9.5)	-0.116
2: July 12 - Aug. 15	456 (18.8)	79 (13.3)	-0.056	201 (20.3)	490 (17.5)	-0.028	657 (19.3)	569 (16.8)	-0.025
3: Aug. 16 - Oct. 17	525 (21.7)	139 (23.4)	0.017	201 (20.3)	587 (21.0)	0.007	726 (21.3)	726 (21.4)	0.001
4: Oct. 18 - Dec. 5	1010 (41.7)	326 (54.8)	0.131	297 (30.1)	1446 (51.8)	0.217	1307 (38.3)	1772 (52.3)	0.140
Site Dexamethasone Prescribing, (%)									
Low	690 (28.5)	84 (14.1)	-0.144	295 (29.9)	421 (15.1)	-0.148	985 (28.9)	505 (14.9)	-0.140
Medium	1473 (60.8)	358 (60.2)	-0.007	572 (57.9)	1665 (59.6)	0.017	2045 (60.0)	2023 (59.7)	-0.003
High	258 (10.7)	153 (25.7)	0.151	121 (12.2)	707 (25.3)	0.131	379 (11.1)	860 (25.4)	0.143
Smoking Status, (%)									
Never Smoked	842 (34.8)	203 (34.1)	-0.007	337 (34.1)	939 (33.6)	-0.005	1179 (34.6)	1142 (33.7)	-0.009
Former Smoker	908 (37.5)	269 (45.2)	0.077	411 (41.6)	1305 (46.7)	0.051	1319 (38.7)	1574 (46.5)	0.078
Current Smoker	626 (25.9)	112 (18.8)	-0.070	211 (21.4)	506 (18.1)	-0.032	837 (24.6)	618 (18.2)	-0.063
Unknown	45 (1.9)	11 (1.8)	0.000	29 (2.9)	43 (1.5)	-0.014	74 (2.2)	54 (1.6)	-0.006
AUDIT-C Score (%)									
0	1489 (61.5)	369 (62.0)	0.005	645 (65.3)	1767 (63.3)	-0.020	2134 (62.6)	2136 (63.0)	0.004
1 – 3	481 (19.9)	132 (22.2)	0.023	204 (20.6)	674 (24.1)	0.035	685 (20.1)	806 (23.8)	0.037
4 – 7	167 (6.9)	34 (5.7)	-0.012	39 (3.9)	147 (5.3)	0.013	206 (6.0)	181 (5.3)	-0.007
8 +	81 (3.3)	15 (2.5)	-0.008	20 (2.0)	43 (1.5)	-0.005	101 (3.0)	58 (1.7)	-0.013
Unknown	203 (8.4)	45 (7.6)	-0.008	80 (8.1)	162 (5.8)	-0.023	283 (8.3)	207 (6.1)	-0.022
Comorbidities									
Myocardial Infarction (%)	208 (8.6)	36 (6.1)	-0.025	89 (9.0)	216 (7.7)	-0.013	297 (8.7)	252 (7.4)	-0.013
Congestive Heart Failure (%)	468 (19.3)	102 (17.1)	-0.022	271 (27.4)	534 (19.1)	-0.083	739 (21.7)	636 (18.8)	-0.029
Cerebrovascular Disease (%)	461 (19.0)	79 (13.3)	-0.058	188 (19.0)	418 (15.0)	-0.041	649 (19.0)	497 (14.7)	-0.044
Dementia (%)	467 (19.3)	59 (9.9)	-0.094	172 (17.4)	252 (9.0)	-0.084	639 (18.7)	311 (9.2)	-0.096
Chronic Obstructive Pulmonary Disease (%)	546 (22.6)	168 (28.2)	0.057	306 (31.0)	923 (33.0)	0.021	852 (25.0)	1091 (32.2)	0.072
Rheumatoid Arthritis (%)	34 (1.4)	9 (1.5)	0.001	14 (1.4)	49 (1.8)	0.003	48 (1.4)	58 (1.7)	0.003

Corticosteroids	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
Peptic ulcer (%)	72 (3.0)	9 (1.5)	-0.015	25 (2.5)	55 (2.0)	-0.006	97 (2.8)	64 (1.9)	-0.010
Liver disease, mild (%)	335 (13.8)	66 (11.1)	-0.027	100 (10.1)	265 (9.5)	-0.006	435 (12.8)	331 (9.8)	-0.030
Diabetes, Uncomplicated (%)	1054 (43.5)	278 (46.7)	0.032	474 (48.0)	1369 (49.0)	0.010	1528 (44.8)	1647 (48.6)	0.038
Diabetes, Complicated (%)	704 (29.1)	168 (28.2)	-0.008	318 (32.2)	819 (29.3)	-0.029	1022 (30.0)	987 (29.1)	-0.008
Hemi or paraplegia (%)	84 (3.5)	10 (1.7)	-0.018	36 (3.6)	52 (1.9)	-0.018	120 (3.5)	62 (1.8)	-0.017
Liver disease, moderate-severe (%)	56 (2.3)	9 (1.5)	-0.008	13 (1.3)	32 (1.1)	-0.002	69 (2.0)	41 (1.2)	-0.008
Metastatic cancer (%)	56 (2.3)	6 (1.0)	-0.013	16 (1.6)	46 (1.6)	0.000	72 (2.1)	52 (1.5)	-0.006
HIV (%)	32 (1.3)	10 (1.7)	0.004	13 (1.3)	20 (0.7)	-0.006	45 (1.3)	30 (0.9)	-0.004
Renal disease (%)	610 (25.2)	140 (23.5)	-0.017	284 (28.7)	656 (23.5)	-0.053	894 (26.2)	796 (23.5)	-0.027
Charlson Comorbidities Count (%)									
0	499 (20.6)	134 (22.5)	0.019	179 (18.1)	518 (18.5)	0.004	678 (19.9)	652 (19.2)	-0.006
1 - 2	737 (30.4)	200 (33.6)	0.032	278 (28.1)	934 (33.4)	0.053	1015 (29.8)	1134 (33.5)	0.037
3 - 4	529 (21.9)	131 (22.0)	0.002	235 (23.8)	702 (25.1)	0.013	764 (22.4)	833 (24.6)	0.022
5 +	656 (27.1)	130 (21.8)	-0.052	296 (30.0)	639 (22.9)	-0.071	952 (27.9)	769 (22.7)	-0.052
Number of Doctors (prior year) (%)									
0	1057 (43.7)	250 (42.0)	-0.016	395 (40.0)	1075 (38.5)	-0.015	1452 (42.6)	1325 (39.1)	-0.035
1	653 (27.0)	182 (30.6)	0.036	246 (24.9)	780 (27.9)	0.030	899 (26.4)	962 (28.4)	0.020
2 - 4	645 (26.6)	155 (26.1)	-0.006	316 (32.0)	879 (31.5)	-0.005	961 (28.2)	1034 (30.5)	0.023
5 +	66 (2.7)	8 (1.3)	-0.014	31 (3.1)	59 (2.1)	-0.010	97 (2.8)	67 (2.0)	-0.009
Specialty clinics attended Cardiology **(%)**	580 (24.0)	147 (24.7)	0.007	296 (30.0)	759 (27.2)	-0.028	876 (25.7)	906 (26.7)	0.010
Coagulation (%)	38 (1.6)	13 (2.2)	0.006	21 (2.1)	31 (1.1)	-0.010	59 (1.7)	44 (1.3)	-0.004
Pacemaker (%)	93 (3.8)	20 (3.4)	-0.005	48 (4.9)	70 (2.5)	-0.024	141 (4.1)	90 (2.7)	-0.015
Dialysis (%)	32 (1.3)	5 (0.8)	-0.005	32 (3.2)	33 (1.2)	-0.021	64 (1.9)	38 (1.1)	-0.008
Gastoenterology (%)	203 (8.4)	61 (10.3)	0.019	86 (8.7)	292 (10.5)	0.018	289 (8.5)	353 (10.4)	0.019
Hepatology (%)	97 (4.0)	10 (1.7)	-0.023	30 (3.0)	64 (2.3)	-0.007	127 (3.7)	74 (2.2)	-0.015
Homeless (%)	199 (8.2)	30 (5.0)	-0.032	58 (5.9)	93 (3.3)	-0.025	257 (7.5)	123 (3.6)	-0.039
Prophylactic Anticoagulants	1267 (52.3)	332 (55.8)	0.035	523 (52.9)	1643 (58.8)	0.059	1790 (52.5)	1975 (58.3)	0.058
Co-medications									
Remdesivir, 1st 48 hours (%)	174 (7.2)	257 (43.2)	0.360	211 (21.4)	2001 (71.6)	0.503	385 (11.3)	2258 (66.6)	0.554
Laboratory Results									
Albumin, g/dL (%)									
3.5 +	1050 (43.4)	218 (36.6)	-0.067	305 (30.9)	781 (28.0)	-0.029	1355 (39.7)	999 (29.5)	-0.103
3 - 3.49	719 (29.7)	203 (34.1)	0.044	344 (34.8)	1005 (36.0)	0.012	1063 (31.2)	1208 (35.7)	0.045
< 3	478 (19.7)	151 (25.4)	0.056	285 (28.8)	928 (33.2)	0.044	763 (22.4)	1079 (31.8)	0.095
Missing	174 (7.2)	23 (3.9)	-0.033	54 (5.5)	79 (2.8)	-0.026	228 (6.7)	102 (3.0)	-0.037
Alanine aminotransferase, IU/L (%)									
< 20	784 (32.4)	148 (24.9)	-0.075	290 (29.4)	578 (20.7)	-0.087	1074 (31.5)	726 (21.4)	-0.101
20 - 39	938 (38.7)	242 (40.7)	0.019	418 (42.3)	1201 (43.0)	0.007	1356 (39.8)	1443 (42.6)	0.028
40 +	533 (22.0)	199 (33.4)	0.114	227 (23.0)	977 (35.0)	0.120	760 (22.3)	1176 (34.7)	0.124
Missing	166 (6.9)	6 (1.0)	-0.058	53 (5.4)	37 (1.3)	-0.040	219 (6.4)	43 (1.3)	-0.052
Asparate aminostransferase, IU/L (%)									
< 20	654 (27.0)	65 (10.9)	-0.161	199 (20.1)	218 (7.8)	-0.123	853 (25.0)	283 (8.4)	-0.167
20 - 39	1098 (45.4)	279 (46.9)	0.015	444 (44.9)	1218 (43.6)	-0.013	1542 (45.2)	1497 (44.2)	-0.010

Corticosteroids	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
40 +	669 (27.6)	251 (42.2)	0.146	345 (34.9)	1357 (48.6)	0.137	1014 (29.7)	1608 (47.5)	0.177
Creatinine, mg/dL (%)									
< 1.2	1223 (50.5)	277 (46.6)	-0.040	423 (42.8)	1324 (47.4)	0.046	1646 (48.3)	1601 (47.3)	-0.010
1.2 – 1.99	797 (32.9)	244 (41.0)	0.081	374 (37.9)	1048 (37.5)	-0.003	1171 (34.4)	1292 (38.1)	0.038
2 +	360 (14.9)	74 (12.4)	-0.024	186 (18.8)	421 (15.1)	-0.038	546 (16.0)	495 (14.6)	-0.014
Missing	41 (1.7)	0 (0.0)	-0.017	5 (0.5)	0 (0.0)	-0.005	46 (1.3)	0 (0.0)	-0.013
Fibrosis-4 Index (%)									
< 1.45	550 (22.7)	129 (21.7)	-0.010	162 (16.4)	411 (14.7)	-0.017	712 (20.9)	540 (15.9)	-0.049
1.45 – 3.25	994 (41.1)	239 (40.2)	-0.009	394 (39.9)	1260 (45.1)	0.052	1388 (40.7)	1499 (44.2)	0.035
3.25 +	697 (28.8)	220 (37.0)	0.082	377 (38.2)	1081 (38.7)	0.005	1074 (31.5)	1301 (38.4)	0.069
Missing	180 (7.4)	7 (1.2)	-0.063	55 (5.6)	41 (1.5)	-0.041	235 (6.9)	48 (1.4)	-0.055
Lactate, mmol/L (%)									
1_1.2	361 (14.9)	118 (19.8)	0.049	172 (17.4)	496 (17.8)	0.003	533 (15.6)	614 (18.1)	0.025
2_1.2LT2	514 (21.2)	172 (28.9)	0.077	254 (25.7)	930 (33.3)	0.076	768 (22.5)	1102 (32.5)	0.100
3_GE2	250 (10.3)	96 (16.1)	0.058	151 (15.3)	413 (14.8)	-0.005	401 (11.8)	509 (15.0)	0.033
Missing	1296 (53.5)	209 (35.1)	-0.184	411 (41.6)	954 (34.2)	-0.074	1707 (50.1)	1163 (34.3)	-0.157
Platelet count per microL (%)									
150 or higher	1631 (67.4)	401 (67.4)	0.000	613 (62.0)	1893 (67.8)	0.057	2244 (65.8)	2294 (67.7)	0.019
< 150	744 (30.7)	194 (32.6)	0.019	371 (37.6)	897 (32.1)	-0.054	1115 (32.7)	1091 (32.2)	-0.005
Missing	46 (1.9)	0 (0.0)	-0.019	4 (0.4)	3 (0.1)	-0.003	50 (1.5)	3 (0.1)	-0.014
Total bilirubin, mg/dL (%)									
< 1	1799 (74.3)	456 (76.6)	0.023	734 (74.3)	2089 (74.8)	0.005	2533 (74.3)	2545 (75.1)	0.008
1 - 1.2	182 (7.5)	49 (8.2)	0.007	94 (9.5)	278 (10.0)	0.004	276 (8.1)	327 (9.7)	0.016
1.2 +	290 (12.0)	86 (14.5)	0.025	111 (11.2)	393 (14.1)	0.028	401 (11.8)	479 (14.1)	0.024
Missing	150 (6.2)	4 (0.7)	-0.055	49 (5.0)	33 (1.2)	-0.038	199 (5.8)	37 (1.1)	-0.047
White Blood Count per microL (%)									
4-10	1494 (61.7)	274 (46.1)	-0.157	564 (57.1)	1261 (45.1)	-0.119	2058 (60.4)	1535 (45.3)	-0.151
<4	606 (25.0)	202 (33.9)	0.089	269 (27.2)	821 (29.4)	0.022	875 (25.7)	1023 (30.2)	0.045
>10	321 (13.3)	119 (20.0)	0.067	155 (15.7)	711 (25.5)	0.098	476 (14.0)	830 (24.5)	0.105
C-reactive protein measured (%)	1281 (52.9)	415 (69.7)	0.168	563 (57.0)	1828 (65.4)	0.085	1844 (54.1)	2243 (66.2)	0.121
D-dimer measured (%)	1712 (70.7)	486 (81.7)	0.110	775 (78.4)	2354 (84.3)	0.058	2487 (73.0)	2840 (83.8)	0.109
Viral Signs									
Highest Temperature (F) (%)									
< 99	1051 (43.4)	198 (33.3)	-0.101	279 (28.2)	816 (29.2)	0.010	1330 (39.0)	1014 (29.9)	-0.091
99 - 100	606 (25.0)	140 (23.5)	-0.015	230 (23.3)	644 (23.1)	-0.002	836 (24.5)	784 (23.1)	-0.014
100 - 102	537 (22.2)	183 (30.8)	0.086	319 (32.3)	878 (31.4)	-0.009	856 (25.1)	1061 (31.3)	0.062
102 +	220 (9.1)	71 (11.9)	0.028	158 (16.0)	438 (15.7)	-0.003	378 (11.1)	509 (15.0)	0.039
Missing	7 (0.3)	3 (0.5)	0.002	2 (0.2)	17 (0.6)	0.004	9 (0.3)	20 (0.6)	0.003
Mean Arterial Pressure, mmHg (%)									
< 60	63 (2.6)	9 (1.5)	-0.011	37 (3.7)	46 (1.6)	-0.021	100 (2.9)	55 (1.6)	-0.013
60 – 69	322 (13.3)	51 (8.6)	-0.047	148 (15.0)	341 (12.2)	-0.028	470 (13.8)	392 (11.6)	-0.022
70 – 89	1575 (65.1)	401 (67.4)	0.023	643 (65.1)	1906 (68.2)	0.032	2218 (65.1)	2307 (68.1)	0.030
90 +	455 (18.8)	133 (22.4)	0.036	159 (16.1)	486 (17.4)	0.013	614 (18.0)	619 (18.3)	0.003

Corticosteroids	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
Missing	6 (0.2)	1 (0.2)	-0.001	1 (0.1)	14 (0.5)	0.004	7 (0.2)	15 (0.4)	0.002
Lowest Oxygen Saturation (%)									
< 88	30 (1.2)	11 (1.8)	0.006	78 (7.9)	338 (12.1)	0.042	108 (3.2)	349 (10.3)	0.071
88 - 92	630 (26.0)	263 (44.2)	0.182	489 (49.5)	1686 (60.4)	0.109	1119 (32.8)	1949 (57.5)	0.247
93 - 95	1198 (49.5)	238 (40.0)	-0.095	311 (31.5)	580 (20.8)	-0.107	1509 (44.3)	818 (24.1)	-0.201
96 +	508 (21.0)	70 (11.8)	-0.092	92 (9.3)	119 (4.3)	-0.051	600 (17.6)	189 (5.6)	-0.120
Missing	55 (2.3)	13 (2.2)	-0.001	18 (1.8)	70 (2.5)	0.007	73 (2.1)	83 (2.4)	0.003

Supplemental Table 2. Sensitivity analyses estimating the average treatment effect in the treated population (ATT) in weighted Cox proportional hazards models for the association of corticosteroids with all-cause 90-day mortality among those not on IRS

	No oxygen supplementation	Nasal cannula	Combined group: no oxygen plus NC
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**
Primary analysis	1.77 (1.25-2.50)	1.26 (0.92-1.74)	1.60 (1.24-2.08)
Subgroup analyses			
Restricted to dexamethasone	1.55 (0.95-2.52)	1.28 (0.84-1.94)	1.49 (1.02-2.18)
Excluding patients admitted to ICU in initial 48 hours	1.62 (1.05-2.49)	1.33 (0.88-1.99)	1.60 (1.15-2.24)
Restricted to patients age 70 and older	1.69 (1.13-2.54)	1.49 (0.99-2.24)	1.72 (1.24-2.40)

Models present the ATT (average treatment effect in treated population).
CI = confidence interval
HR = hazard ratio
IRS = intensive respiratory support

Supplemental Table 3. Sensitivity analyses with unweighted, multivariable Cox proportional hazards regression models for the association of corticosteroids with all-cause 90-day mortality

	No oxygen supplementation	Nasal cannula	Combined group: no oxygen plus NC
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**
Primary analysis	1.87 (1.36-2.57)	1.39 (1.10-1.76)	1.66 (1.39-1.99)
Subgroup analyses			
Restricted to dexamethasone	1.87 (1.32-2.66)	1.37 (1.08-1.74)	1.66 (1.38-1.99)
Excluding patients admitted to ICU in initial 48 hours	1.85 (1.31-2.62)	1.31 (1.01-1.69)	1.63 (1.34-1.98)
Restricted to patients age 70 and older	2.02 (1.40-2.89)	1.41 (1.09-1.82)	1.66 (1.36-2.02)

CI = confidence interval
HR = hazard ratio
IRS = intensive respiratory support

Supplemental Table 4. STROBE Checklist of items for cohort studies

	Item No	Recommendation	Section/Paragraph
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Abstract: Methods
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract: Methods, Findings, Interpretation
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Introduction: Paragraphs 1-2
Objectives	3	State specific objectives, including any prespecified hypotheses	Introduction: Paragraph 3
Methods			
Study design	4	Present key elements of study design early in the paper	Methods: Paragraph 1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods: Paragraph 1
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Methods: Paragraphs 1-2
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A

Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Methods: Paragraphs 3-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Methods: Paragraphs 3-6
Bias	9	Describe any efforts to address potential sources of bias	Methods: Paragraphs 7-8
Study size	10	Explain how the study size was arrived at	All hospitalized COVID+ patients with at least 48h stay, concatenating length of stay to include emergency department/ observational status
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Methods: paragraphs 4, 6, Table 2, Supplemental Table 1
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Methods: paragraphs 7, 8
		(*b*) Describe any methods used to examine subgroups and interactions	Methods: paragraph 9

		(*c*) Explain how missing data were addressed	Methods: paragraph 8, Table 2, Supplemental Table 1
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	Methods: paragraph 9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Methods: paragraph 1-2 Results: paragraph 1 Figure 1
		(b) Give reasons for non-participation at each stage	Methods: paragraph 2 Figure 1
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Results: paragraphs 1-2 Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 2, Supplemental Table 1
		(c) Summarise follow-up time (eg, average and total amount)	Figure 2

Outcome data	15*	Report numbers of outcome events or summary measures over time	Results: paragraph 2 Table 1, Figure 2, Figure 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Results: paragraph 2 Results: paragraphs 4, 5 Table 3
		(*b*) Report category boundaries when continuous variables were categorized	Table 2 and Supplemental Table 1
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Results: paragraph 6
Discussion			
Key results	18	Summarise key results with reference to study objectives	Discussion: paragraph 1-2
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Discussion: paragraph 7

Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion: paragraphs 1, 2, 3, 5, 6
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussion: paragraph 3, 4, 5, 6
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Metadata

*Give information separately for exposed and unexposed groups.