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Early View

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Dexamethasone in hospitalised coronavirus-19 patients not on intensive respiratory support

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Title: Dexamethasone in hospitalized coronavirus-19 patients not on intensive respiratory support

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Take Home Message

Although commonly used, dexamethasone within 48 hours of admission was associated with increased 90-day mortality in patients hospitalized with COVID-19 not on oxygen, and with no mortality benefit in patients on low-flow nasal cannula.

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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*.

Contributions: KC, JT, MG, BJ, VM, MEO, CTR, MRB, ACJ and KMA conceived (formulated or helped in the evolution) of the study. JT, RD, PRA and CTR curated the data. RD and JT performed the formal analysis. KC, PRA, ACJ and KMA acquired funding. KC, RD, JT, PRA, MEO, CTR, ACJ, and KMA designed the methodology. RD, JT, and SS managed and coordinated the project. KC, JT, PRA, BJ, and KMA contributed to validation. KC, RD, JT, and KMA wrote the first draft of the manuscript. All authors fulfill ICJME criteria for authorship; all authors participated in interpretation of the data; in critically revising the manuscript for important intellectual content; and approved the final version to be published. All authors agree to be accountable for the work and ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. KC and KMA are joint

principal investigators. KC, RD, JT, and KMA are guarantors. The corresponding author attests that all listed authors meet authorship criteria. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

ABSTRACT

Introduction: Dexamethasone decreases mortality in coronavirus disease 2019 (COVID-19) patients on intensive respiratory support (IRS) but is of uncertain benefit if less severely ill. We determined whether early (within 48 hours) dexamethasone was associated with mortality in patients hospitalized with COVID-19 not on IRS.

Methods: We included patients admitted to Veterans Affairs hospitals between June 7, 2020-May 31, 2021 within 14-days after SARS-CoV-2 positive test. Exclusions included recent prior corticosteroids and IRS within 48 hours. We used inverse probability of treatment weights (IPTW) to balance exposed and unexposed groups, and Cox proportional hazards models to determine 90-day all-cause mortality.

Results: Of 19,973 total patients (95% men, median age 71, 27% black), 15,404 (77%) were without IRS within 48 hours. Of these, 3,514/9,450 (34%) patients on no oxygen received dexamethasone and 1,042 (11%) died; 4,472/5,954 (75%) patients on low-flow nasal cannula (NC) received dexamethasone and 857 (14%) died. In IPTW stratified models, patients on no oxygen who received dexamethasone experienced 76% increased risk for 90-day mortality (hazard ratio [HR] 1.76, 95% confidence interval [CI] 1.47 to 2.12); there was no association with mortality among patients on NC (HR 1.08, 95% CI 0.86 to 1.36).

Conclusion: In patients hospitalized with COVID-19, early initiation of dexamethasone was common and was associated with no mortality benefit among those on no oxygen or NC in the first 48 hours; instead, we found evidence of potential harm. These real-world findings do not support the use of early dexamethasone in hospitalized COVID-19 patients without IRS.

INTRODUCTION

Corticosteroids have emerged as an effective therapy for critically ill patients with COVID-19. The large United Kingdom RECOVERY trial RCT of corticosteroids in COVID-19 patients demonstrated an overall 2.8% absolute decrease in mortality for patients treated with dexamethasone compared to usual care.[1] When stratified by respiratory support at randomization, dexamethasone was associated with greater benefit amongst those on invasive mechanical ventilation (IMV) versus supplemental oxygen (inclusive of non-invasive mechanical ventilation [NIV]); dexamethasone was not significantly associated with mortality in those not on oxygen. Dissemination of these and other results led to rapid uptake in use of corticosteroids for COVID-19 patients, particularly those receiving more intensive respiratory support (IRS) such as high-flow nasal cannula (HFNC), NIV and IMV.[2-6]

However, whether corticosteroids are beneficial in all patients with COVID-19 remains uncertain. The association between corticosteroids and outcomes among a wider group of patients with COVID-19 – including a larger proportion without IRS than in the RECOVERY trial – has been mixed.[7-11] Variability in the effect of corticosteroids may be due to numerous factors. A recent Cochrane review concluded that systemic corticosteroids "probably reduce all-cause mortality slightly" but that there is an "urgent need for good-quality evidence for specific subgroups of disease severity, for which we propose level of respiratory support at randomization."[12]

We determined the association between corticosteroids and 90-day all-cause mortality using real-world clinical data from the Department of Veterans Affairs (VA), the largest integrated

healthcare system in the United States. In a 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, mainly dexamethasone, we focused on those who were without IRS. We used propensity score weighting to account for confounding by indication. We hypothesized that dexamethasone would not be associated with mortality benefit in patients without IRS.

METHODS

Study Design and Population

We conducted an observational cohort study of 27,168 patients 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 May 31, 2021 (to allow 90-day follow-up on all).[13, 14] Before June 7 corticosteroids were mostly initiated after 48 hours. Index date was defined as date of presentation, including emergency room and time under observation status if not admitted directly. We determined length of stay by concatenating episodes of care separated by <24 hours, with first episode on the index date as day one. Due to changes in COVID-19 incidence and treatment protocols over time, we divided the observation period into seven time phases (Table 1). Additional methodological details are in the online Supplement.

Exclusions: Of 27,168 patients, we excluded 7,195, yielding a cohort of 19,973 patients (Figure 1 and Supplement). The most common exclusion was length of stay less than 48-hours as these patients had insufficient time to receive dexamethasone, followed by any systemic corticosteroid exposure prior to index date. This was defined as any corticosteroids within 14 days, or receipt of

corticosteroids for ≥14 days in the preceding 45 days. For mortality analyses, we further excluded 454 patients because they were at sites where no or all patients received dexamethasone (n=277), received hydroxychloroquine (n=89), or received vasopressors in the first 48 hours (n=90), as these patients may have had an alternative indication for corticosteroids.

Exposures, Outcomes, and Covariates

All data came from VA electronic health record (EHR) extracts, which provide directly analyzable demographics, comorbidities, medications, vital signs and laboratory results as well as notes that require text processing.

Dexamethasone Exposure: Exposure was defined as at least one dose of oral or parenteral dexamethasone within 48 hours after index date as determined from bar code medication administration (BCMA) data. We also determined administration of other systemic corticosteroids (prednisone, prednisolone, methylprednisolone and/or hydrocortisone).

Outcome: The primary outcome was 90-day all-cause mortality, ascertained using inpatient records and VA death registry data to capture deaths outside of hospitalization.

Respiratory Support: We stratified patients by highest level of respiratory support during the initial 48 hours of hospitalization into the following categories: 1) no oxygen support; 2) low-flow oxygen via nasal cannula (NC) that was not identified as a high-flow or other delivery device; 3) other supplemental oxygen/NIV, including face mask, non-rebreather mask, or other delivery not identifiable as low-flow NC or high-flow; 4) high-flow oxygen/HFNC; and 5) 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), validated with manual chart review to identify key terms indicative of respiratory support (Supplement).

Covariates: We obtained age, race, ethnicity, sex, comorbidities, additional medications, vital signs and laboratory results. We calculated the Charlson Comorbidity Index (CCI)[15] and the Veterans Health Administration COVID-19 (VACO) Index (Table 2 and Supplement Table 1).[16] We focused on routinely collected laboratory tests that have been associated with increased mortality in COVID-19[17] including albumin, liver function, lactate, white blood cell count, and creatinine (Table 2 and Supplemental Table 1). We selected the worst laboratory, temperature, blood pressure, and pulse oximetry within the initial 48 hours. To account for potential effects of co-prescribed medications, we included use of remdesivir and prophylactic anticoagulants within the initial 48 hours.[14] Intensive care unit (ICU) admission was determined using VA bedsection codes.[14, 18] As there was generally very little missing data (<5%), an explicit level for missingness was used for selected covariates.

Statistical analysis

We first compared COVID-19 patients by the five respiratory support categories using summary statistics (Table 1). Because nearly all patients on IMV or HFNC received dexamethasone, there was insufficient variability to allow generation of propensity score weights. Category 3, Other/NIV, was heterogenous with respect to respiratory support used and illness severity. For

these reasons, as well as the greater clinical equipoise, we restricted our analysis to patients without IRS (specifically, no oxygen or only low-flow NC support).

In those without IRS, we compared mortality by exposure to dexamethasone overall and stratified by NC. To account for confounding by indication, we generated propensity scores for the probability of receiving dexamethasone in the first 48 hours using logistic regression. Models included covariates associated with dexamethasone exposure and mortality: comorbidities, laboratory results, vital signs, site utilization patterns, co-medications and the time phases (Table 2 and Supplement 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.[19] In our primary analysis, we used average treatment effect (ATE) weights, reflecting the overall population from which the sample was taken. We used stabilized weights and trimmed from analysis the ten patients with the most extreme high and low weights.[20] We calculated standardized mean differences (SMD) between treatment groups and considered 0.2 or less as balanced. Using days since index date as the time scale, we compared differences in survival using weighted Kaplan-Meier (KM) plots [21] and estimated ATE using Cox proportional hazards models to generate hazard ratio (HR) and confidence limits using a robust variance estimator. We included the VACO Index in outcome models to further account for residual confounding.[16]

Subgroup and sensitivity analyses: In subgroup analyses, we excluded patients admitted to the ICU within the first 48 hours, and restricted to those age 70 and older. In sensitivity analyses, we limited the window between a positive SARS-CoV-2 test to within 24 or 48 hours of index date;

In addition, we considered exposure to any systemic corticosteroids within the first 48 hours. We also evaluated the average treatment effect among the treated (ATT) population that received dexamethasone in weighted Cox proportional hazards models, and constructed unweighted, but multivariable adjusted models for all primary and subgroup analyses (Supplement 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 (Supplement Table 4).

RESULTS

Patient characteristics, dexamethasone exposure and respiratory support

Patients hospitalized during the seven phases (n=19,973) 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 (83%) were admitted within one day after positive SARS-CoV-2 test. More than half overall (60%) received corticosteroids within 48 hours, of whom 95% received dexamethasone. Concurrent remdesivir and prophylactic anticoagulants initiated within 48 hours of admission were more common in those who received dexamethasone than in those who did not (remdesivir 43% vs. 13%; anticoagulants 46% vs. 10%, respectively).

When stratified by highest level of respiratory support in the first 48 hours of admission, 77% of patients were on either no oxygen (47%) or NC only (30%) (Table 1). Dexamethasone was administered to 34% without oxygen, 75% on NC, 69% on other supplemental oxygen/NIV, 91% on HFNC, and 90% on IMV. Use of dexamethasone generally increased over time (Figure 2). Overall, unadjusted 90-day mortality was 17% and varied by respiratory support (Figure 2).

Dexamethasone and mortality in patients without IRS

Amongst patients without IRS, the median duration of inpatient dexamethasone administration was 5 days (IQR 3-8) 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 341 (3.6%) and 115 (1.9%) patients, respectively, received only one day of inpatient dexamethasone.

After propensity score weighting, our samples (pseudopopulations) were well-balanced (Table 2 and Supplement Table 1). Among patients without oxygen, weighted KM curves (Figure 3) show that those who received dexamethasone had higher mortality over 90-days than those who did not, with differences beginning to appear 10-days after index date. In ATE estimates (Table 3), patients without oxygen who received dexamethasone had an 76% increased hazard of 90-day mortality (HR 1.76, 95% CI 1.47 to 2.12).

In patients on NC, 90-day mortality was similar in those who did and did not receive dexamethasone, as shown in weighted KM curves (Figure 3). ATE estimates demonstrated a non-significant 8% increased mortality risk (HR 1.08, 95% CI 0.86 to 1.37) in patients on NC

who received dexamethasone. When combining patients on no oxygen or NC, dexamethasone was associated with approximately 60% or more increased mortality risk.

Subgroup and sensitivity analyses

Results were similar in subgroup analyses excluding patients admitted to ICU within the first 48 hours and limiting the sample to patients age 70 and older (Table 3). Findings were also consistent considering SARS-CoV-2 testing within 24 or 48 hours of index date, exposure to all corticosteroids, and when using ATT or multivariable Cox models (Supplement Tables 2 and 3). Among patients on NC, HRs were similar using ATT estimates, but dexamethasone was associated with a statistically significant increase in mortality in multivariable Cox models (HR 1.31, 95% CI 1.08-1.60, Supplemental Table 3).

DISCUSSION

In this US national cohort of hospitalized patients with COVID-19, dexamethasone use was common and increased over time. Among patients on IRS, 90% received dexamethasone within 48 hours of admission. Focusing on patients without IRS, where there is less evidence supporting corticosteroid use, we found that among patients without oxygen in the first 48 hours, dexamethasone was administered in 34% and was associated with 76% increased 90-day mortality. Among those on NC in the first 48 hours, dexamethasone was administered in 75% and was associated with no mortality benefit. This real-world evidence does not support the use of dexamethasone in hospitalized COVID-19 patients without IRS in the first 48 hours.

While we cannot rule out residual confounding, our findings were robust employing several different approaches and in subgroup and sensitivity analyses, including limiting the time window for SARS-CoV-2 test result, exposure to any systemic corticosteroid, restricted to patients over age 70 and excluding those who were admitted to the ICU within 48 hours. Results were consistent using ATE, reflecting the overall population from which the sample was taken, and using ATT, reflecting the population who received dexamethasone. They were also consistent controlling for potential confounders such as demographics, phase of the pandemic, site prescribing patterns, comorbidities, vital signs, laboratory values and co-administration of medications including remdesivir.[16]

Importantly, patients without IRS in the initial 48 hours represent the majority (77%) of COVID-19 admissions in the cohort; thus, our findings have important clinical implications on the potential unintended consequences of widespread dexamethasone adoption for COVID-19 amongst patients who are without IRS. We found that uptake of dexamethasone for COVID-19 patients hospitalized in the VA was rapid after release of the RECOVERY trial results in early June 2020. By mid-July 2020 most facilities had increased the proportion of patients administered dexamethasone to 90% of patients on HFNC or IMV within 48 hours of admission, exceeding national estimates from other health systems.[6] However, sites also increased use of dexamethasone for patients with less severe COVID-19, including those not on oxygen or only on NC (Figure 2), suggesting indication creep.

Our results provide real world evidence of practice patterns and extend findings from RECOVERY.[1] We provide clinically actionable evidence demonstrating significantly and substantially increased mortality in hospitalized COVID-19 patients not on oxygen who received early dexamethasone. Moreover, our results inform an area of significant clinical uncertainty, namely the use of dexamethasone in COVID-19 patients with less severe respiratory failure. Clinical guidelines issued by the US National Institutes of Health provide a moderate recommendation for corticosteroids in hospitalized COVID-19 patients "on supplemental oxygen."[22] While dexamethasone was associated with improved outcomes in patients on oxygen support in RECOVERY, this category included all forms of oxygen, except for IMV, but inclusive of NIV. We further stratified patients by level of oxygen support during the initial 48 hours of hospitalization, addressing a significant knowledge gap.[12] We found a lack of benefit associated with dexamethasone in patients on only low-flow NC within 48 hours of admission, suggesting that use of corticosteroids in this population should be re-considered and requires further prospective study.

Even before COVID-19, the impact of corticosteroids has been inconsistent in other causes of pneumonia including influenza, community-acquired pneumonia (CAP), and the original severe acute respiratory syndrome (SARS).[8, 23-26]. The impact of corticosteroids likely depends on multiple factors, including patient age and other characteristics, heterogeneity in host response to infection, etiology of pneumonia, time since onset of infection and presence and severity of acute respiratory distress syndrome (ARDS).[8, 10, 27-31] While corticosteroids may decrease host inflammatory response, potentially modulating lung injury, they may also have harmful side

effects or unintended consequences on adaptive immune responses that may be important to resolution of infection and increase risk of secondary infection.

There remain unanswered questions regarding the use of dexamethasone for patients hospitalized with COVID-19, particularly those without IRS. For some patients, initiation within 48 hours of hospitalization may be too early and could impair viral clearance.[32] While most patients in our cohort had positive SARS-CoV-2 testing within one day of hospitalization, we do not know how long symptoms preceded seeking medical attention and testing. Corticosteroids may also have a differential effect depending on degree of inflammation,[33] but often extensive missing data and selection bias in obtaining tests such as C-reactive protein (CRP) and interleukin-6 (IL-6) make this difficult to explore in real-world data. Further, it is unclear whether the dexamethasone regimen used in RECOVERY is optimal or whether the formulation, dose and duration of corticosteroids should vary by factors such as patient age or severity of COVID-19.[2-4, 32] While most corticosteroid use in our cohort was dexamethasone, we found consistent results when including all systemic corticosteroids, and also when restricting to individuals over age 70, although other reports have found a potential for increased harm in older persons.[31] It is also unknown whether corticosteroids have a differential effect in breakthrough COVID-19 after vaccination or different variants of SARS-CoV-2.

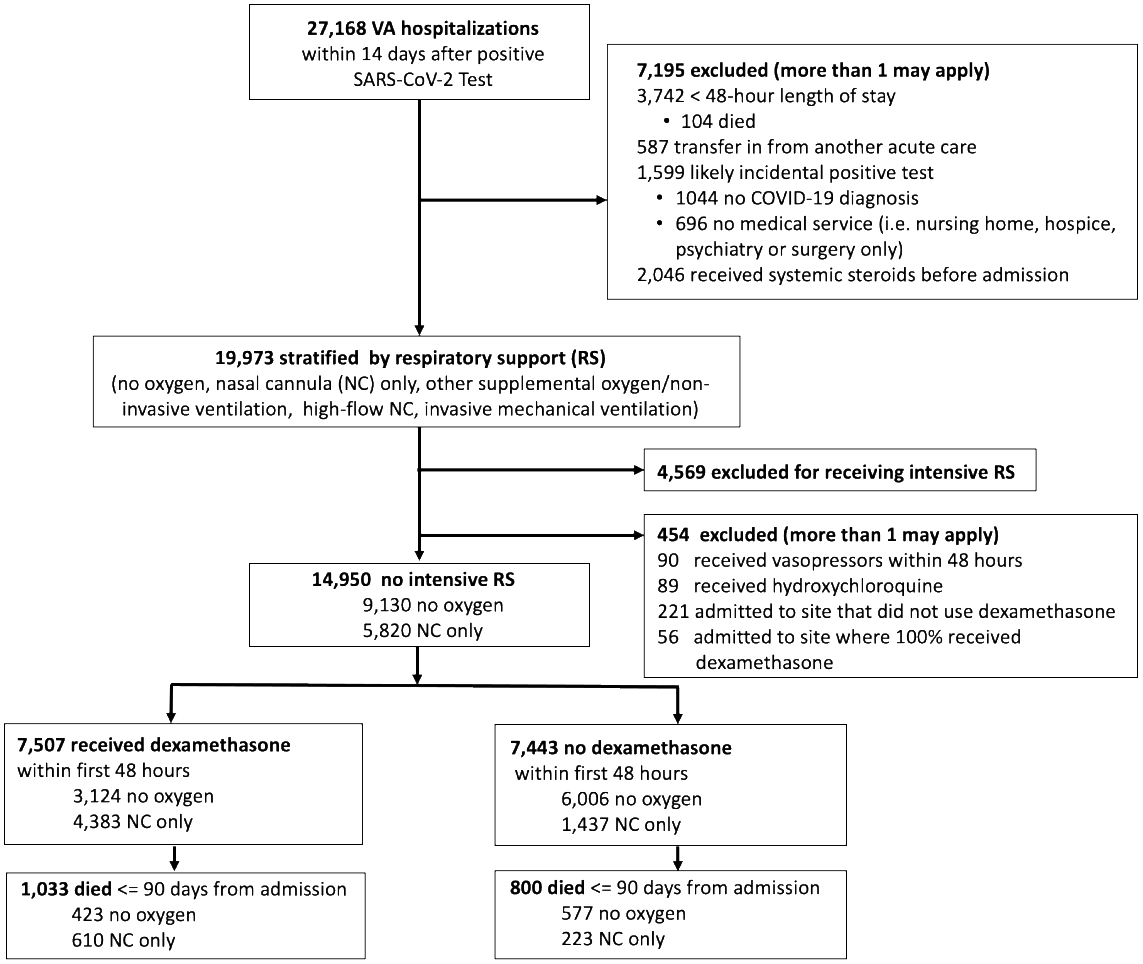
There are several limitations to our study. First, the study was observational. While we used detailed clinical data that included measures reflecting illness severity and administration of co-medications in a large population well balanced by propensity for treatment, residual confounding for severity of illness could have contributed to greater mortality in those exposed

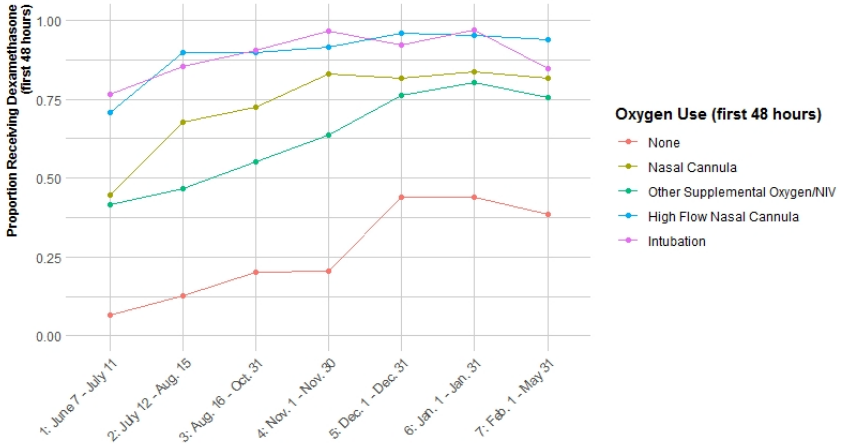
to dexamethasone. Some laboratory results could have occurred after dexamethasone exposure, as both were ascertained within 48 hours. However, the impact of dexamethasone on acute laboratory results is likely limited and this approach allowed an equal time window to detect worst results in patients exposed and unexposed to dexamethasone. Although respiratory support algorithms were manually reviewed and validated, some misclassification may have occurred; but substantial separation in Kaplan-Meier curves showing increasing mortality with greater respiratory support, provides face validity. We also cannot rule out alternative indications for dexamethasone beyond COVID-19 in patients not on oxygen or on NC. However, we excluded those on corticosteroids prior to admission and patients on vasopressors within the initial 48 hours. Further, we did not calculate dose and only assessed days of inpatient dexamethasone exposure. However, most patients had length of inpatient dexamethasone treatment equal to their hospital length of stay, and very few received only one dose of dexamethasone (<4%). Finally, our cohort consisted predominantly of male Veterans, but had excellent racial and geographic variability.

In summary, we found no evidence of mortality benefit at 90-days associated with early initiation of dexamethasone in patients hospitalized with COVID-19 among those on no oxygen or NC within the first 48 hours of admission, and instead found evidence of potential harm. These findings come from a large population with detailed clinical data providing real-world evidence that was consistent using different analytic approaches to control for confounding and remained robust in a variety of subgroup and sensitivity analyses. Given the frequent and continued administration of dexamethasone to a substantial proportion of patients who are not on oxygen or are only on low-flow NC, the real-world evidence presented here highlights the non-

beneficial and potentially harmful expansion in use of dexamethasone in hospitalized COVID-19 patients without IRS. Future work should also evaluate dexamethasone and associated outcomes among hospitalized patients with COVID-19 breakthrough infections and different SARS-CoV-2 variants.

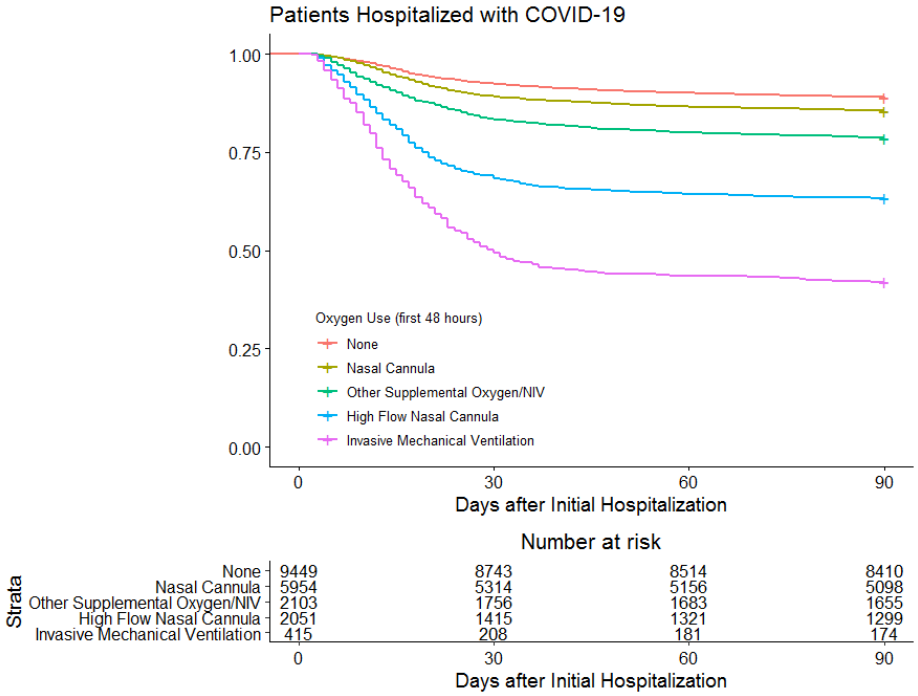
Figure 1. Derivation of Study Population





Time period of admission from June 7, 2020 through May 31, 2021

A.



B.

Figure 2. Proportion of patients exposed to dexamethasone (A) and unadjusted Kaplan Meier survival curves for 90-day mortality (B) according to respiratory support level.
Note that the RECOVERY trial was halted on June 8, 2020, with press release of results on June 16, 2020.

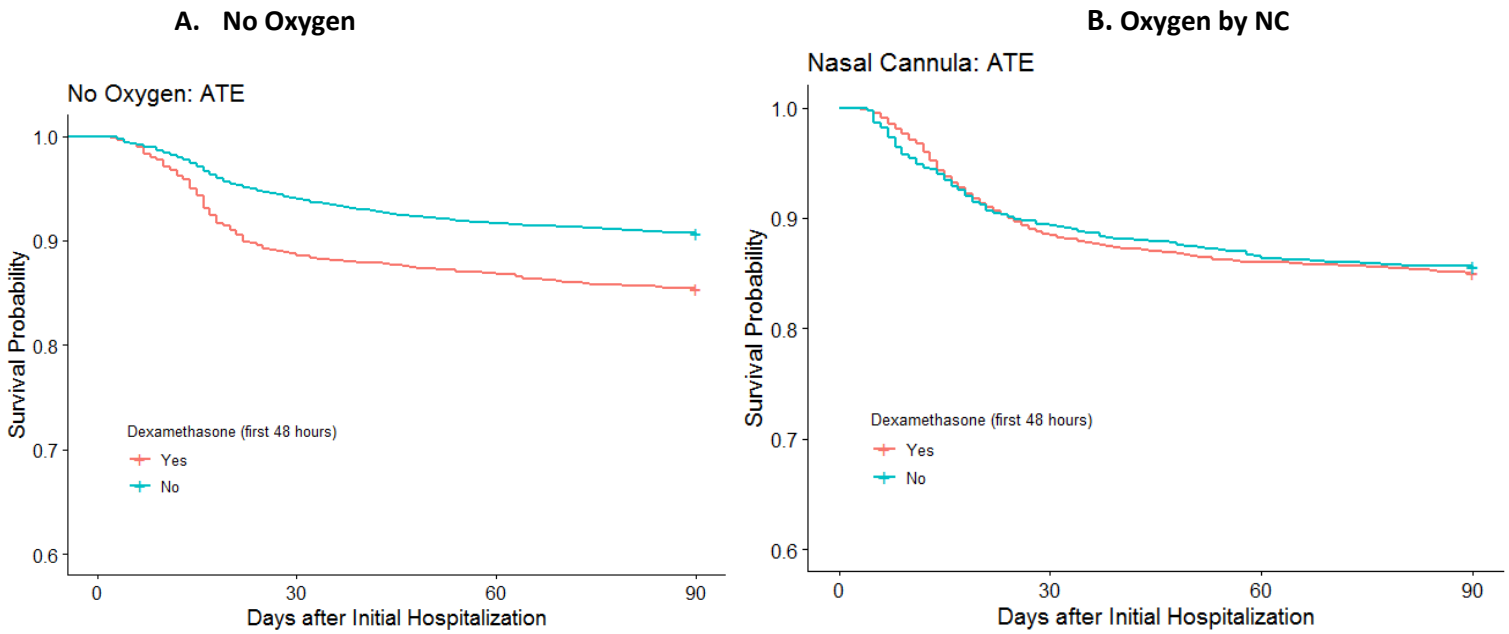


Figure 3. IPTW Kaplan Meier survival curves for 90-day mortality by corticosteroid use among those on no oxygen or NC

ATE = Average Treatment Effect

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 (NC)	Other Supplemental Oxygen/NIV	High Flow Nasal Cannula (HFNC)	Invasive Mechanical Ventilation (IMV)
Overall Cohort, n	19,973	9,450	5,954	2,103	2,051	415
Demographics						
Age, n (%)						
<50	1,760 (9%)	1,013 (11%)	459 (8%)	138 (7%)	120 (6%)	30 (7%)
50-59	2,361 (12%)	1,205 (13%)	691 (12%)	204 (10%)	216 (11%)	45 (11%)
60-69	4,677 (23%)	2,194 (23%)	1,340 (23%)	490 (23%)	536 (26%)	117 (28%)
70-79	7,230 (36%)	3,155 (33%)	2,235 (38%)	833 (40%)	837 (41%)	170 (41%)
80+	3,945 (20%)	1,883 (20%)	1,229 (21%)	438 (21%)	342 (17%)	53 (13%)
Sex: Male, n (%)	18,993 (95%)	8,948 (95%)	5,651 (95%)	2,002 (95%)	1,991 (97%)	401 (97%)
Race, n (%)						
White, non-Hispanic	11,033 (55%)	5,019 (53%)	3,387 (57%)	1,253 (60%)	1,161 (57%)	213 (51%)
Black, non-Hispanic	5,449 (27%)	2,854 (30%)	1,522 (26%)	498 (24%)	481 (23%)	94 (23%)
Hispanic	1,738 (9%)	773 (8%)	526 (9%)	167 (8%)	216 (11%)	56 (13%)
Other	1,144 (6%)	510 (5%)	330 (6%)	134 (6%)	134 (7%)	36 (9%)
Unknown	609 (3%)	294 (3%)	189 (3%)	51 (2%)	59 (3%)	16 (4%)
Phase (Admission Date, 2020), n (%)						
1: June 7 - July 11	1,505 (8%)	590 (6%)	592 (10%)	115 (5%)	161 (8%)	47 (11%)
2: July 12 - Aug. 15	1,688 (8%)	602 (6%)	714 (12%)	148 (7%)	190 (9%)	34 (8%)
3: Aug. 16 - Oct. 31	2,724 (14%)	931 (10%)	1,145 (19%)	254 (12%)	319 (16%)	75 (18%)
4: Nov. 1 - Nov. 30	2,842 (14%)	891 (9%)	1,215 (20%)	273 (13%)	405 (20%)	58 (14%)
5: Dec. 1 - Dec. 31	4,052 (20%)	2,204 (23%)	866 (15%)	519 (25%)	387 (19%)	76 (18%)
6: Jan. 1 - Jan. 31	3,588 (18%)	2,045 (22%)	749 (13%)	428 (20%)	300 (15%)	66 (16%)
7: Feb. 1 - May 31	3,574 (18%)	2,187 (23%)	673 (11%)	366 (17%)	289 (14%)	59 (14%)
Selected Conditions						
Dementia, n (%)	2,357 (12%)	1,290 (14%)	659 (11%)	240 (11%)	137 (7%)	31 (7%)
CHF, n (%)	4,356 (22%)	1,981 (21%)	1,339 (22%)	555 (26%)	401 (20%)	80 (19%)
COPD/Asthma, n (%)	5,903 (30%)	2,433 (26%)	1,978 (33%)	738 (35%)	636 (31%)	118 (28%)
Charlson Comorbidity Index, n (%)						
0	3,718 (19%)	1,885 (20%)	1,034 (17%)	316 (15%)	407 (20%)	76 (18%)
1-2	6,336 (32%)	2,939 (31%)	1,897 (32%)	627 (30%)	718 (35%)	155 (37%)
3-4	4,622 (23%)	2,102 (22%)	1,457 (24%)	520 (25%)	457 (22%)	86 (21%)
5+	5,297 (27%)	2,524 (27%)	1,566 (26%)	640 (30%)	469 (23%)	98 (24%)
Medication Use						
Corticosteroid, Any Systemic, n (%)						
First 48 Hours	11,970 (60%)	3,514 (37%)	4,627 (78%)	1,521 (72%)	1,923 (94%)	385 (93%)
Later than 48 Hours	1,607 (8%)	870 (9%)	467 (8%)	202 (10%)	47 (2%)	21 (5%)
None	6,396 (32%)	5,066 (54%)	860 (14%)	380 (18%)	81 (4%)	9 (2%)

		Oxygen Support first 48 hours				
	Overall	None	Nasal Cannula (NC)	Other Supplemental Oxygen/NIV	High Flow Nasal Cannula (HFNC)	Invasive Mechanical Ventilation (IMV)
Dexamethasone, n (%)						
First 48 Hours	11,361 (57%)	3,198 (34%)	4,472 (75%)	1,447 (69%)	1,871 (91%)	373 (90%)
Later than 48 Hours	1,586 (8%)	833 (9%)	473 (8%)	201 (10%)	55 (3%)	24 (6%)
None	7,026 (35%)	5,419 (57%)	1,009 (17%)	455 (22%)	125 (6%)	18 (4%)
Remdesivir, n (%)						
First 48 Hours	9,533 (48%)	2,716 (29%)	3,706 (62%)	1,197 (57%)	1,637 (80%)	277 (67%)
Later than 48 Hours	1,607 (8%)	768 (8%)	532 (9%)	188 (9%)	88 (4%)	31 (7%)
None	8,833 (44%)	5,966 (63%)	1,716 (29%)	718 (34%)	326 (16%)	107 (26%)
Prophylactic Anticoagulant, n (%)						
First 48 Hours	14,708 (74%)	6,820 (72%)	4,502 (76%)	1,576 (75%)	1,514 (74%)	296 (71%)
Later than 48 Hours	1,752 (9%)	842 (9%)	463 (8%)	183 (9%)	212 (10%)	52 (13%)
None	3,513 (18%)	1,788 (19%)	989 (17%)	344 (16%)	325 (16%)	67 (16%)
Therapeutic Anticoagulant, n (%)						
First 48 Hours	4,550 (23%)	1,815 (19%)	1,446 (24%)	516 (25%)	647 (32%)	126 (30%)
Later than 48 Hours	13,921 (70%)	6,627 (70%)	4,220 (71%)	1,478 (70%)	1,333 (65%)	263 (63%)
None	1,502 (8%)	1,008 (11%)	288 (5%)	109 (5%)	71 (3%)	26 (6%)
Vasopressors, n (%)						
First 48 Hours	391 (2%)	55 (1%)	35 (1%)	22 (1%)	42 (2%)	237 (57%)
Later than 48 Hours	1,197 (6%)	272 (3%)	272 (5%)	132 (6%)	417 (20%)	104 (25%)
None	18,385 (92%)	9,123 (97%)	5,647 (95%)	1,949 (93%)	1,592 (78%)	74 (18%)
Intensive Care, n (%)						
First 48 Hours	4,143 (21%)	1,172 (12%)	884 (15%)	427 (20%)	1,275 (62%)	385 (93%)
Later than 48 Hours	1,468 (7%)	465 (5%)	554 (9%)	211 (10%)	221 (11%)	17 (4%)
None	14,362 (72%)	7,813 (83%)	4,516 (76%)	1,465 (70%)	555 (27%)	13 (3%)
Intubation, n (%)						
First 48 Hours	415 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	415 (100%)
Later than 48 Hours	1,078 (5%)	257 (3%)	259 (4%)	121 (6%)	441 (22%)	0 (0%)
None	18,480 (93%)	9,193 (97%)	5,695 (96%)	1,982 (94%)	1,610 (78%)	0 (0%)
Hospital Length of Stay, n (%)						
< 7 days	10,604 (53%)	5,633 (60%)	3,316 (56%)	1,098 (52%)	501 (24%)	56 (13%)
7-13 days	5,365 (27%)	2,248 (24%)	1,613 (27%)	602 (29%)	788 (38%)	114 (27%)
14+ days	4,004 (20%)	1,569 (17%)	1,025 (17%)	403 (19%)	762 (37%)	245 (59%)
Mortality (unadjusted, cumulative incidence)						
30 Days, n (%)	2,587 (13%)	728 (8%)	650 (11%)	351 (17%)	648 (32%)	210 (51%)
60 Days, n (%)	3,125 (16%)	940 (10%)	799 (13%)	421 (20%)	731 (36%)	234 (56%)
90 Days, n (%)	3,340 (17%)	1,042 (11%)	857 (14%)	448 (21%)	752 (37%)	241 (58%)

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)

Dexamethasone	Combined Cohort of patients on no oxygen or on NC only		
	No	Yes	SMD
Cohort, n	11963.6	12887.0	
Age, (%)			
<50	1082.7 (9.0)	1142.0 (8.9)	-0.002
50-59	1367.3 (11.4)	1551.5 (12.0)	0.006
60-69	2800.3 (23.4)	2959.5 (23.0)	-0.004
70-79	4206.0 (35.2)	4662.9 (36.2)	0.010
80+	2507.4 (21.0)	2571.2 (20.0)	-0.010
Sex: Male, (%)	11323.9 (94.7)	12237.6 (95.0)	0.003
Race, (%)			
White, non-Hispanic	6430.7 (53.8)	7170.0 (55.6)	0.019
Black, non-Hispanic	3567.0 (29.8)	3507.0 (27.2)	-0.026
Hispanic	940.7 (7.9)	1120.5 (8.7)	0.008
Other	666.5 (5.6)	673.5 (5.2)	-0.003
Unknown	358.7 (3.0)	416.1 (3.2)	0.002
Phase (Admission Date) , (%)			
1: June 7 - July 11	1112.0 (9.3)	865.6 (6.7)	-0.026
2: July 12 - Aug. 15	1063.1 (8.9)	1074.1 (8.3)	-0.006
3: Aug. 16 - Oct. 17	1764.3 (14.7)	1784.1 (13.8)	-0.009
4: Oct. 18 - Nov. 30	1567.9 (13.1)	1894.9 (14.7)	0.016
5: Dec. 1 - Dec. 31	2347.1 (19.6)	2693.3 (20.9)	0.013
6: Jan. 1 - Jan. 31	1998.7 (16.7)	2315.6 (18.0)	0.013
7: Feb. 1 - May 31	2110.5 (17.6)	2259.4 (17.5)	-0.001
Site Dexamethasone Prescribing, (%)			
Low	3173.2 (26.5)	2421.9 (18.8)	-0.077
Medium	7115.5 (59.5)	7480.7 (58.0)	-0.014
High	1674.9 (14.0)	2984.5 (23.2)	0.092
Smoking Status, (%)			
Unknown	384.8 (3.2)	384.5 (3.0)	-0.002
Never Smoker	4080.9 (34.1)	4491.1 (34.8)	0.007
Former Smoker	4576.0 (38.2)	5277.6 (41.0)	0.027
Current Smoker	2921.8 (24.4)	2734.0 (21.2)	-0.032
AUDIT-C Score (%)			
Unknown	441.7 (3.7)	431.4 (3.3)	-0.003
0	7978.6 (66.7)	8489.5 (65.9)	-0.008
1-3	2456.4 (20.5)	2962.0 (23.0)	0.025
4-7	734.5 (6.1)	719.6 (5.6)	-0.006
8+	352.5 (2.9)	284.6 (2.2)	-0.007
Comorbidities			
Myocardial Infarction (%)	1078.8 (9.0)	1096.0 (8.5)	-0.005
Congestive Heart Failure (%)	2678.1 (22.4)	2865.7 (22.2)	-0.001
Cerebrovascular Disease (%)	2113.7 (17.7)	2094.2 (16.3)	-0.014
Dementia (%)	1748.8 (14.6)	1448.8 (11.2)	-0.034
Chronic Obstructive Pulmonary Disease (%)	3131.2 (26.2)	3760.1 (29.2)	0.030
Rheumatoid Arthritis (%)	186.2 (1.6)	206.8 (1.6)	0.000
Peptic ulcer (%)	272.0 (2.3)	270.9 (2.1)	-0.002
Liver disease, mild (%)	1504.2 (12.6)	1452.8 (11.3)	-0.013
Diabetes, Uncomplicated (%)	5683.8 (47.5)	6182.6 (48.0)	0.005
Diabetes, Complicated (%)	3873.3 (32.4)	3969.4 (30.8)	-0.016
Hemi or paraplegia (%)	341.0 (2.9)	285.3 (2.2)	-0.006
Renal disease (%)	3228.2 (27.0)	3422.0 (26.6)	-0.004
Liver disease, moderate-severe (%)	226.5 (1.9)	205.6 (1.6)	-0.003
Metastatic cancer (%)	293.0 (2.4)	256.2 (2.0)	-0.005
HIV (%)	153.5 (1.3)	150.8 (1.2)	-0.001
Charlson Comorbidities Count (%)			
0	2212.6 (18.5)	2412.7 (18.7)	0.002

Dexamethasone	Combined Cohort of patients on no oxygen or on NC only		
	No	Yes	SMD
1-2	3634.1 (30.4)	4065.3 (31.5)	0.012
3-4	2780.0 (23.2)	3018.6 (23.4)	0.002
5+	3336.9 (27.9)	3390.4 (26.3)	-0.016
Number of Doctors (prior year) (%)			
0	4815.2 (40.2)	5033.7 (39.1)	-0.012
1	3240.7 (27.1)	3585.3 (27.8)	0.007
2-4	3564.9 (29.8)	3946.2 (30.6)	0.008
5+	342.8 (2.9)	321.8 (2.5)	-0.004
Specialty clinics attended			
Cardiology **(%)**	3108.1 (26.0)	3528.6 (27.4)	0.014
Coagulation (%)	192.2 (1.6)	214.1 (1.7)	0.001
Pacemaker (%)	428.2 (3.6)	424.7 (3.3)	-0.003
Dialysis (%)	206.6 (1.7)	218.6 (1.7)	0.000
Gastoenterology (%)	1147.9 (9.6)	1277.5 (9.9)	0.003
Hepatology (%)	426.1 (3.6)	359.0 (2.8)	-0.008
Homeless (%)	817.4 (6.8)	596.1 (4.6)	-0.022
Co-Medications			
Prophylactic Anticoagulants 1st 48 hours (%)	8665.8 (72.4)	9589.0 (74.4)	0.020
Remdesivir, 1st 48 hours (%)	3664.1 (30.6)	6050.4 (46.9)	0.163
Laboratory values			
Albumin, g/dL (%)			
3.5 +	4070.5 (34.0)	3839.1 (29.8)	-0.042
3 - 3.49	3935.0 (32.9)	4550.6 (35.3)	0.024
< 3	3361.2 (28.1)	3986.4 (30.9)	0.028
Missing	596.9 (5.0)	510.9 (4.0)	-0.010
Alanine aminotransferase, IU/L (%)			
< 20	3461.5 (28.9)	3151.6 (24.5)	-0.045
20 - 39	4786.1 (40.0)	5418.4 (42.0)	0.020
40 +	3195.2 (26.7)	3995.4 (31.0)	0.043
Missing	520.8 (4.4)	321.6 (2.5)	-0.019
Asparate aminostransferase, IU/L (%)			
< 20	2285.0 (19.1)	1586.6 (12.3)	-0.068
20 - 39	5309.3 (44.4)	5767.2 (44.8)	0.004
40 +	4369.3 (36.5)	5533.2 (42.9)	0.064
Creatinine, mg/dL (%)			
< 1.2	5238.4 (43.8)	5616.3 (43.6)	-0.002
1.2 – 1.99	4423.3 (37.0)	4862.7 (37.7)	0.008
2 +	2196.7 (18.4)	2367.4 (18.4)	0.000
Missing	105.2 (0.9)	40.6 (0.3)	-0.006
Fibrosis-4 Index (%)			
< 1.45	2289.3 (19.1)	2087.1 (16.2)	-0.029
1.45 – 3.25	4791.3 (40.0)	5341.2 (41.4)	0.014
3.25 +	4308.2 (36.0)	5107.3 (39.6)	0.036
Missing	574.8 (4.8)	351.5 (2.7)	-0.021
Lactate, mmol/L (%)			
<1.2	1764.8 (14.8)	2009.6 (15.6)	0.008
1.2 - <2.0	3020.2 (25.2)	3732.9 (29.0)	0.037
2.0+	1626.1 (13.6)	2027.5 (15.7)	0.021
Missing	5552.5 (46.4)	5117.0 (39.7)	-0.067
Platelet count per microL (%)			
150 or higher	7892.8 (66.0)	8381.1 (65.0)	-0.009
< 150	3988.7 (33.3)	4482.4 (34.8)	0.014
Missing	82.1 (0.7)	23.6 (0.2)	-0.005
Total bilirubin, mg/dL (%)			
<1	8779.4 (73.4)	9524.9 (73.9)	0.005
1 - 1.2	1004.1 (8.4)	1187.0 (9.2)	0.008
1.2 +	1664.4 (13.9)	1857.2 (14.4)	0.005
Missing	515.7 (4.3)	318.0 (2.5)	-0.018
White Blood Count per microL (%)			
4-10	6641.3 (55.5)	6266.6 (48.6)	-0.069

Dexamethasone	Combined Cohort of patients on no oxygen or on NC only		
	No	Yes	SMD
<4	3139.3 (26.2)	3812.3 (29.6)	0.033
>10	2183.1 (18.2)	2808.2 (21.8)	0.035
C-reactive protein measured (%)	6674.9 (55.8)	7810.0 (60.6)	0.048
D-dimer measured (%)	8791.6 (73.5)	10350.8 (80.3)	0.068
Vital Signs			
Highest Temperature (F) (%)			
< 99	4466.1 (37.3)	4443.3 (34.5)	-0.029
99 - 100	2919.2 (24.4)	3106.8 (24.1)	-0.003
100 - 102	3077.0 (25.7)	3567.9 (27.7)	0.020
102 +	1459.9 (12.2)	1719.3 (13.3)	0.011
Missing	41.4 (0.3)	49.7 (0.4)	0.000
Mean Arterial Pressure, mmHg (%)			
< 60	320.4 (2.7)	282.2 (2.2)	-0.005
60 – 69	1627.5 (13.6)	1682.2 (13.1)	-0.006
70 – 89	7805.2 (65.2)	8623.3 (66.9)	0.017
90 +	2183.3 (18.2)	2266.1 (17.6)	-0.007
Missing	27.2 (0.2)	33.3 (0.3)	0.000
Lowest Oxygen Saturation (%)			
< 88	643.0 (5.4)	1099.6 (8.5)	0.032
88 - 92	4961.0 (41.5)	6515.0 (50.6)	0.091
93 - 95	4459.7 (37.3)	3888.3 (30.2)	-0.071
96 +	1651.6 (13.8)	1106.9 (8.6)	-0.052
Missing	248.3 (2.1)	277.2 (2.2)	0.001

Table 3. IPTW Cox proportional hazards models for 90-day mortality associated with early dexamethasone exposure in patients hospitalized for COVID-19 without IRS

	No oxygen supplementation	**Nasal cannula**	**Combined group: no oxygen plus NC**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**
Primary analysis	1.76 (1.47 to 2.12)	1.08 (0.86 to 1.36)	1.59 (1.39 to 1.81)
Sensitivity and subgroup analyses			
Restricted to positive SARS-CoV-2 test within 24 hours	1.94 (1.50 to 2.53)	1.23 (0.93 to 1.64)	1.54 (1.26 to 1.87)
Restricted to positive SARS-CoV-2 test within 48 hours	2.01 (1.55 to 2.60)	1.27 (0.96 to 1.68)	1.58 (1.30 to 1.92)
Any systemic corticosteroid	1.77 (1.49 to 2.11)	1.15 (0.92 to 1.43)	1.61 (1.41 to 1.84)
Excluding patients admitted to ICU in initial 48 hours	1.80 (1.36 to 1.74)	1.18 (0.89 to 1.58)	1.45 (1.19 to 1.67)
Restricted to patients age 70 and older	1.76 (1.36 to 2.28)	1.30 (0.99 to 1.72)	1.53 (1.27 to 1.84)

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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Online Supplement

Methods

Study Population and Exclusions:

We conducted an observational cohort study using VA electronic health record (EHR) data. We identified patients 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 May 31, 2021. The cohort inception date of June 7, 2020 was selected because prior to this there was substantial variability in the timing of initiation of corticosteroids (greater use of late corticosteroids, more than 48 hours after admission) and in the type of corticosteroid used in hospitalized COVID-19 patients. After June 7, 2020, there was a substantial increase in initiation of corticosteroids – particularly dexamethasone – within 48 hours of hospitalization. Notably, this time period coincides with the announcement that recruitment was halted in the RECOVERY trial on June 8, 2020, and the subsequent press release that indicated benefit from dexamethasone on June 16, 2020. In addition, we omitted early months of the pandemic from March-May 2020 because there was significant variability in other aspects of care, including availability of testing and use of respiratory support and co-medications. The date of May 31, 2021 was selected as the end date for the cohort in order to have at least 90 days of follow-up for all individuals at the time of the analyses.

From the initial 27,168 patients identified, we excluded 7,195, yielding a cohort of 19,973 patients who were then stratified by category of respiratory support (Figure 1). More than one

exclusion criteria could apply; the most common reason was length of stay less than 48-hours (n=3,742; 104 deaths) as these patients had insufficient time to receive dexamethasone. This was followed by any systemic corticosteroid exposure prior to index date (n=2,046), defined as any corticosteroids within 14 days, or receipt of corticosteroids for ≥14 days in the preceding 45 days. 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.

In modeling mortality analyses restricted to patients who were not on oxygen or were on low-flow nasal cannula (NC) only, we excluded an additional 454 total patients; more than one exclusion criteria could also apply. Within each phase, we restricted to facilities with at least 10 cases of COVID-19 and with at least one dexamethasone prescription (n=221), and where not 100% of patients with COVID-19 received dexamethasone (n=56) to have sufficient variation and number of events at each site. We also excluded patients prescribed hydroxychloroquine (n=89) as it was falling out of favor over the study time period; the temporal variation combined with the small number of participants made balancing them by site and across groups challenging. We excluded participants who were on vasopressors in the first 48 hours (n=90) as these patients may have had a different clinical indication (namely persistent shock) for dexamethasone or other corticosteroids and thus less likely to fall into a group for whom there is clinical equipoise, yielding a final analytic sample of 14,950 patients.

Respiratory Support: We stratified patients by highest level of respiratory support during the initial 48 hours of hospitalization. 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 by performing manual full chart review including of all clinician, nursing and respiratory therapy notes, 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 of 100%. On chart review, no cases were found to have received oxygen that were not also identified by NLP as being on oxygen. Specificity and positive predictive value were 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.

Dexamethasone Exposure: In each phase, we defined administration by site as low ($<25^{th}$ percentile), medium (between 25-75% percentile), or high ($>75^{th}$ percentile) based on the proportion in the sample receiving corticosteroids.

Supplemental Table E1. Unweighted and propensity weighted pseudo populations
A. Unweighted population

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
Cohort, n	5726	3124		1290	4383		7016	7507	
Age, (%)									
<50	657 (11.5)	310 (9.9)	-0.016	80 (6.2)	356 (8.1)	0.019	737 (10.5)	666 (8.9)	-0.016
50-59	681 (11.9)	438 (14.0)	0.021	143 (11.1)	521 (11.9)	0.008	824 (11.7)	959 (12.8)	0.010
60-69	1339 (23.4)	718 (23.0)	-0.004	282 (21.9)	995 (22.7)	0.008	1621 (23.1)	1713 (22.8)	-0.003
70-79	1843 (32.2)	1072 (34.3)	0.021	462 (35.8)	1664 (38.0)	0.022	2305 (32.9)	2736 (36.4)	0.036
80+	1206 (21.1)	586 (18.8)	-0.023	323 (25.0)	847 (19.3)	-0.057	1529 (21.8)	1433 (19.1)	-0.027
Sex: Male, (%)	5428 (94.8)	2963 (94.8)	0.001	1227 (95.1)	4168 (95.1)	0.000	6655 (94.9)	7131 (95.0)	0.001
Race, (%)									
White, non-Hispanic	2996 (52.3)	1711 (54.8)	0.024	724 (56.1)	2507 (57.2)	0.011	3720 (53.0)	4218 (56.2)	0.032
Black, non-Hispanic	1816 (31.7)	820 (26.2)	-0.055	361 (28.0)	1077 (24.6)	-0.034	2177 (31.0)	1897 (25.3)	-0.058
Hispanic	437 (7.6)	300 (9.6)	0.020	90 (7.0)	414 (9.4)	0.025	527 (7.5)	714 (9.5)	0.020
Other	308 (5.4)	176 (5.6)	0.003	74 (5.7)	244 (5.6)	-0.002	382 (5.4)	420 (5.6)	0.002
Unknown	169 (3.0)	117 (3.7)	0.008	41 (3.2)	141 (3.2)	0.000	210 (3.0)	258 (3.4)	0.004
Phase (Admission Date) , (%)									
1: June 7 - July 11	426 (7.4)	38 (1.2)	-0.062	289 (22.4)	258 (5.9)	-0.165	715 (10.2)	296 (3.9)	-0.062
2: July 12 - Aug. 15	457 (8.0)	64 (2.0)	-0.059	201 (15.6)	468 (10.7)	-0.049	658 (9.4)	532 (7.1)	-0.023
3: Aug. 16 - Oct. 17	694 (12.1)	186 (6.0)	-0.062	277 (21.5)	812 (18.5)	-0.029	971 (13.8)	998 (13.3)	-0.005
4: Oct. 18 - Nov. 30	676 (11.8)	180 (5.8)	-0.060	183 (14.2)	993 (22.7)	0.085	859 (12.2)	1173 (15.6)	0.034
5: Dec. 1 - Dec. 31	1158 (20.2)	947 (30.3)	0.101	137 (10.6)	696 (15.9)	0.053	1295 (18.5)	1643 (21.9)	0.034
6: Jan. 1 - Jan. 31	1063 (18.6)	878 (28.1)	0.095	99 (7.7)	608 (13.9)	0.062	1162 (16.6)	1486 (19.8)	0.032
7: Feb. 1 - May 31	1252 (21.9)	831 (26.6)	0.047	104 (8.1)	548 (12.5)	0.044	1356 (19.3)	1379 (18.4)	-0.010
Site Dexamethasone Prescribing, (%)									
Low	1689 (29.5)	405 (13.0)	-0.165	399 (30.9)	594 (13.6)	-0.174	2088 (29.8)	999 (13.3)	-0.165
Medium	3406 (59.5)	1787 (57.2)	-0.023	729 (56.5)	2451 (55.9)	-0.006	4135 (58.9)	4238 (56.5)	-0.025
High	631 (11.0)	932 (29.8)	0.188	162 (12.6)	1338 (30.5)	0.180	793 (11.3)	2270 (30.2)	0.189
Smoking Status, (%)									
Unknown	210 (3.7)	91 (2.9)	-0.008	49 (3.8)	117 (2.7)	-0.011	259 (3.7)	208 (2.8)	-0.009
Never Smoker	1958 (34.2)	1173 (37.5)	0.034	430 (33.3)	1479 (33.7)	0.004	2388 (34.0)	2652 (35.3)	0.013
Former Smoker	1934 (33.8)	1268 (40.6)	0.068	524 (40.6)	1936 (44.2)	0.036	2458 (35.0)	3204 (42.7)	0.076

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
Current Smoker	1624 (28.4)	592 (19.0)	-0.094	287 (22.2)	851 (19.4)	-0.028	1911 (27.2)	1443 (19.2)	-0.080
AUDIT-C Score (%)									
Unknown	250 (4.4)	86 (2.8)	-0.016	62 (4.8)	125 (2.9)	-0.020	312 (4.4)	211 (2.8)	-0.016
0	3663 (64.0)	2048 (65.6)	0.016	898 (69.6)	2928 (66.8)	-0.028	4561 (65.0)	4976 (66.3)	0.013
1-3	1164 (20.3)	756 (24.2)	0.039	255 (19.8)	1055 (24.1)	0.043	1419 (20.2)	1811 (24.1)	0.039
4-7	389 (6.8)	182 (5.8)	-0.010	53 (4.1)	204 (4.7)	0.005	442 (6.3)	386 (5.1)	-0.012
8+	260 (4.5)	52 (1.7)	-0.029	22 (1.7)	71 (1.6)	-0.001	282 (4.0)	123 (1.6)	-0.024
Comorbidities									
Myocardial Infarction (%)	534 (9.3)	228 (7.3)	-0.020	128 (9.9)	354 (8.1)	-0.018	662 (9.4)	582 (7.8)	-0.017
Congestive Heart Failure (%)	1226 (21.4)	618 (19.8)	-0.016	374 (29.0)	898 (20.5)	-0.085	1600 (22.8)	1516 (20.2)	-0.026
Cerebrovascular Disease (%)	1110 (19.4)	425 (13.6)	-0.058	248 (19.2)	657 (15.0)	-0.042	1358 (19.4)	1082 (14.4)	-0.049
Dementia (%)	946 (16.5)	269 (8.6)	-0.079	222 (17.2)	405 (9.2)	-0.080	1168 (16.6)	674 (9.0)	-0.077
Chronic Obstructive Pulmonary Disease (%)	1312 (22.9)	888 (28.4)	0.055	417 (32.3)	1416 (32.3)	0.000	1729 (24.6)	2304 (30.7)	0.060
Rheumatoid Arthritis (%)	78 (1.4)	54 (1.7)	0.004	19 (1.5)	71 (1.6)	0.001	97 (1.4)	125 (1.7)	0.003
Peptic ulcer (%)	159 (2.8)	44 (1.4)	-0.014	35 (2.7)	85 (1.9)	-0.008	194 (2.8)	129 (1.7)	-0.010
Liver disease, mild (%)	834 (14.6)	327 (10.5)	-0.041	147 (11.4)	435 (9.9)	-0.015	981 (14.0)	762 (10.2)	-0.038
Diabetes, Uncomplicated (%)	2581 (45.1)	1492 (47.8)	0.027	631 (48.9)	2149 (49.0)	0.001	3212 (45.8)	3641 (48.5)	0.027
Diabetes, Complicated (%)	1771 (30.9)	922 (29.5)	-0.014	427 (33.1)	1314 (30.0)	-0.031	2198 (31.3)	2236 (29.8)	-0.015
Hemi or paraplegia (%)	203 (3.5)	48 (1.5)	-0.020	51 (4.0)	78 (1.8)	-0.022	254 (3.6)	126 (1.7)	-0.019
Renal disease (%)	1541 (26.9)	733 (23.5)	-0.034	380 (29.5)	1074 (24.5)	-0.050	1921 (27.4)	1807 (24.1)	-0.033
Liver disease, moderate-severe (%)	124 (2.2)	48 (1.5)	-0.006	24 (1.9)	46 (1.0)	-0.008	148 (2.1)	94 (1.3)	-0.009
Metastatic cancer (%)	138 (2.4)	48 (1.5)	-0.009	24 (1.9)	80 (1.8)	0.000	162 (2.3)	128 (1.7)	-0.006
HIV (%)	69 (1.2)	37 (1.2)	0.000	17 (1.3)	39 (0.9)	-0.004	86 (1.2)	76 (1.0)	-0.002
Charlson Comorbidities Count (%)									
0	1128 (19.7)	655 (21.0)	0.013	209 (16.2)	793 (18.1)	0.019	1337 (19.1)	1448 (19.3)	0.002
1-2	1698 (29.7)	1047 (33.5)	0.039	362 (28.1)	1441 (32.9)	0.048	2060 (29.4)	2488 (33.1)	0.038
3-4	1268 (22.1)	704 (22.5)	0.004	310 (24.0)	1097 (25.0)	0.010	1578 (22.5)	1801 (24.0)	0.015
5+	1632 (28.5)	718 (23.0)	-0.055	409 (31.7)	1052 (24.0)	-0.077	2041 (29.1)	1770 (23.6)	-0.055
Number of Doctors (prior year) (%)									
0	2421 (42.3)	1291 (41.3)	-0.010	493 (38.2)	1639 (37.4)	-0.008	2914 (41.5)	2930 (39.0)	-0.025
1	1493 (26.1)	872 (27.9)	0.018	337 (26.1)	1268 (28.9)	0.028	1830 (26.1)	2140 (28.5)	0.024
2-4	1665 (29.1)	901 (28.8)	-0.002	413 (32.0)	1368 (31.2)	-0.008	2078 (29.6)	2269 (30.2)	0.006
5+	147 (2.6)	60 (1.9)	-0.006	47 (3.6)	108 (2.5)	-0.012	194 (2.8)	168 (2.2)	-0.005

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
Specialty clinics attended									
Cardiology **(%)**	1394 (24.3)	809 (25.9)	0.016	405 (31.4)	1262 (28.8)	-0.026	1799 (25.6)	2071 (27.6)	0.019
Coagulation (%)	93 (1.6)	59 (1.9)	0.003	24 (1.9)	58 (1.3)	-0.005	117 (1.7)	117 (1.6)	-0.001
Pacemaker (%)	198 (3.5)	81 (2.6)	-0.009	67 (5.2)	127 (2.9)	-0.023	265 (3.8)	208 (2.8)	-0.010
Dialysis (%)	93 (1.6)	29 (0.9)	-0.007	38 (2.9)	53 (1.2)	-0.017	131 (1.9)	82 (1.1)	-0.008
Gastoenterology (%)	493 (8.6)	292 (9.3)	0.007	107 (8.3)	434 (9.9)	0.016	600 (8.6)	726 (9.7)	0.011
Hepatology (%)	224 (3.9)	72 (2.3)	-0.016	41 (3.2)	109 (2.5)	-0.007	265 (3.8)	181 (2.4)	-0.014
Homeless (%)	517 (9.0)	124 (4.0)	-0.051	78 (6.0)	139 (3.2)	-0.029	595 (8.5)	263 (3.5)	-0.050
Co-Medications									
Prophylactic Anticoagulants 1st 48 hours (%)	4006 (70.0)	2375 (76.0)	0.061	883 (68.4)	3404 (77.7)	0.092	4889 (69.7)	5779 (77.0)	0.073
Remdesivir, 1st 48 hours (%)	445 (7.8)	2115 (67.7)	0.599	268 (20.8)	3302 (75.3)	0.546	713 (10.2)	5417 (72.2)	0.620
Laboratory values									
Albumin, g/dL (%)									
3.5 +	2300 (40.2)	916 (29.3)	-0.108	384 (29.8)	1122 (25.6)	-0.042	2684 (38.3)	2038 (27.1)	-0.111
3 - 3.49	1720 (30.0)	1116 (35.7)	0.057	434 (33.6)	1581 (36.1)	0.024	2154 (30.7)	2697 (35.9)	0.052
< 3	1315 (23.0)	971 (31.1)	0.081	399 (30.9)	1550 (35.4)	0.044	1714 (24.4)	2521 (33.6)	0.092
Missing	391 (6.8)	121 (3.9)	-0.030	73 (5.7)	130 (3.0)	-0.027	464 (6.6)	251 (3.3)	-0.033
Alanine aminotransferase, IU/L (%)									
< 20	1864 (32.6)	633 (20.3)	-0.123	409 (31.7)	931 (21.2)	-0.105	2273 (32.4)	1564 (20.8)	-0.116
20 - 39	2170 (37.9)	1348 (43.1)	0.053	511 (39.6)	1873 (42.7)	0.031	2681 (38.2)	3221 (42.9)	0.047
40 +	1290 (22.5)	1105 (35.4)	0.128	300 (23.3)	1526 (34.8)	0.116	1590 (22.7)	2631 (35.0)	0.124
Missing	402 (7.0)	38 (1.2)	-0.058	70 (5.4)	53 (1.2)	-0.042	472 (6.7)	91 (1.2)	-0.055
Asparate aminostransferase, IU/L (%)									
< 20	1565 (27.3)	287 (9.2)	-0.181	276 (21.4)	331 (7.6)	-0.138	1841 (26.2)	618 (8.2)	-0.180
20 - 39	2501 (43.7)	1344 (43.0)	-0.007	574 (44.5)	1848 (42.2)	-0.023	3075 (43.8)	3192 (42.5)	-0.013
40 +	1660 (29.0)	1493 (47.8)	0.188	440 (34.1)	2204 (50.3)	0.162	2100 (29.9)	3697 (49.2)	0.193
Creatinine, mg/dL (%)									
< 1.2	2726 (47.6)	1427 (45.7)	-0.019	540 (41.9)	2015 (46.0)	0.041	3266 (46.6)	3442 (45.9)	-0.007
1.2 – 1.99	1899 (33.2)	1235 (39.5)	0.064	479 (37.1)	1655 (37.8)	0.006	2378 (33.9)	2890 (38.5)	0.046
2 +	1013 (17.7)	443 (14.2)	-0.035	258 (20.0)	706 (16.1)	-0.039	1271 (18.1)	1149 (15.3)	-0.028
Missing	88 (1.5)	19 (0.6)	-0.009	13 (1.0)	7 (0.2)	-0.008	101 (1.4)	26 (0.3)	-0.011
Fibrosis-4 Index (%)									

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
< 1.45	1391 (24.3)	539 (17.3)	-0.070	210 (16.3)	599 (13.7)	-0.026	1601 (22.8)	1138 (15.2)	-0.077
1.45 – 3.25	2232 (39.0)	1313 (42.0)	0.030	512 (39.7)	1923 (43.9)	0.042	2744 (39.1)	3236 (43.1)	0.040
3.25 +	1661 (29.0)	1226 (39.2)	0.102	496 (38.4)	1800 (41.1)	0.026	2157 (30.7)	3026 (40.3)	0.096
Missing	442 (7.7)	46 (1.5)	-0.062	72 (5.6)	61 (1.4)	-0.042	514 (7.3)	107 (1.4)	-0.059
Lactate, mmol/L (%)									
<1.2	739 (12.9)	482 (15.4)	0.025	215 (16.7)	707 (16.1)	-0.005	954 (13.6)	1189 (15.8)	0.022
1.2 - <2.0	1164 (20.3)	929 (29.7)	0.094	331 (25.7)	1423 (32.5)	0.068	1495 (21.3)	2352 (31.3)	0.100
2.0+	667 (11.6)	564 (18.1)	0.064	193 (15.0)	727 (16.6)	0.016	860 (12.3)	1291 (17.2)	0.049
Missing	3156 (55.1)	1149 (36.8)	-0.183	551 (42.7)	1526 (34.8)	-0.079	3707 (52.8)	2675 (35.6)	-0.172
Platelet count per microL (%)									
150 or higher	3900 (68.1)	2099 (67.2)	-0.009	803 (62.2)	2962 (67.6)	0.053	4703 (67.0)	5061 (67.4)	0.004
< 150	1741 (30.4)	1019 (32.6)	0.022	479 (37.1)	1416 (32.3)	-0.048	2220 (31.6)	2435 (32.4)	0.008
Missing	85 (1.5)	6 (0.2)	-0.013	8 (0.6)	5 (0.1)	-0.005	93 (1.3)	11 (0.1)	-0.012
Total bilirubin, mg/dL (%)									
<1	4102 (71.6)	2299 (73.6)	0.020	954 (74.0)	3219 (73.4)	-0.005	5056 (72.1)	5518 (73.5)	0.014
1 - 1.2	449 (7.8)	295 (9.4)	0.016	113 (8.8)	467 (10.7)	0.019	562 (8.0)	762 (10.2)	0.021
1.2 +	797 (13.9)	473 (15.1)	0.012	156 (12.1)	640 (14.6)	0.025	953 (13.6)	1113 (14.8)	0.012
Missing	378 (6.6)	57 (1.8)	-0.048	67 (5.2)	57 (1.3)	-0.039	445 (6.3)	114 (1.5)	-0.048
White Blood Count per microL (%)									
4-10	3426 (59.8)	1443 (46.2)	-0.136	732 (56.7)	1890 (43.1)	-0.136	4158 (59.3)	3333 (44.4)	-0.149
<4	1320 (23.1)	915 (29.3)	0.062	346 (26.8)	1344 (30.7)	0.038	1666 (23.7)	2259 (30.1)	0.063
>10	980 (17.1)	766 (24.5)	0.074	212 (16.4)	1149 (26.2)	0.098	1192 (17.0)	1915 (25.5)	0.085
C-reactive protein measured (%)	2786 (48.7)	1947 (62.3)	0.137	723 (56.0)	2793 (63.7)	0.077	3509 (50.0)	4740 (63.1)	0.131
D-dimer measured (%)	3676 (64.2)	2635 (84.3)	0.201	986 (76.4)	3682 (84.0)	0.076	4662 (66.4)	6317 (84.1)	0.177
Vital Signs									
Highest Temperature (F) (%)									
< 99	2620 (45.8)	1071 (34.3)	-0.115	396 (30.7)	1409 (32.1)	0.014	3016 (43.0)	2480 (33.0)	-0.100
99 - 100	1441 (25.2)	752 (24.1)	-0.011	312 (24.2)	1026 (23.4)	-0.008	1753 (25.0)	1778 (23.7)	-0.013
100 - 102	1176 (20.5)	888 (28.4)	0.079	386 (29.9)	1316 (30.0)	0.001	1562 (22.3)	2204 (29.4)	0.071
102 +	475 (8.3)	397 (12.7)	0.044	194 (15.0)	614 (14.0)	-0.010	669 (9.5)	1011 (13.5)	0.039
Missing	14 (0.2)	16 (0.5)	0.003	2 (0.2)	18 (0.4)	0.003	16 (0.2)	34 (0.5)	0.002
Mean Arterial Pressure, mmHg (%)									
< 60	155 (2.7)	55 (1.8)	-0.009	51 (4.0)	74 (1.7)	-0.023	206 (2.9)	129 (1.7)	-0.012

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
60 – 69	787 (13.7)	342 (10.9)	-0.028	222 (17.2)	550 (12.5)	-0.047	1009 (14.4)	892 (11.9)	-0.025
70 – 89	3629 (63.4)	2092 (67.0)	0.036	828 (64.2)	2998 (68.4)	0.042	4457 (63.5)	5090 (67.8)	0.043
90 +	1144 (20.0)	625 (20.0)	0.000	188 (14.6)	747 (17.0)	0.025	1332 (19.0)	1372 (18.3)	-0.007
Missing	11 (0.2)	10 (0.3)	0.001	1 (0.1)	14 (0.3)	0.002	12 (0.2)	24 (0.3)	0.001
Lowest Oxygen Saturation (%)									
< 88	118 (2.1)	319 (10.2)	0.082	106 (8.2)	622 (14.2)	0.060	224 (3.2)	941 (12.5)	0.093
88 - 92	1603 (28.0)	1660 (53.1)	0.251	643 (49.8)	2702 (61.6)	0.118	2246 (32.0)	4362 (58.1)	0.261
93 - 95	2690 (47.0)	863 (27.6)	-0.194	401 (31.1)	794 (18.1)	-0.130	3091 (44.1)	1657 (22.1)	-0.220
96 +	1193 (20.8)	216 (6.9)	-0.139	118 (9.1)	165 (3.8)	-0.054	1311 (18.7)	381 (5.1)	-0.136
Missing	122 (2.1)	66 (2.1)	0.000	22 (1.7)	100 (2.3)	0.006	144 (2.1)	166 (2.2)	0.002

B. Propensity weighted pseudo population estimating the average treatment effect in the entire population (ATE)

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
Cohort, n	8072.1	6801.3		3594.6	5602.9		11963.6	12887.0	
Age, (%)									
<50	807.0 (10.0)	648.8 (9.5)	-0.005	271.7 (7.6)	436.5 (7.8)	0.002	1082.7 (9.0)	1142.0 (8.9)	-0.002
50-59	991.0 (12.3)	847.1 (12.5)	0.002	376.8 (10.5)	657.9 (11.7)	0.013	1367.3 (11.4)	1551.5 (12.0)	0.006
60-69	1863.5 (23.1)	1658.1 (24.4)	0.013	802.6 (22.3)	1254.6 (22.4)	0.001	2800.3 (23.4)	2959.5 (23.0)	-0.004
70-79	2694.9 (33.4)	2283.9 (33.6)	0.002	1331.8 (37.0)	2122.6 (37.9)	0.008	4206.0 (35.2)	4662.9 (36.2)	0.010
80+	1715.8 (21.3)	1363.5 (20.0)	-0.012	811.8 (22.6)	1131.3 (20.2)	-0.024	2507.4 (21.0)	2571.2 (20.0)	-0.010
Sex: Male, (%)	7651.9 (94.8)	6471.7 (95.2)	0.004	3392.6 (94.4)	5332.5 (95.2)	0.008	11323.9 (94.7)	12237.6 (95.0)	0.003
Race, (%)									
White, non-Hispanic	4298.8 (53.3)	3657.7 (53.8)	0.005	2017.2 (56.1)	3172.8 (56.6)	0.005	6430.7 (53.8)	7170.0 (55.6)	0.019
Black, non-Hispanic	2443.2 (30.3)	1883.4 (27.7)	-0.026	933.2 (26.0)	1416.2 (25.3)	-0.007	3567.0 (29.8)	3507.0 (27.2)	-0.026
Hispanic	666.2 (8.3)	673.0 (9.9)	0.016	272.0 (7.6)	483.8 (8.6)	0.011	940.7 (7.9)	1120.5 (8.7)	0.008
Other	428.3 (5.3)	348.7 (5.1)	-0.002	236.1 (6.6)	341.5 (6.1)	-0.005	666.5 (5.6)	673.5 (5.2)	-0.003
Unknown	235.5 (2.9)	238.5 (3.5)	0.006	136.2 (3.8)	188.6 (3.4)	-0.004	358.7 (3.0)	416.1 (3.2)	0.002
Phase (Admission Date) , (%)									
1: June 7 - July 11	444.3 (5.5)	212.1 (3.1)	-0.024	607.5 (16.9)	576.6 (10.3)	-0.066	1112.0 (9.3)	865.6 (6.7)	-0.026
2: July 12 - Aug. 15	501.3 (6.2)	225.4 (3.3)	-0.029	569.6 (15.8)	656.1 (11.7)	-0.041	1063.1 (8.9)	1074.1 (8.3)	-0.006
3: Aug. 16 - Oct. 17	937.0 (11.6)	674.2 (9.9)	-0.017	824.3 (22.9)	1101.0 (19.7)	-0.033	1764.3 (14.7)	1784.1 (13.8)	-0.009
4: Oct. 18 - Nov. 30	895.1 (11.1)	628.7 (9.2)	-0.018	560.0 (15.6)	1163.1 (20.8)	0.052	1567.9 (13.1)	1894.9 (14.7)	0.016
5: Dec. 1 - Dec. 31	1841.7 (22.8)	1806.4 (26.6)	0.037	384.9 (10.7)	809.7 (14.5)	0.037	2347.1 (19.6)	2693.3 (20.9)	0.013
6: Jan. 1 - Jan. 31	1620.7 (20.1)	1653.3 (24.3)	0.042	350.0 (9.7)	676.4 (12.1)	0.023	1998.7 (16.7)	2315.6 (18.0)	0.013
7: Feb. 1 - May 31	1832.1 (22.7)	1601.3 (23.5)	0.008	298.4 (8.3)	620.1 (11.1)	0.028	2110.5 (17.6)	2259.4 (17.5)	-0.001
Site Dexamethasone Prescribing, (%)									
Low	2026.5 (25.1)	1094.8 (16.1)	-0.090	938.8 (26.1)	974.2 (17.4)	-0.087	3173.2 (26.5)	2421.9 (18.8)	-0.077
Medium	4815.2 (59.7)	4102.3 (60.3)	0.007	2151.7 (59.9)	3175.9 (56.7)	-0.032	7115.5 (59.5)	7480.7 (58.0)	-0.014
High	1230.4 (15.2)	1604.2 (23.6)	0.083	504.1 (14.0)	1452.7 (25.9)	0.119	1674.9 (14.0)	2984.5 (23.2)	0.092
Smoking Status, (%)									
Unknown	262.5 (3.3)	187.8 (2.8)	-0.005	109.3 (3.0)	158.1 (2.8)	-0.002	384.8 (3.2)	384.5 (3.0)	-0.002
Never Smoker	2848.7 (35.3)	2590.4 (38.1)	0.028	1201.3 (33.4)	1886.7 (33.7)	0.003	4080.9 (34.1)	4491.1 (34.8)	0.007
Former Smoker	2952.7 (36.6)	2577.3 (37.9)	0.013	1481.1 (41.2)	2425.1 (43.3)	0.021	4576.0 (38.2)	5277.6 (41.0)	0.027
Current Smoker	2008.2 (24.9)	1445.8 (21.3)	-0.036	802.9 (22.3)	1133.0 (20.2)	-0.021	2921.8 (24.4)	2734.0 (21.2)	-0.032

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
AUDIT-C Score (%)									
Unknown	302.2 (3.7)	195.8 (2.9)	-0.009	122.4 (3.4)	166.8 (3.0)	-0.004	441.7 (3.7)	431.4 (3.3)	-0.003
0	5274.8 (65.3)	4451.1 (65.4)	0.001	2454.8 (68.3)	3800.4 (67.8)	-0.005	7978.6 (66.7)	8489.5 (65.9)	-0.008
1-3	1648.0 (20.4)	1553.9 (22.8)	0.024	795.5 (22.1)	1293.3 (23.1)	0.010	2456.4 (20.5)	2962.0 (23.0)	0.025
4-7	562.1 (7.0)	435.6 (6.4)	-0.006	169.8 (4.7)	253.7 (4.5)	-0.002	734.5 (6.1)	719.6 (5.6)	-0.006
8+	285.1 (3.5)	164.9 (2.4)	-0.011	52.0 (1.4)	88.7 (1.6)	0.001	352.5 (2.9)	284.6 (2.2)	-0.007
Comorbidities									
Myocardial Infarction (%)	714.1 (8.8)	504.4 (7.4)	-0.014	373.0 (10.4)	495.4 (8.8)	-0.015	1078.8 (9.0)	1096.0 (8.5)	-0.005
Congestive Heart Failure (%)	1718.5 (21.3)	1375.3 (20.2)	-0.011	921.3 (25.6)	1282.0 (22.9)	-0.027	2678.1 (22.4)	2865.7 (22.2)	-0.001
Cerebrovascular Disease (%)	1437.7 (17.8)	1065.1 (15.7)	-0.022	655.4 (18.2)	930.5 (16.6)	-0.016	2113.7 (17.7)	2094.2 (16.3)	-0.014
Dementia (%)	1177.4 (14.6)	727.9 (10.7)	-0.039	530.7 (14.8)	635.2 (11.3)	-0.034	1748.8 (14.6)	1448.8 (11.2)	-0.034
Chronic Obstructive Pulmonary Disease (%)	1970.4 (24.4)	1759.3 (25.9)	0.015	1124.8 (31.3)	1812.0 (32.3)	0.010	3131.2 (26.2)	3760.1 (29.2)	0.030
Rheumatoid Arthritis (%)	124.1 (1.5)	94.5 (1.4)	-0.001	69.5 (1.9)	86.0 (1.5)	-0.004	186.2 (1.6)	206.8 (1.6)	0.000
Peptic ulcer (%)	179.7 (2.2)	103.2 (1.5)	-0.007	88.0 (2.4)	127.5 (2.3)	-0.002	272.0 (2.3)	270.9 (2.1)	-0.002
Liver disease, mild (%)	1053.4 (13.0)	848.3 (12.5)	-0.006	364.9 (10.1)	577.9 (10.3)	0.002	1504.2 (12.6)	1452.8 (11.3)	-0.013
Diabetes, Uncomplicated (%)	3704.1 (45.9)	3265.6 (48.0)	0.021	1757.1 (48.9)	2760.5 (49.3)	0.004	5683.8 (47.5)	6182.6 (48.0)	0.005
Diabetes, Complicated (%)	2520.2 (31.2)	2086.1 (30.7)	-0.005	1167.4 (32.5)	1714.2 (30.6)	-0.019	3873.3 (32.4)	3969.4 (30.8)	-0.016
Hemi or paraplegia (%)	235.8 (2.9)	140.1 (2.1)	-0.009	99.2 (2.8)	120.2 (2.1)	-0.006	341.0 (2.9)	285.3 (2.2)	-0.006
Renal disease (%)	2155.8 (26.7)	1794.8 (26.4)	-0.003	1062.6 (29.6)	1449.3 (25.9)	-0.037	3228.2 (27.0)	3422.0 (26.6)	-0.004
Liver disease, moderate-severe (%)	170.9 (2.1)	125.7 (1.8)	-0.003	42.0 (1.2)	68.6 (1.2)	0.001	226.5 (1.9)	205.6 (1.6)	-0.003
Metastatic cancer (%)	189.7 (2.4)	135.6 (2.0)	-0.004	66.2 (1.8)	108.0 (1.9)	0.001	293.0 (2.4)	256.2 (2.0)	-0.005
HIV (%)	99.5 (1.2)	94.0 (1.4)	0.002	66.2 (1.8)	71.8 (1.3)	-0.006	153.5 (1.3)	150.8 (1.2)	-0.001
Charlson Comorbidities Count (%)									
0	1564.1 (19.4)	1339.5 (19.7)	0.003	617.6 (17.2)	973.5 (17.4)	0.002	2212.6 (18.5)	2412.7 (18.7)	0.002
1-2	2451.6 (30.4)	2182.3 (32.1)	0.017	1031.5 (28.7)	1768.4 (31.6)	0.029	3634.1 (30.4)	4065.3 (31.5)	0.012
3-4	1831.3 (22.7)	1492.8 (21.9)	-0.007	883.1 (24.6)	1378.4 (24.6)	0.000	2780.0 (23.2)	3018.6 (23.4)	0.002
5+	2225.1 (27.6)	1786.7 (26.3)	-0.013	1062.4 (29.6)	1482.5 (26.5)	-0.031	3336.9 (27.9)	3390.4 (26.3)	-0.016
Number of Doctors (prior year) (%)									
0	3355.1 (41.6)	2775.9 (40.8)	-0.007	1306.9 (36.4)	2073.4 (37.0)	0.006	4815.2 (40.2)	5033.7 (39.1)	-0.012
1	2145.1 (26.6)	1870.4 (27.5)	0.009	955.4 (26.6)	1622.0 (28.9)	0.024	3240.7 (27.1)	3585.3 (27.8)	0.007
2-4	2373.8 (29.4)	2010.5 (29.6)	0.002	1214.9 (33.8)	1764.0 (31.5)	-0.023	3564.9 (29.8)	3946.2 (30.6)	0.008
5+	198.1 (2.5)	144.5 (2.1)	-0.003	117.4 (3.3)	143.5 (2.6)	-0.007	342.8 (2.9)	321.8 (2.5)	-0.004
Specialty clinics attended									

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
Cardiology **(%)**	2009.2 (24.9)	1732.1 (25.5)	0.006	1097.7 (30.5)	1680.2 (30.0)	-0.005	3108.1 (26.0)	3528.6 (27.4)	0.014
Coagulation (%)	137.3 (1.7)	116.6 (1.7)	0.000	44.3 (1.2)	82.1 (1.5)	0.002	192.2 (1.6)	214.1 (1.7)	0.001
Pacemaker (%)	261.0 (3.2)	176.0 (2.6)	-0.006	161.9 (4.5)	191.6 (3.4)	-0.011	428.2 (3.6)	424.7 (3.3)	-0.003
Dialysis (%)	117.2 (1.5)	115.0 (1.7)	0.002	99.4 (2.8)	94.2 (1.7)	-0.011	206.6 (1.7)	218.6 (1.7)	0.000
Gastoenterology (%)	752.9 (9.3)	581.6 (8.6)	-0.008	332.9 (9.3)	528.2 (9.4)	0.002	1147.9 (9.6)	1277.5 (9.9)	0.003
Hepatology (%)	276.9 (3.4)	193.4 (2.8)	-0.006	106.1 (3.0)	153.4 (2.7)	-0.002	426.1 (3.6)	359.0 (2.8)	-0.008
Homeless (%)	619.4 (7.7)	362.9 (5.3)	-0.023	198.0 (5.5)	221.2 (3.9)	-0.016	817.4 (6.8)	596.1 (4.6)	-0.022
Co-Medications									
Prophylactic Anticoagulants 1st 48 hours (%)	5781.6 (71.6)	5062.6 (74.4)	0.028	2604.7 (72.5)	4253.2 (75.9)	0.034	8665.8 (72.4)	9589.0 (74.4)	0.020
Remdesivir, 1st 48 hours (%)	1867.5 (23.1)	2555.9 (37.6)	0.144	1522.2 (42.3)	3510.2 (62.7)	0.203	3664.1 (30.6)	6050.4 (46.9)	0.163
Laboratory values									
Albumin, g/dL (%)									
3.5 +	2971.4 (36.8)	2217.8 (32.6)	-0.042	1039.5 (28.9)	1501.5 (26.8)	-0.021	4070.5 (34.0)	3839.1 (29.8)	-0.042
3 - 3.49	2643.7 (32.8)	2356.3 (34.6)	0.019	1238.6 (34.5)	1983.4 (35.4)	0.009	3935.0 (32.9)	4550.6 (35.3)	0.024
< 3	2004.0 (24.8)	1951.3 (28.7)	0.039	1168.2 (32.5)	1931.2 (34.5)	0.020	3361.2 (28.1)	3986.4 (30.9)	0.028
Missing	453.0 (5.6)	276.0 (4.1)	-0.016	148.3 (4.1)	186.8 (3.3)	-0.008	596.9 (5.0)	510.9 (4.0)	-0.010
Alanine aminotransferase, IU/L (%)									
< 20	2424.1 (30.0)	1771.8 (26.1)	-0.040	975.1 (27.1)	1310.1 (23.4)	-0.037	3461.5 (28.9)	3151.6 (24.5)	-0.045
20 - 39	3144.7 (39.0)	2722.1 (40.0)	0.011	1510.6 (42.0)	2396.5 (42.8)	0.007	4786.1 (40.0)	5418.4 (42.0)	0.020
40 +	2098.6 (26.0)	2136.3 (31.4)	0.054	1006.2 (28.0)	1789.2 (31.9)	0.039	3195.2 (26.7)	3995.4 (31.0)	0.043
Missing	404.7 (5.0)	171.0 (2.5)	-0.025	102.7 (2.9)	107.1 (1.9)	-0.009	520.8 (4.4)	321.6 (2.5)	-0.019
Asparate aminostransferase, IU/L (%)									
< 20	1758.6 (21.8)	934.8 (13.7)	-0.080	502.6 (14.0)	572.1 (10.2)	-0.038	2285.0 (19.1)	1586.6 (12.3)	-0.068
20 - 39	3510.0 (43.5)	2998.7 (44.1)	0.006	1591.8 (44.3)	2437.9 (43.5)	-0.008	5309.3 (44.4)	5767.2 (44.8)	0.004
40 +	2803.5 (34.7)	2867.8 (42.2)	0.074	1500.3 (41.7)	2592.9 (46.3)	0.045	4369.3 (36.5)	5533.2 (42.9)	0.064
Creatinine, mg/dL (%)									
< 1.2	3692.5 (45.7)	2972.3 (43.7)	-0.020	1471.4 (40.9)	2501.2 (44.6)	0.037	5238.4 (43.8)	5616.3 (43.6)	-0.002
1.2 – 1.99	2892.6 (35.8)	2574.4 (37.9)	0.020	1399.8 (38.9)	2118.8 (37.8)	-0.011	4423.3 (37.0)	4862.7 (37.7)	0.008
2 +	1387.3 (17.2)	1224.0 (18.0)	0.008	708.7 (19.7)	974.1 (17.4)	-0.023	2196.7 (18.4)	2367.4 (18.4)	0.000
Missing	99.6 (1.2)	30.6 (0.4)	-0.008	14.8 (0.4)	8.8 (0.2)	-0.003	105.2 (0.9)	40.6 (0.3)	-0.006
Fibrosis-4 Index (%)									
< 1.45	1753.2 (21.7)	1263.6 (18.6)	-0.031	507.7 (14.1)	791.1 (14.1)	0.000	2289.3 (19.1)	2087.1 (16.2)	-0.029

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
1.45 – 3.25	3175.6 (39.3)	2785.6 (41.0)	0.016	1477.8 (41.1)	2418.4 (43.2)	0.021	4791.3 (40.0)	5341.2 (41.4)	0.014
3.25 +	2686.8 (33.3)	2565.5 (37.7)	0.044	1502.2 (41.8)	2276.9 (40.6)	-0.012	4308.2 (36.0)	5107.3 (39.6)	0.036
Missing	456.5 (5.7)	186.6 (2.7)	-0.029	107.0 (3.0)	116.5 (2.1)	-0.009	574.8 (4.8)	351.5 (2.7)	-0.021
Lactate, mmol/L (%)									
<1.2	1079.9 (13.4)	1033.2 (15.2)	0.018	606.2 (16.9)	924.8 (16.5)	-0.004	1764.8 (14.8)	2009.6 (15.6)	0.008
1.2 - <2.0	1932.7 (23.9)	1911.1 (28.1)	0.042	1028.3 (28.6)	1747.7 (31.2)	0.026	3020.2 (25.2)	3732.9 (29.0)	0.037
2.0+	1091.5 (13.5)	1077.5 (15.8)	0.023	579.7 (16.1)	908.6 (16.2)	0.001	1626.1 (13.6)	2027.5 (15.7)	0.021
Missing	3968.0 (49.2)	2779.5 (40.9)	-0.083	1380.4 (38.4)	2021.8 (36.1)	-0.023	5552.5 (46.4)	5117.0 (39.7)	-0.067
Platelet count per microL (%)									
150 or higher	5456.1 (67.6)	4504.8 (66.2)	-0.014	2273.1 (63.2)	3709.6 (66.2)	0.030	7892.8 (66.0)	8381.1 (65.0)	-0.009
< 150	2542.9 (31.5)	2288.1 (33.6)	0.021	1312.2 (36.5)	1885.7 (33.7)	-0.029	3988.7 (33.3)	4482.4 (34.8)	0.014
Missing	73.1 (0.9)	8.5 (0.1)	-0.008	9.3 (0.3)	7.7 (0.1)	-0.001	82.1 (0.7)	23.6 (0.2)	-0.005
Total bilirubin, mg/dL (%)									
<1	5850.6 (72.5)	5009.8 (73.7)	0.012	2738.6 (76.2)	4170.8 (74.4)	-0.017	8779.4 (73.4)	9524.9 (73.9)	0.005
1 - 1.2	650.1 (8.1)	602.3 (8.9)	0.008	291.0 (8.1)	556.4 (9.9)	0.018	1004.1 (8.4)	1187.0 (9.2)	0.008
1.2 +	1163.5 (14.4)	1014.1 (14.9)	0.005	461.2 (12.8)	769.4 (13.7)	0.009	1664.4 (13.9)	1857.2 (14.4)	0.005
Missing	407.9 (5.1)	175.2 (2.6)	-0.025	103.9 (2.9)	106.3 (1.9)	-0.010	515.7 (4.3)	318.0 (2.5)	-0.018
White Blood Count per microL (%)									
4-10	4515.2 (55.9)	3361.8 (49.4)	-0.065	1926.9 (53.6)	2578.4 (46.0)	-0.076	6641.3 (55.5)	6266.6 (48.6)	-0.069
<4	2095.3 (26.0)	1972.6 (29.0)	0.030	997.2 (27.7)	1699.2 (30.3)	0.026	3139.3 (26.2)	3812.3 (29.6)	0.033
>10	1461.7 (18.1)	1466.9 (21.6)	0.035	670.6 (18.7)	1325.3 (23.7)	0.050	2183.1 (18.2)	2808.2 (21.8)	0.035
C-reactive protein measured (%)	4320.2 (53.5)	4113.1 (60.5)	0.070	2174.7 (60.5)	3484.6 (62.2)	0.017	6674.9 (55.8)	7810.0 (60.6)	0.048
D-dimer measured (%)	5648.2 (70.0)	5406.0 (79.5)	0.095	2876.9 (80.0)	4655.2 (83.1)	0.031	8791.6 (73.5)	10350.8 (80.3)	0.068
Vital Signs									
Highest Temperature (F) (%)									
< 99	3407.6 (42.2)	2500.0 (36.8)	-0.055	986.1 (27.4)	1746.3 (31.2)	0.037	4466.1 (37.3)	4443.3 (34.5)	-0.029
99 - 100	1974.6 (24.5)	1607.0 (23.6)	-0.008	799.8 (22.3)	1331.8 (23.8)	0.015	2919.2 (24.4)	3106.8 (24.1)	-0.003
100 - 102	1848.1 (22.9)	1773.1 (26.1)	0.032	1163.4 (32.4)	1708.9 (30.5)	-0.019	3077.0 (25.7)	3567.9 (27.7)	0.020
102 +	811.4 (10.1)	881.4 (13.0)	0.029	639.1 (17.8)	800.7 (14.3)	-0.035	1459.9 (12.2)	1719.3 (13.3)	0.011
Missing	30.4 (0.4)	39.8 (0.6)	0.002	6.1 (0.2)	15.2 (0.3)	0.001	41.4 (0.3)	49.7 (0.4)	0.000
Mean Arterial Pressure, mmHg (%)									
< 60	212.6 (2.6)	149.6 (2.2)	-0.004	97.1 (2.7)	106.8 (1.9)	-0.008	320.4 (2.7)	282.2 (2.2)	-0.005
60 – 69	1044.4 (12.9)	827.9 (12.2)	-0.008	625.3 (17.4)	784.1 (14.0)	-0.034	1627.5 (13.6)	1682.2 (13.1)	-0.006

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
70 – 89	5161.5 (63.9)	4474.7 (65.8)	0.018	2372.0 (66.0)	3785.1 (67.6)	0.016	7805.2 (65.2)	8623.3 (66.9)	0.017
90 +	1632.3 (20.2)	1325.1 (19.5)	-0.007	495.4 (13.8)	915.0 (16.3)	0.025	2183.3 (18.2)	2266.1 (17.6)	-0.007
Missing	21.3 (0.3)	24.0 (0.4)	0.001	4.8 (0.1)	11.9 (0.2)	0.001	27.2 (0.2)	33.3 (0.3)	0.000
Lowest Oxygen Saturation (%)									
< 88	269.7 (3.3)	412.6 (6.1)	0.027	386.2 (10.7)	709.6 (12.7)	0.019	643.0 (5.4)	1099.6 (8.5)	0.032
88 - 92	2760.1 (34.2)	3021.3 (44.4)	0.102	1974.6 (54.9)	3319.6 (59.2)	0.043	4961.0 (41.5)	6515.0 (50.6)	0.091
93 - 95	3462.4 (42.9)	2437.4 (35.8)	-0.071	967.7 (26.9)	1188.9 (21.2)	-0.057	4459.7 (37.3)	3888.3 (30.2)	-0.071
96 +	1387.7 (17.2)	776.4 (11.4)	-0.058	209.8 (5.8)	272.9 (4.9)	-0.010	1651.6 (13.8)	1106.9 (8.6)	-0.052
Missing	192.3 (2.4)	153.7 (2.3)	-0.001	56.4 (1.6)	111.8 (2.0)	0.004	248.3 (2.1)	277.2 (2.2)	0.001

C. Propensity weighted pseudo population estimating the average treatment effect in the treated population (ATT)

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
Cohort, n	1800.0	3124.0		2324.6	4383.0		4425.3	7507.0	
Age, (%)									
<50	145.5 (8.1)	310.0 (9.9)	0.018	194.6 (8.4)	356.0 (8.1)	-0.003	333.7 (7.5)	666.0 (8.9)	0.013
50-59	205.6 (11.4)	438.0 (14.0)	0.026	239.3 (10.3)	521.0 (11.9)	0.016	471.6 (10.7)	959.0 (12.8)	0.021
60-69	444.3 (24.7)	718.0 (23.0)	-0.017	517.6 (22.3)	995.0 (22.7)	0.004	1057.7 (23.9)	1713.0 (22.8)	-0.011
70-79	644.3 (35.8)	1072.0 (34.3)	-0.015	876.1 (37.7)	1664.0 (38.0)	0.003	1601.2 (36.2)	2736.0 (36.4)	0.003
80+	360.4 (20.0)	586.0 (18.8)	-0.013	497.0 (21.4)	847.0 (19.3)	-0.021	961.1 (21.7)	1433.0 (19.1)	-0.026
Sex: Male, (%)	1703.4 (94.6)	2963.0 (94.8)	0.002	2182.6 (93.9)	4168.0 (95.1)	0.012	4194.1 (94.8)	7131.0 (95.0)	0.002
Race, (%)									
White, non-Hispanic	1015.8 (56.4)	1711.0 (54.8)	-0.017	1327.6 (57.1)	2507.0 (57.2)	0.001	2417.5 (54.6)	4218.0 (56.2)	0.016
Black, non-Hispanic	517.0 (28.7)	820.0 (26.2)	-0.025	567.3 (24.4)	1077.0 (24.6)	0.002	1271.0 (28.7)	1897.0 (25.3)	-0.035
Hispanic	137.4 (7.6)	300.0 (9.6)	0.020	186.8 (8.0)	414.0 (9.4)	0.014	375.2 (8.5)	714.0 (9.5)	0.010
Other	83.3 (4.6)	176.0 (5.6)	0.010	161.8 (7.0)	244.0 (5.6)	-0.014	223.5 (5.1)	420.0 (5.6)	0.005
Unknown	46.5 (2.6)	117.0 (3.7)	0.012	81.1 (3.5)	141.0 (3.2)	-0.003	138.1 (3.1)	258.0 (3.4)	0.003
Phase (Admission Date) , (%)									
1: June 7 - July 11	41.3 (2.3)	38.0 (1.2)	-0.011	318.1 (13.7)	258.0 (5.9)	-0.078	396.8 (9.0)	296.0 (3.9)	-0.050
2: July 12 - Aug. 15	54.0 (3.0)	64.0 (2.0)	-0.010	355.4 (15.3)	468.0 (10.7)	-0.046	361.2 (8.2)	532.0 (7.1)	-0.011
3: Aug. 16 - Oct. 17	181.4 (10.1)	186.0 (6.0)	-0.041	541.2 (23.3)	812.0 (18.5)	-0.048	640.1 (14.5)	998.0 (13.3)	-0.012
4: Oct. 18 - Nov. 30	164.4 (9.1)	180.0 (5.8)	-0.034	396.0 (17.0)	993.0 (22.7)	0.056	640.5 (14.5)	1173.0 (15.6)	0.012
5: Dec. 1 - Dec. 31	510.4 (28.4)	947.0 (30.3)	0.020	258.9 (11.1)	696.0 (15.9)	0.047	917.8 (20.7)	1643.0 (21.9)	0.011
6: Jan. 1 - Jan. 31	444.1 (24.7)	878.0 (28.1)	0.034	256.9 (11.1)	608.0 (13.9)	0.028	765.3 (17.3)	1486.0 (19.8)	0.025
7: Feb. 1 - May 31	404.4 (22.5)	831.0 (26.6)	0.041	198.1 (8.5)	548.0 (12.5)	0.040	703.5 (15.9)	1379.0 (18.4)	0.025
Site Dexamethasone Prescribing, (%)									
Low	381.1 (21.2)	405.0 (13.0)	-0.082	525.1 (22.6)	594.0 (13.6)	-0.090	1013.6 (22.9)	999.0 (13.3)	-0.096
Medium	1063.0 (59.1)	1787.0 (57.2)	-0.019	1434.4 (61.7)	2451.0 (55.9)	-0.058	2622.1 (59.3)	4238.0 (56.5)	-0.028
High	355.9 (19.8)	932.0 (29.8)	0.101	365.1 (15.7)	1338.0 (30.5)	0.148	789.6 (17.8)	2270.0 (30.2)	0.124
Smoking Status, (%)									
Unknown	48.2 (2.7)	91.0 (2.9)	0.002	61.1 (2.6)	117.0 (2.7)	0.000	116.3 (2.6)	208.0 (2.8)	0.001
Never Smoker	635.5 (35.3)	1173.0 (37.5)	0.022	772.0 (33.2)	1479.0 (33.7)	0.005	1534.1 (34.7)	2652.0 (35.3)	0.007
Former Smoker	734.7 (40.8)	1268.0 (40.6)	-0.002	970.5 (41.7)	1936.0 (44.2)	0.024	1837.5 (41.5)	3204.0 (42.7)	0.012
Current Smoker	381.6 (21.2)	592.0 (19.0)	-0.023	521.0 (22.4)	851.0 (19.4)	-0.030	937.3 (21.2)	1443.0 (19.2)	-0.020
AUDIT-C Score (%)									

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
Unknown	50.1 (2.8)	86.0 (2.8)	0.000	61.3 (2.6)	125.0 (2.9)	0.002	117.6 (2.7)	211.0 (2.8)	0.002
0	1222.6 (67.9)	2048.0 (65.6)	-0.024	1574.6 (67.7)	2928.0 (66.8)	-0.009	3016.6 (68.2)	4976.0 (66.3)	-0.019
1-3	381.2 (21.2)	756.0 (24.2)	0.030	539.9 (23.2)	1055.0 (24.1)	0.008	980.1 (22.1)	1811.0 (24.1)	0.020
4-7	111.0 (6.2)	182.0 (5.8)	-0.003	117.8 (5.1)	204.0 (4.7)	-0.004	250.1 (5.7)	386.0 (5.1)	-0.005
8+	35.1 (1.9)	52.0 (1.7)	-0.003	30.9 (1.3)	71.0 (1.6)	0.003	61.0 (1.4)	123.0 (1.6)	0.003
Comorbidities									
Myocardial Infarction (%)	149.5 (8.3)	228.0 (7.3)	-0.010	249.5 (10.7)	354.0 (8.1)	-0.027	405.6 (9.2)	582.0 (7.8)	-0.014
Congestive Heart Failure (%)	394.0 (21.9)	618.0 (19.8)	-0.021	561.2 (24.1)	898.0 (20.5)	-0.037	988.4 (22.3)	1516.0 (20.2)	-0.021
Cerebrovascular Disease (%)	294.5 (16.4)	425.0 (13.6)	-0.028	415.9 (17.9)	657.0 (15.0)	-0.029	747.4 (16.9)	1082.0 (14.4)	-0.025
Dementia (%)	201.7 (11.2)	269.0 (8.6)	-0.026	311.9 (13.4)	405.0 (9.2)	-0.042	540.9 (12.2)	674.0 (9.0)	-0.032
Chronic Obstructive Pulmonary Disease (%)	489.4 (27.2)	888.0 (28.4)	0.012	724.0 (31.1)	1416.0 (32.3)	0.012	1297.3 (29.3)	2304.0 (30.7)	0.014
Rheumatoid Arthritis (%)	32.4 (1.8)	54.0 (1.7)	-0.001	50.5 (2.2)	71.0 (1.6)	-0.006	77.7 (1.8)	125.0 (1.7)	-0.001
Peptic ulcer (%)	27.7 (1.5)	44.0 (1.4)	-0.001	53.8 (2.3)	85.0 (1.9)	-0.004	81.9 (1.9)	129.0 (1.7)	-0.001
Liver disease, mild (%)	204.4 (11.4)	327.0 (10.5)	-0.009	225.4 (9.7)	435.0 (9.9)	0.002	465.3 (10.5)	762.0 (10.2)	-0.004
Diabetes, Uncomplicated (%)	873.7 (48.5)	1492.0 (47.8)	-0.008	1125.6 (48.4)	2149.0 (49.0)	0.006	2210.3 (49.9)	3641.0 (48.5)	-0.014
Diabetes, Complicated (%)	565.8 (31.4)	922.0 (29.5)	-0.019	728.2 (31.3)	1314.0 (30.0)	-0.013	1416.1 (32.0)	2236.0 (29.8)	-0.022
Hemi or paraplegia (%)	39.8 (2.2)	48.0 (1.5)	-0.007	47.8 (2.1)	78.0 (1.8)	-0.003	91.9 (2.1)	126.0 (1.7)	-0.004
Renal disease (%)	467.3 (26.0)	733.0 (23.5)	-0.025	684.9 (29.5)	1074.0 (24.5)	-0.050	1208.8 (27.3)	1807.0 (24.1)	-0.032
Liver disease, moderate-severe (%)	29.3 (1.6)	48.0 (1.5)	-0.001	18.9 (0.8)	46.0 (1.0)	0.002	64.8 (1.5)	94.0 (1.3)	-0.002
Metastatic cancer (%)	40.7 (2.3)	48.0 (1.5)	-0.007	43.1 (1.9)	80.0 (1.8)	0.000	115.9 (2.6)	128.0 (1.7)	-0.009
HIV (%)	30.5 (1.7)	37.0 (1.2)	-0.005	50.1 (2.2)	39.0 (0.9)	-0.013	68.4 (1.5)	76.0 (1.0)	-0.005
Charlson Comorbidities Count (%)									
0	329.4 (18.3)	655.0 (21.0)	0.027	415.9 (17.9)	793.0 (18.1)	0.002	747.7 (16.9)	1448.0 (19.3)	0.024
1-2	582.7 (32.4)	1047.0 (33.5)	0.011	686.0 (29.5)	1441.0 (32.9)	0.034	1435.8 (32.4)	2488.0 (33.1)	0.007
3-4	419.5 (23.3)	704.0 (22.5)	-0.008	552.6 (23.8)	1097.0 (25.0)	0.013	1051.8 (23.8)	1801.0 (24.0)	0.002
5+	468.5 (26.0)	718.0 (23.0)	-0.030	670.0 (28.8)	1052.0 (24.0)	-0.048	1190.0 (26.9)	1770.0 (23.6)	-0.033
Number of Doctors (prior year) (%)									
0	739.6 (41.1)	1291.0 (41.3)	0.002	834.3 (35.9)	1639.0 (37.4)	0.015	1756.5 (39.7)	2930.0 (39.0)	-0.007
1	502.8 (27.9)	872.0 (27.9)	0.000	633.0 (27.2)	1268.0 (28.9)	0.017	1170.1 (26.4)	2140.0 (28.5)	0.021
2-4	512.8 (28.5)	901.0 (28.8)	0.004	785.9 (33.8)	1368.0 (31.2)	-0.026	1359.5 (30.7)	2269.0 (30.2)	-0.005
5+	44.9 (2.5)	60.0 (1.9)	-0.006	71.4 (3.1)	108.0 (2.5)	-0.006	139.2 (3.1)	168.0 (2.2)	-0.009
Specialty clinics attended									

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
Cardiology **(%)**	441.0 (24.5)	809.0 (25.9)	0.014	709.1 (30.5)	1262.0 (28.8)	-0.017	1159.7 (26.2)	2071.0 (27.6)	0.014
Coagulation (%)	28.7 (1.6)	59.0 (1.9)	0.003	23.2 (1.0)	58.0 (1.3)	0.003	64.5 (1.5)	117.0 (1.6)	0.001
Pacemaker (%)	54.2 (3.0)	81.0 (2.6)	-0.004	95.8 (4.1)	127.0 (2.9)	-0.012	145.2 (3.3)	208.0 (2.8)	-0.005
Dialysis (%)	24.2 (1.3)	29.0 (0.9)	-0.004	61.1 (2.6)	53.0 (1.2)	-0.014	75.6 (1.7)	82.0 (1.1)	-0.006
Gastoenterology (%)	174.2 (9.7)	292.0 (9.3)	-0.003	228.9 (9.8)	434.0 (9.9)	0.001	448.6 (10.1)	726.0 (9.7)	-0.005
Hepatology (%)	50.6 (2.8)	72.0 (2.3)	-0.005	66.8 (2.9)	109.0 (2.5)	-0.004	122.8 (2.8)	181.0 (2.4)	-0.004
Homeless (%)	97.2 (5.4)	124.0 (4.0)	-0.014	120.5 (5.2)	139.0 (3.2)	-0.020	199.0 (4.5)	263.0 (3.5)	-0.010
Co-Medications									
Prophylactic Anticoagulants 1st 48 hours (%)	1351.7 (75.1)	2375.0 (76.0)	0.009	1726.9 (74.3)	3404.0 (77.7)	0.034	3315.3 (74.9)	5779.0 (77.0)	0.021
Remdesivir, 1st 48 hours (%)	800.6 (44.5)	2115.0 (67.7)	0.232	1275.1 (54.9)	3302.0 (75.3)	0.205	2391.0 (54.0)	5417.0 (72.2)	0.181
Laboratory values									
Albumin, g/dL (%)									
3.5 +	542.4 (30.1)	916.0 (29.3)	-0.008	632.6 (27.2)	1122.0 (25.6)	-0.016	1291.8 (29.2)	2038.0 (27.1)	-0.020
3 - 3.49	642.2 (35.7)	1116.0 (35.7)	0.000	826.5 (35.6)	1581.0 (36.1)	0.005	1479.2 (33.4)	2697.0 (35.9)	0.025
< 3	539.9 (30.0)	971.0 (31.1)	0.011	790.4 (34.0)	1550.0 (35.4)	0.014	1493.7 (33.8)	2521.0 (33.6)	-0.002
Missing	75.4 (4.2)	121.0 (3.9)	-0.003	75.0 (3.2)	130.0 (3.0)	-0.003	160.6 (3.6)	251.0 (3.3)	-0.003
Alanine aminotransferase, IU/L (%)									
< 20	492.9 (27.4)	633.0 (20.3)	-0.071	556.7 (23.9)	931.0 (21.2)	-0.027	1117.4 (25.2)	1564.0 (20.8)	-0.044
20 - 39	759.2 (42.2)	1348.0 (43.1)	0.010	1010.7 (43.5)	1873.0 (42.7)	-0.007	1883.3 (42.6)	3221.0 (42.9)	0.003
40 +	515.2 (28.6)	1105.0 (35.4)	0.067	724.9 (31.2)	1526.0 (34.8)	0.036	1351.1 (30.5)	2631.0 (35.0)	0.045
Missing	32.7 (1.8)	38.0 (1.2)	-0.006	32.3 (1.4)	53.0 (1.2)	-0.002	73.5 (1.7)	91.0 (1.2)	-0.004
Asparate aminostransferase, IU/L (%)									
< 20	232.9 (12.9)	287.0 (9.2)	-0.038	227.3 (9.8)	331.0 (7.6)	-0.022	480.6 (10.9)	618.0 (8.2)	-0.026
20 - 39	837.7 (46.5)	1344.0 (43.0)	-0.035	1043.5 (44.9)	1848.0 (42.2)	-0.027	2013.5 (45.5)	3192.0 (42.5)	-0.030
40 +	729.4 (40.5)	1493.0 (47.8)	0.073	1053.8 (45.3)	2204.0 (50.3)	0.050	1931.2 (43.6)	3697.0 (49.2)	0.056
Creatinine, mg/dL (%)									
< 1.2	774.8 (43.0)	1427.0 (45.7)	0.026	947.0 (40.7)	2015.0 (46.0)	0.052	1816.1 (41.0)	3442.0 (45.9)	0.048
1.2 – 1.99	695.2 (38.6)	1235.0 (39.5)	0.009	928.6 (39.9)	1655.0 (37.8)	-0.022	1742.2 (39.4)	2890.0 (38.5)	-0.009
2 +	326.3 (18.1)	443.0 (14.2)	-0.039	447.4 (19.2)	706.0 (16.1)	-0.031	840.9 (19.0)	1149.0 (15.3)	-0.037
Missing	3.7 (0.2)	19.0 (0.6)	0.004	1.5 (0.1)	7.0 (0.2)	0.001	26.1 (0.6)	26.0 (0.3)	-0.002
Fibrosis-4 Index (%)									
< 1.45	327.4 (18.2)	539.0 (17.3)	-0.009	302.8 (13.0)	599.0 (13.7)	0.006	667.6 (15.1)	1138.0 (15.2)	0.001

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
1.45 – 3.25	743.3 (41.3)	1313.0 (42.0)	0.007	990.9 (42.6)	1923.0 (43.9)	0.012	1836.7 (41.5)	3236.0 (43.1)	0.016
3.25 +	683.9 (38.0)	1226.0 (39.2)	0.013	996.3 (42.9)	1800.0 (41.1)	-0.018	1834.5 (41.5)	3026.0 (40.3)	-0.011
Missing	45.5 (2.5)	46.0 (1.5)	-0.011	34.6 (1.5)	61.0 (1.4)	-0.001	86.4 (2.0)	107.0 (1.4)	-0.005
Lactate, mmol/L (%)									
<1.2	299.2 (16.6)	482.0 (15.4)	-0.012	404.8 (17.4)	707.0 (16.1)	-0.013	718.7 (16.2)	1189.0 (15.8)	-0.004
1.2 - <2.0	495.8 (27.5)	929.0 (29.7)	0.022	717.7 (30.9)	1423.0 (32.5)	0.016	1307.9 (29.6)	2352.0 (31.3)	0.018
2.0+	276.8 (15.4)	564.0 (18.1)	0.027	376.3 (16.2)	727.0 (16.6)	0.004	672.5 (15.2)	1291.0 (17.2)	0.020
Missing	728.3 (40.5)	1149.0 (36.8)	-0.037	825.9 (35.5)	1526.0 (34.8)	-0.007	1726.1 (39.0)	2675.0 (35.6)	-0.034
Platelet count per microL (%)									
150 or higher	1175.4 (65.3)	2099.0 (67.2)	0.019	1500.3 (64.5)	2962.0 (67.6)	0.030	2834.3 (64.0)	5061.0 (67.4)	0.034
< 150	617.5 (34.3)	1019.0 (32.6)	-0.017	823.2 (35.4)	1416.0 (32.3)	-0.031	1579.1 (35.7)	2435.0 (32.4)	-0.032
Missing	7.1 (0.4)	6.0 (0.2)	-0.002	1.2 (0.0)	5.0 (0.1)	0.001	11.9 (0.3)	11.0 (0.1)	-0.001
Total bilirubin, mg/dL (%)									
<1	1336.7 (74.3)	2299.0 (73.6)	-0.007	1793.5 (77.2)	3219.0 (73.4)	-0.037	3313.1 (74.9)	5518.0 (73.5)	-0.014
1 - 1.2	163.8 (9.1)	295.0 (9.4)	0.003	181.8 (7.8)	467.0 (10.7)	0.028	395.4 (8.9)	762.0 (10.2)	0.012
1.2 +	266.5 (14.8)	473.0 (15.1)	0.003	312.8 (13.5)	640.0 (14.6)	0.011	620.3 (14.0)	1113.0 (14.8)	0.008
Missing	33.0 (1.8)	57.0 (1.8)	0.000	36.4 (1.6)	57.0 (1.3)	-0.003	96.4 (2.2)	114.0 (1.5)	-0.007
White Blood Count per microL (%)									
4-10	937.2 (52.1)	1443.0 (46.2)	-0.059	1198.0 (51.5)	1890.0 (43.1)	-0.084	2251.8 (50.9)	3333.0 (44.4)	-0.065
<4	512.2 (28.5)	915.0 (29.3)	0.008	655.4 (28.2)	1344.0 (30.7)	0.025	1271.5 (28.7)	2259.0 (30.1)	0.014
>10	350.6 (19.5)	766.0 (24.5)	0.050	471.2 (20.3)	1149.0 (26.2)	0.059	902.0 (20.4)	1915.0 (25.5)	0.051
C-reactive protein measured (%)	1092.7 (60.7)	1947.0 (62.3)	0.016	1472.5 (63.3)	2793.0 (63.7)	0.004	2725.4 (61.6)	4740.0 (63.1)	0.016
D-dimer measured (%)	1430.4 (79.5)	2635.0 (84.3)	0.049	1925.8 (82.8)	3682.0 (84.0)	0.012	3590.4 (81.1)	6317.0 (84.1)	0.030
Vital Signs									
Highest Temperature (F) (%)									
< 99	652.8 (36.3)	1071.0 (34.3)	-0.020	602.2 (25.9)	1409.0 (32.1)	0.062	1392.3 (31.5)	2480.0 (33.0)	0.016
99 - 100	443.5 (24.6)	752.0 (24.1)	-0.006	489.9 (21.1)	1026.0 (23.4)	0.023	1007.8 (22.8)	1778.0 (23.7)	0.009
100 - 102	439.7 (24.4)	888.0 (28.4)	0.040	776.7 (33.4)	1316.0 (30.0)	-0.034	1325.2 (29.9)	2204.0 (29.4)	-0.006
102 +	247.6 (13.8)	397.0 (12.7)	-0.010	451.6 (19.4)	614.0 (14.0)	-0.054	673.5 (15.2)	1011.0 (13.5)	-0.018
Missing	16.4 (0.9)	16.0 (0.5)	-0.004	4.1 (0.2)	18.0 (0.4)	0.002	26.4 (0.6)	34.0 (0.5)	-0.001
Mean Arterial Pressure, mmHg (%)									
< 60	51.8 (2.9)	55.0 (1.8)	-0.011	45.7 (2.0)	74.0 (1.7)	-0.003	93.5 (2.1)	129.0 (1.7)	-0.004
60 – 69	224.7 (12.5)	342.0 (10.9)	-0.015	410.9 (17.7)	550.0 (12.5)	-0.051	630.6 (14.3)	892.0 (11.9)	-0.024

Dexamethasone	No Oxygen			Nasal Canula			Combined Cohort		
	No	Yes	SMD	No	Yes	SMD	No	Yes	SMD
70 – 89	1182.3 (65.7)	2092.0 (67.0)	0.013	1546.3 (66.5)	2998.0 (68.4)	0.019	2968.3 (67.1)	5090.0 (67.8)	0.007
90 +	330.9 (18.4)	625.0 (20.0)	0.016	317.8 (13.7)	747.0 (17.0)	0.034	716.7 (16.2)	1372.0 (18.3)	0.021
Missing	10.3 (0.6)	10.0 (0.3)	- 0.003	3.8 (0.2)	14.0 (0.3)	0.002	16.2 (0.4)	24.0 (0.3)	0.000
Lowest Oxygen Saturation (%)									
< 88	98.5 (5.5)	319.0 (10.2)	0.047	274.2 (11.8)	622.0 (14.2)	0.024	383.4 (8.7)	941.0 (12.5)	0.039
88 - 92	850.7 (47.3)	1660.0 (53.1)	0.059	1355.9 (58.3)	2702.0 (61.6)	0.033	2262.9 (51.1)	4362.0 (58.1)	0.070
93 - 95	629.6 (35.0)	863.0 (27.6)	- 0.073	566.8 (24.4)	794.0 (18.1)	- 0.063	1357.3 (30.7)	1657.0 (22.1)	- 0.086
96 +	172.2 (9.6)	216.0 (6.9)	- 0.026	93.3 (4.0)	165.0 (3.8)	- 0.002	315.4 (7.1)	381.0 (5.1)	- 0.021
Missing	49.2 (2.7)	66.0 (2.1)	- 0.006	34.4 (1.5)	100.0 (2.3)	0.008	106.3 (2.4)	166.0 (2.2)	- 0.002

Supplemental Table E2. Sensitivity analyses estimating the average treatment effect in the treated population (ATT) in weighted Cox proportional hazards models for 90-day mortality associated with early dexamethasone exposure in patients hospitalized for COVID-19 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	1.99 (1.60-2.48)	1.04 (0.78-1.39)	1.60 (1.32-1.94)
Sensitivity and subgroup analyses			
Restricted to positive SARS-CoV-2 test within 24 hours	1.50 (1.04-2.17)	1.30 (0.90-1.88)	1.39 (1.03-1.88)
Restricted to positive SARS-CoV-2 test within 48 hours	1.52 (1.05-2.21)	1.32 (0.92-1.90)	1.43 (1.06-1.92)
Any systemic corticosteroids	1.90 (1.53-2.36)	1.15 (0.88-1.52)	1.58 (1.31-1.90)
Excluding patients admitted to ICU in initial 48 hours	1.23 (0.88-1.74)	1.28 (0.88-1.86)	1.27 (0.96-1.67)
Restricted to patients age 70 and older	1.45 (1.05-2.01)	1.33 (0.93-1.89)	1.45 (1.11-1.91)

Models present the ATT (average treatment effect in treated population).

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

Supplemental Table E3. Sensitivity analyses with unweighted, multivariable Cox proportional hazards models for 90-day mortality associated with early dexamethasone exposure in patients hospitalized for COVID-19 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	1.75 (1.47-2.07)	1.31 (1.08-1.60)	1.63 (1.44-1.85)
Sensitivity and subgroup analyses			
Restricted to positive SARS-CoV-2 test within 24 hours	1.86 (1.55-2.23)	1.33 (1.08-1.64)	1.69 (1.48-1.93)
Restricted to positive SARS-CoV-2 test within 48 hours	1.89 (1.58-2.26)	1.33 (1.08-1.63)	1.70 (1.49-1.94)
Any systemic corticosteroids	1.69 (1.44-1.99)	1.33 (1.09-1.61)	1.61 (1.43-1.82)
Excluding patients admitted to ICU in initial 48 hours	1.63 (1.35-1.98)	1.18 (0.96-1.44)	1.49 (1.30-1.70)
Restricted to patients age 70 and older	1.76 (1.46-2.12)	1.31 (1.06-1.60)	1.61 (1.41-1.84)

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