Supplemental Online Content

Fawzy A, Wu TD, Wang K, et al. Racial and ethnic discrepancy in pulse oximetry and delayed identification of treatment eligibility among patients with COVID-19. *JAMA Intern Med*. Published online May 31, 2022. doi:10.1001/jamainternmed.2022.1906

This supplemental material has been provided by the authors to give readers additional information about their work.

© 2022 American Medical Association. All rights reserved.

eMethods 1: Linear Mixed-Effects Model

The association between race/ethnic category and the difference in paired SpO_2 and SaO_2 measurements (response variable) was examined using an unadjusted linear mixed-effects model with race/ethnicity included in the fixed effect and a random intercept. This was investigated in the overall sample and a sub-sample limited to patients with SpO_2 88-96%. Given there were four race/ethnic categories, three comparisons were made (with White as the reference) and statistical significance was defined as $p<0.017$ based on Bonferroni correction. The linear mixed-effects model was then adjusted for age, sex, history of diabetes, Charleston Comorbidity Index (score of 1-4 vs. 5+), time-varying vital signs (mean arterial pressure and temperature) and laboratory results (creatinine, hemoglobin, and total bilirubin), and the time-varying oxygen device used by patients (room air or oxygen by mask or nasal prongs vs. high-flow nasal cannula or non-invasive vs. mechanical ventilation). These covariates were chosen based on their known or theoretical impact on pulse oximetry accuracy or association with COVID-19 clinical trajectory. Paired SpO_2-SaO_2 measurements were mapped to the nearest mean arterial pressure and temperature measurements collected 4 hours before or 2 hours after, and to the nearest laboratory results in the preceding 48 hours. Only paired measurements with complete data for covariates were included in the analysis. All covariates and their interactions with race/ethnicity were included as fixed effects, and only those interactions with p-value < 0.05 were retained in the final model. An intercept, time-varying vitals and lab measurements were included as random effects at the individual level to account for within-subject variation and dependency of repeated measurements. An unstructured variance-covariance structure was employed for each random effect and separate random effects were considered to be independent.

© 2022 American Medical Association. All rights reserved.

eMethods 2: Sensitivity Analysis Methods

A sensitivity analysis was conducted excluding observations where titration of supplemental oxygen may have occurred between the measurement times of SpO_2 and SaO_2. Specifically, we excluded observations where there was a mismatch in oxygen device, liters per minute, or fraction of inspired oxygen (FiO_2). The majority of exclusions were due to missing or incomplete data. The linear mixed-effects models were re-fitted with the new sample. The analysis of unrecognized or delayed treatment eligibility was repeated using the alternative adjusted linear mixed-effects model.

© 2022 American Medical Association. All rights reserved.

eResults 1: Sensitivity Analysis Results

The sensitivity analysis excluding observations where titration of oxygen may have occurred between SpO_2 and SaO_2 measurements included 1,030 patients with 29,198 concurrent SaO_2 and SpO_2 measurements for unadjusted linear mixed-effects model, and 976 patients with 26,857 concurrent SaO_2 and SpO_2 measurements and complete covariates used to fit the adjusted linear mixed-effects model. In unadjusted analysis, compared with White patients SpO_2 overestimated SaO_2 by 1.2% for Black patients, 0.5% for non-Black Hispanic patients and 1.5% for Asian patients ($p<0.017$ for all). Occult hypoxemia ($SaO_2<88\%$ with concurrent SpO_2 measurement 92-96%) was identified in 3.6% of Black patient samples, 2.8% of non-Black Hispanic patient samples, 3.6% of Asian patient samples, and 1.7% of White patient samples. At the patient level, 30.7% of Black patients, 31.8% of non-Black Hispanic patients, 30.4% of Asian patients, and 20.0% of White patients had occult hypoxemia at some point during the hospital encounter. In the adjusted linear mixed-effects model, compared with White patients, SpO_2 overestimated SaO_2 by an average of 1.1% among Black patients (95% confidence interval [CI]: 0.5% to 1.7%; p=0.0002), 1.0% among non-Black Hispanic patients (95% CI: 0.3% to 1.8%; p=0.007), and 1.9% among Asian patients (95% CI: 0.7% to 3.0%; p=0.002).

There were 1934 patients with predicted $SaO_2 \leq 94\%$ before measured $SpO_2 \leq 94\%$ or oxygen initiation. Compared to White patients, Black patients had a 28% lower hazard of eligibility recognition (hazard ratio [HR] 0.72; 95% CI 0.64-0.81; $p<0.0001$) and non-Black Hispanic patients had a 24% lower hazard of eligibility recognition (HR 0.76; 95% CI 0.66-0.81; p=0.0002) with no difference between White and Asian patients (HR 1.00; 95% CI 0.76-1.31; p=0.98). There were 455 patients with unrecognized treatment indication and their distribution by race was similar to the main analysis (50.5% Black, 29.2% non-Black Hispanic,17.3% White, and 3% Asian). The median (IQR) treatment delay was attenuated for Asian patients but similar to the main analysis for other race/ethnicities: 6.9 (2.0-20.9) hours for Black patients, 5.0 (1.1-15.0) for non-Black Hispanic patients, 5.6 (1.4-14.9) for White patients, and 5.0 (1.7-13.0) for Asian patients. Similar to the main analysis, compared with White patients, Black patients were the only group that had a significantly higher median difference in time to recognition of eligibility by 1.0 hour (95% CI: 0.22 to 1.9 hours; p=0.007).

© 2022 American Medical Association. All rights reserved.

eTable 1: Pre-defined race categories available in the Johns Hopkins Health System electronic medical record.

White or Caucasian
Black or African American
American Indian or Alaska Native
Asian
Native Hawaiian or Other Pacific Islander
Other
Patient Refused
Unknown
Two or More Races
Declined to Answer
Hispanic
Native Hawaiian
Other Pacific Islander

© 2022 American Medical Association. All rights reserved.

eTable 2: Unadjusted linear mixed-effects model evaluating the association of race with SaO_2-SpO_2 for the full cohort and limited to SpO_2 between 88% and 96%

	Full dataset (N=1,216; 32,282 paired observations)			Limited to SpO2 88-96% (N=950; 15,984 paired observations)		
	Mean Difference (Standard Error)	p-value	95% Confidence Interval	Mean Difference (Standard Error)	p-value	95% Confidence Interval
White	-0.751(0.093)	$2.59x10^{-15}$	-0.93, -0.57	-0.03 (0.128)	0.8	-0.28, 0.22
Black	-1.156 (0.129)	$1.65x10^{-18}$	-1.4, -0.90	-1.4 (0.179)	$1.05x10^{-14}$	-1.8, -1.1
Hispanic	-0.556 (0.160)	0.0005	-0.87, -0.24	-0.78 (0.215)	0.0003	-1.2, -0.36
Asian	-1.583 (0.265)	$3.18x10^{-9}$	-2.1, -1.1	-2.1 (0.360)	$5.77x10^{-9}$	-2.8, -1.4

© 2022 American Medical Association. All rights reserved.

eTable 3: Adjusted fully specified linear mixed-effects model including interactions between race and each covariate as fixed effects

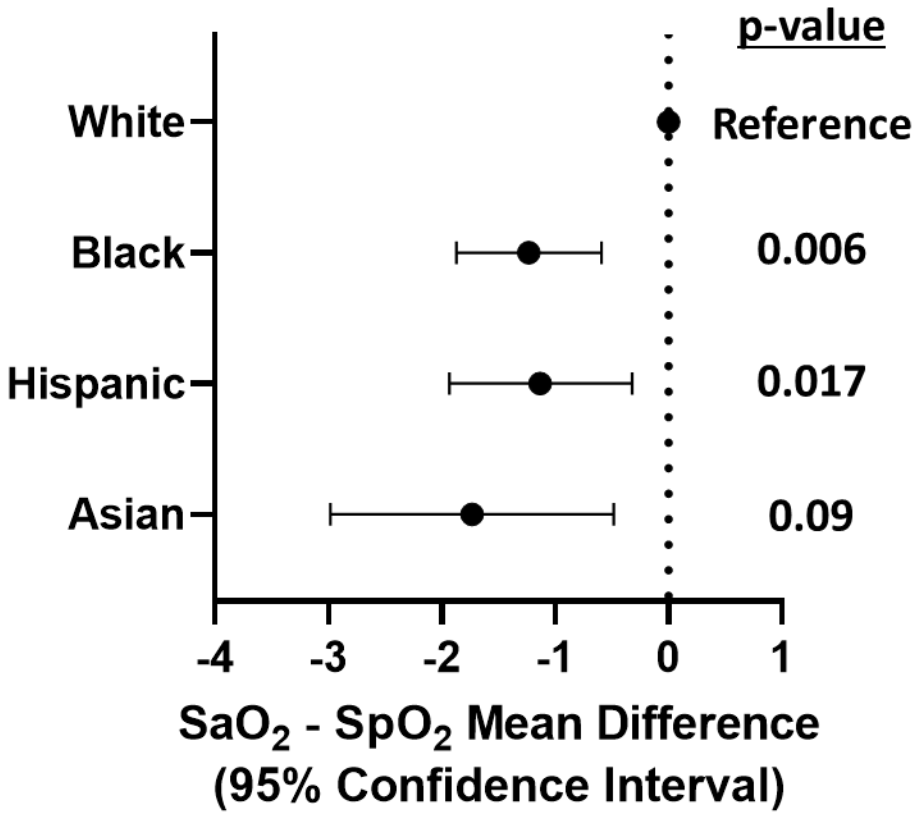
	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	-0.135	1.365	-0.099	0.921
Race:				
Asian	-3.170	3.778	-0.839	0.402
Black	0.395	1.828	0.216	0.829
Hispanic	-4.195	2.046	-2.051	0.041
SpO2	-1.777	0.122	-14.620	0.000
Race : SpO2				
Asian : SpO2	1.543	0.334	4.622	0.000
Black : SpO2	0.403	0.166	2.427	0.016
Hispanic : SpO2	0.585	0.200	2.921	0.004
MAP	-0.080	0.062	-1.282	0.201
Temperature	-0.036	0.065	-0.559	0.577
Age	-0.032	0.024	-1.350	0.178
Age ≥ 65	0.202	0.696	0.290	0.772
Male	0.136	0.444	0.306	0.760
O2 device:				
WHO = 5	0.359	0.484	0.742	0.458
WHO = 6 or 7	0.717	0.383	1.870	0.061
HGB	-0.068	0.106	-0.643	0.521
Creatinine	0.216	0.168	1.285	0.200
Bilirubin	-0.837	0.768	-1.089	0.277
Diabetes	0.425	0.475	0.894	0.372
CCI 1-4	0.055	0.753	0.072	0.942
CCI ≥5	0.511	0.936	0.546	0.585
Race : MAP				
Asian : MAP	-0.040	0.162	-0.245	0.807
Black : MAP	0.043	0.082	0.522	0.602
Hispanic : MAP	-0.143	0.098	-1.452	0.147
Race : Temperature				
Asian : Temperature	-0.022	0.173	-0.128	0.898
Black : Temperature	0.000	0.088	0.004	0.997
Hispanic : Temperature	0.048	0.103	0.463	0.643
Race : Age				
Asian : Age	0.078	0.059	1.326	0.186
Black : Age	-0.025	0.032	-0.776	0.438
Hispanic : Age	0.026	0.036	0.724	0.469
Race : Age ≥ 65				
Asian : Age ≥ 65	-2.180	1.690	-1.290	0.198

© 2022 American Medical Association. All rights reserved.

	Estimate	Std. Error	t value	Pr(>|t|)
Black : Age ≥ 65	0.765	0.953	0.803	0.422
Hispanic : Age ≥ 65	0.442	1.148	0.385	0.700
Race : Male				
Asian : Male	-0.019	1.280	-0.015	0.988
Black : Male	0.189	0.602	0.315	0.753
Hispanic : Male	0.021	0.819	0.026	0.979
Race : O2 device				
Asian : WHO = 5	-2.337	1.585	-1.475	0.140
Black : WHO = 5	-0.252	0.662	-0.380	0.704
Hispanic : WHO = 5	2.088	0.807	2.588	0.010
Asian : WHO = 6 or 7	-1.447	1.286	-1.125	0.260
Black : WHO = 6 or 7	0.274	0.523	0.523	0.601
Hispanic : WHO = 6 or 7	1.421	0.637	2.231	0.026
Race : HGB				
Asian : HGB	0.066	0.276	0.240	0.810
Black : HGB	0.365	0.145	2.522	0.012
Hispanic : HGB	0.237	0.166	1.433	0.153
Race : Creatinine				
Asian : Creatinine	-0.754	0.437	-1.724	0.086
Black : Creatinine	-0.168	0.215	-0.783	0.434
Hispanic : Creatinine	0.073	0.286	0.253	0.800
Race : Bilirubin				
Asian : Bilirubin	-1.260	2.019	-0.624	0.533
Black : Bilirubin	1.763	1.046	1.686	0.093
Hispanic : Bilirubin	-0.657	1.208	-0.544	0.587
Race : Diabetes				
Asian : Diabetes	-2.689	1.463	-1.839	0.067
Black : Diabetes	-1.106	0.661	-1.674	0.095
Hispanic : Diabetes	-1.125	0.843	-1.335	0.183
Race : CCI				
Asian : CCI 1-4	0.483	1.761	0.274	0.784
Black : CCI 1-4	0.020	1.043	0.019	0.985
Hispanic : CCI 1-4	0.838	1.085	0.772	0.440
Asian : CCI ≥ 5	-1.768	2.559	-0.691	0.490
Black : CCI ≥ 5	-0.329	1.282	-0.256	0.798
Hispanic : CCI ≥ 5	-0.421	1.998	-0.211	0.833

© 2022 American Medical Association. All rights reserved.

eFigure 1: Average relative marginal effects by race from the adjusted fully specified linear mixed-effects model



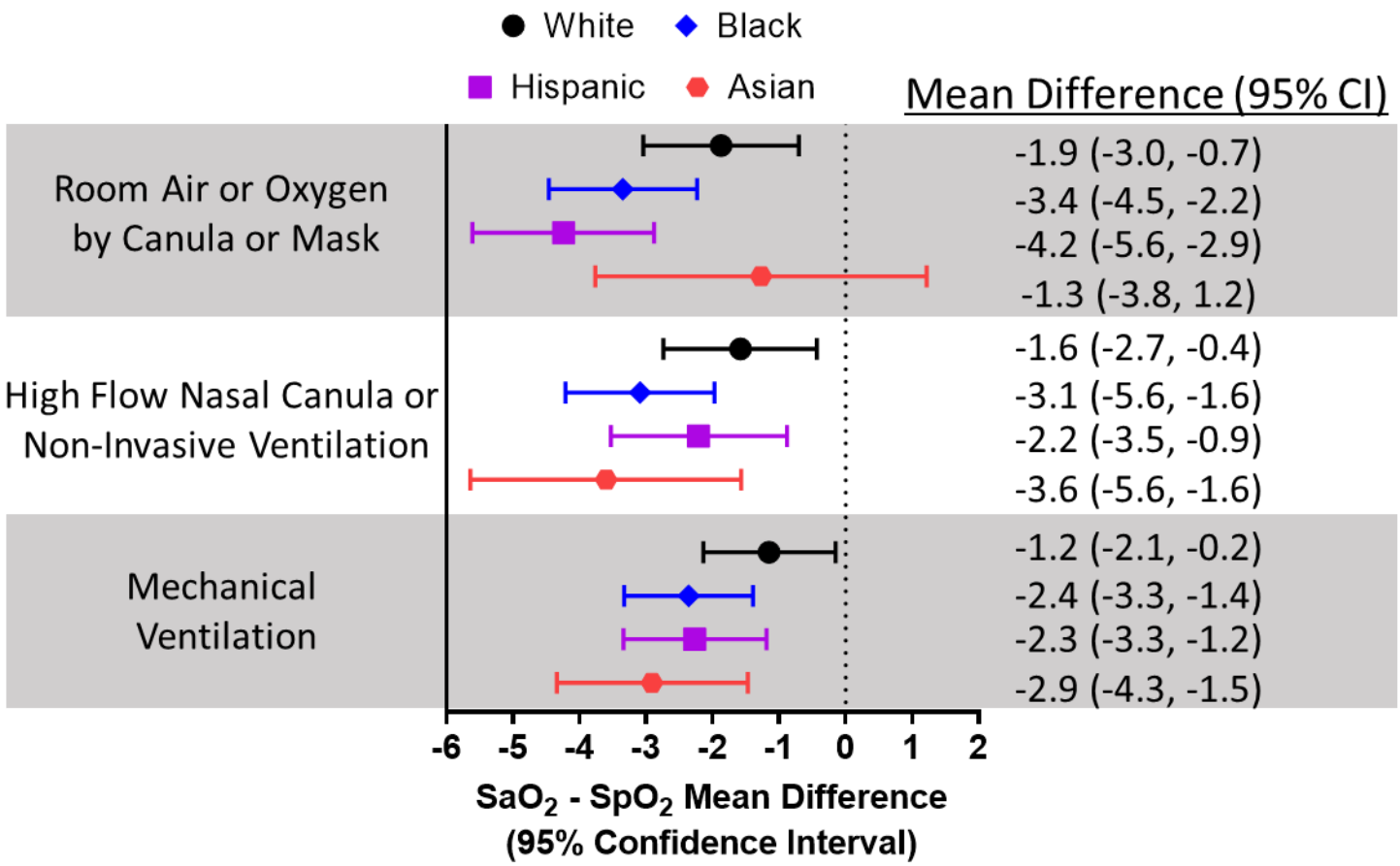
© 2022 American Medical Association. All rights reserved.

eTable 4: Adjusted parsimonious linear mixed-effects model including significant interactions of race with SpO_2 and oxygen device as fixed effects

	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	0.340	0.888	0.383	0.702
Race:				
Asian	0.618	1.258	0.491	0.624
Black	-1.473	0.544	-2.708	0.007
Hispanic	-2.369	0.681	-3.479	0.001
SpO2	-1.779	0.124	-14.346	0.000
Race : SpO2				
Asian : SpO2	1.398	0.338	4.141	0.000
Black : SpO2	0.333	0.169	1.974	0.049
Hispanic : SpO2	0.567	0.204	2.779	0.006
MAP	-0.092	0.034	-2.672	0.008
Temperature	-0.028	0.037	-0.758	0.449
Age	-0.038	0.014	-2.711	0.007
Age ≥ 65	0.342	0.433	0.790	0.430
Male	0.208	0.284	0.730	0.466
O2 device:				
Non-invasive ventilation or high-flow	0.284	0.465	0.610	0.542
Intubation and Mechanical Ventilation	0.722	0.358	2.015	0.044
HGB	0.126	0.064	1.980	0.048
Creatinine	0.081	0.111	0.735	0.463
Bilirubin	-0.352	0.462	-0.762	0.447
Diabetes	-0.238	0.311	-0.764	0.445
CCI 1-4	0.102	0.440	0.233	0.816
CCI ≥5	0.439	0.584	0.751	0.453
Race : O2 device				
Asian : Non-invasive and HFNC	-2.616	1.437	-1.821	0.069
Black : Non-invasive and HFNC	-0.028	0.633	-0.044	0.965
Hispanic : Non-invasive and HFNC	1.754	0.770	2.277	0.023
Asian : Ventilator	-2.358	1.148	-2.054	0.040
Black : Ventilator	0.260	0.490	0.530	0.596
Hispanic : Ventilator	1.257	0.595	2.110	0.035

© 2022 American Medical Association. All rights reserved.

eFigure 2: Average absolute differences between SaO_2 and SpO_2 by race stratified by oxygen device



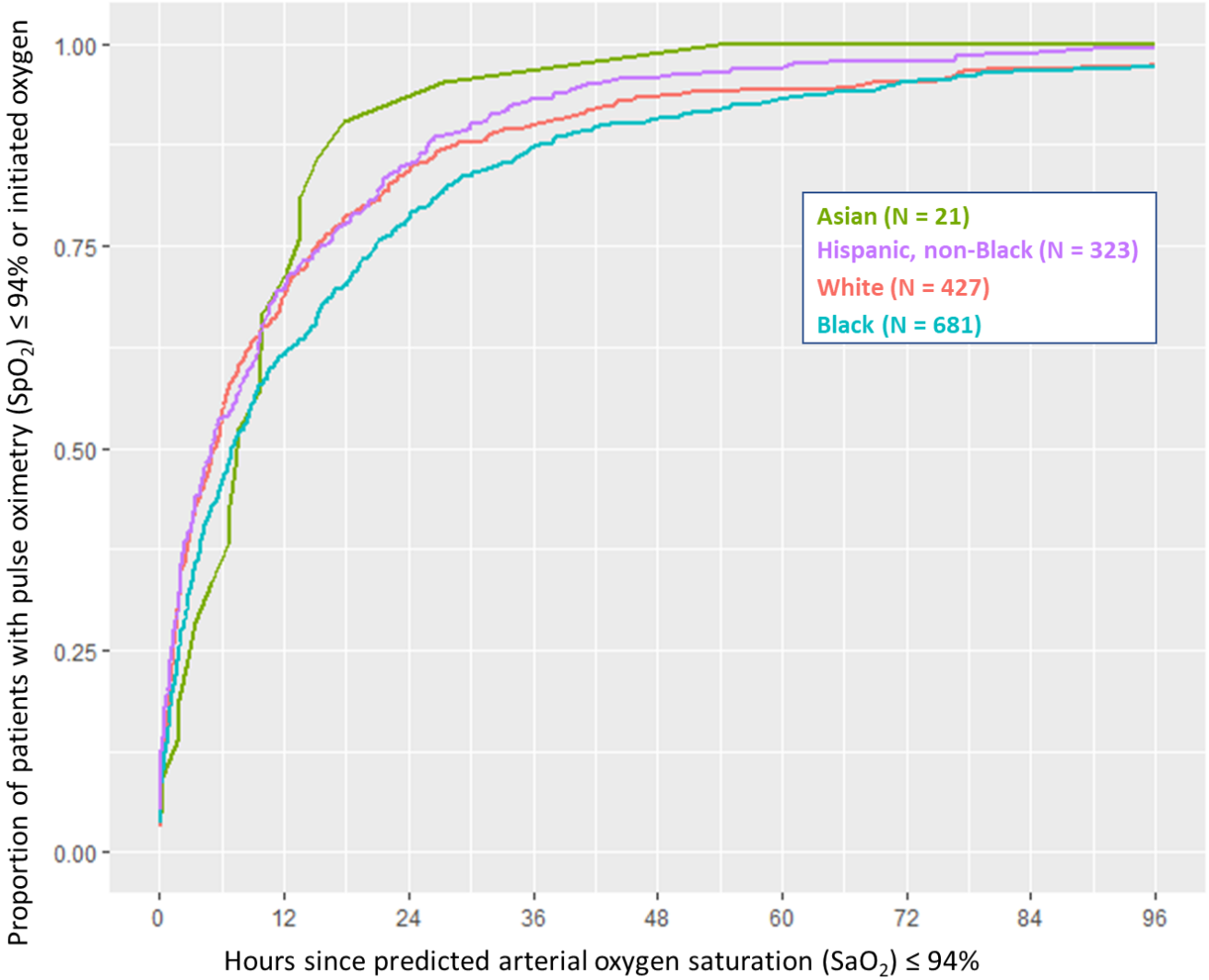
© 2022 American Medical Association. All rights reserved.

eTable 5: Baseline characteristics of patients testing positive for COVID-19 with predicted $SaO_2 \leq 94\%$ before $SpO_2 \leq 94\%$ or oxygen initiation included in the analysis of unrecognized or delayed treatment eligibility

Characteristic [mean ± SD or N (%) unless otherwise specified]	**White, non-Hispanic (N = 505)**	**Black (N = 928)**	**Hispanic (excluding Black Hispanic) (N = 445)**	**Asian (N = 25)**
Age (years)	74.9 ±13.3	59.5 ±17.1	48.4 ±16.9	78.1 ±12.3
Female	246 (48.7%)	510 (55%)	200 (44.9%)	16 (64%)
Location				
Johns Hopkins Hospital	92 (18.2%)	449 (48.4%)	143 (32.1%)	3 (12%)
Bayview Medical Center	125 (24.8%)	141 (15.2%)	101 (22.7%)	3 (12%)
Howard County General Hospital	113 (22.4%)	173 (18.6%)	77 (17.3%)	11 (44%)
Sibley Memorial Hospital	54 (10.7%)	86 (9.3%)	18 (4%)	0 (0%)
Suburban Hospital	121 (24%)	75 (8.1%)	102 (22.9%)	8 (32%)
Hemoglobin on admission (g/dL)	12.7 ±2.1	12.3 ±2.2	13.2 ±2.2	12.2 ±2.4
Bilirubin on admission (mg/dL)	0.7 ±1.7	0.6 ±0.9	0.6 ±1.2	0.5 ±0.4
Creatinine on admission (mg/dL)	1.3 ±0.9	1.8 ±2.2	1.1 ±1.5	1.6 ±1.3
Body Mass Index	27.0 ±5.6	31 ±8.6	29.4 ±6.3	23.5 ±3.2
Charleston Comorbidity Index				
Charleston Comorbidity Index 1-4	373 (73.9%)	611 (65.8%)	221 (49.7%)	14 (56%)
Charleston Comorbidity Index ≥ 5	51 (10.1%)	142 (15.3%)	13 (2.9%)	3 (12%)
Diabetes	180 (35.6%)	417 (44.9%)	129 (29%)	13 (52%)
Chronic Obstructive Pulmonary Disease	136 (26.9%)	291 (31.4%)	68 (15.3%)	4 (16%)
Peripheral Vascular Disease	86 (17%)	153 (16.5%)	20 (4.5%)	1 (4%)
Chronic Kidney Disease	144 (28.5%)	304 (32.8%)	46 (10.3%)	7 (28%)
Maximum Respiratory Support Needed				
Room air or oxygen by mask or nasal prongs	482 (95.4%)	882 (95.0%)	426 (95.7%)	23 (92.0%)
Non-invasive ventilation or high-flow oxygen	4 (0.8%)	8 (0.9%)	2 (0.4%)	0 (0%)
Mechanical Ventilation	19 (3.8%)	38 (4.1%)	17 (3.9%)	2 (8.0%)

© 2022 American Medical Association. All rights reserved.

eFigure 3: Proportion of patients with pulse oximetry (SpO_2) ≤94% or initiated oxygen since predicted arterial oxygen saturation (SaO_2) ≤94% among patients diagnosed with COVID-19 among patients ultimately having SpO_2 ≤ 94% or initiated oxygen



© 2022 American Medical Association. All rights reserved.

eTable 6: Absolute and relative treatment eligibility delay by race among 1,452 patients with predicted $SaO_2 \leq 94\%$ before $SpO_2 \leq 94\%$ or oxygen initiation

Race	White	Black	Hispanic	Asian
N	427	681	323	21
Mean (SD) Absolute Treatment Eligibility Delay	14.8 (28.9) hours	18.6 (35.7) hours	15.4 (74.8) hours	10.8 (11.9) hours
Median (IQR) Absolute Treatment Eligibility Delay	5.3 (1.4 - 15.2) hours	7.0 (1.9 - 20.8) hours	5.0 (1.2 - 15.8) hours	7.7 (3.5 - 13.6) hours
Difference in Location* (95% Confidence Interval)	Reference	1.0 (0.23, 1.9) hours	-0.14 (-0.87, 0.48) hours	1.4 (-1.7, 4.8) hours
p-value**	Reference	0.006	0.3	0.6

*Median of the difference between samples **Wilcoxon Rank-Sum Test

© 2022 American Medical Association. All rights reserved.