

## Supplemental Online Content

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**eTable 1.** Characteristics of SARS-CoV-2-Positive Veterans With or Without G6PD Deficiency

**eFigure 1.** COVID+ Veterans With and Without G6PD Deficiency

**eFigure 2.** Odds of Developing Severe Outcomes with SARS-CoV-2 Infection in the Presence of G6PD Deficiency

**eTable 2.** COVID-19 Outcomes in US Veterans With and Without G6PD Deficiency

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

**eTable 1. Characteristics of SARS-CoV-2-Positive Veterans with or without G6PD Deficiency**

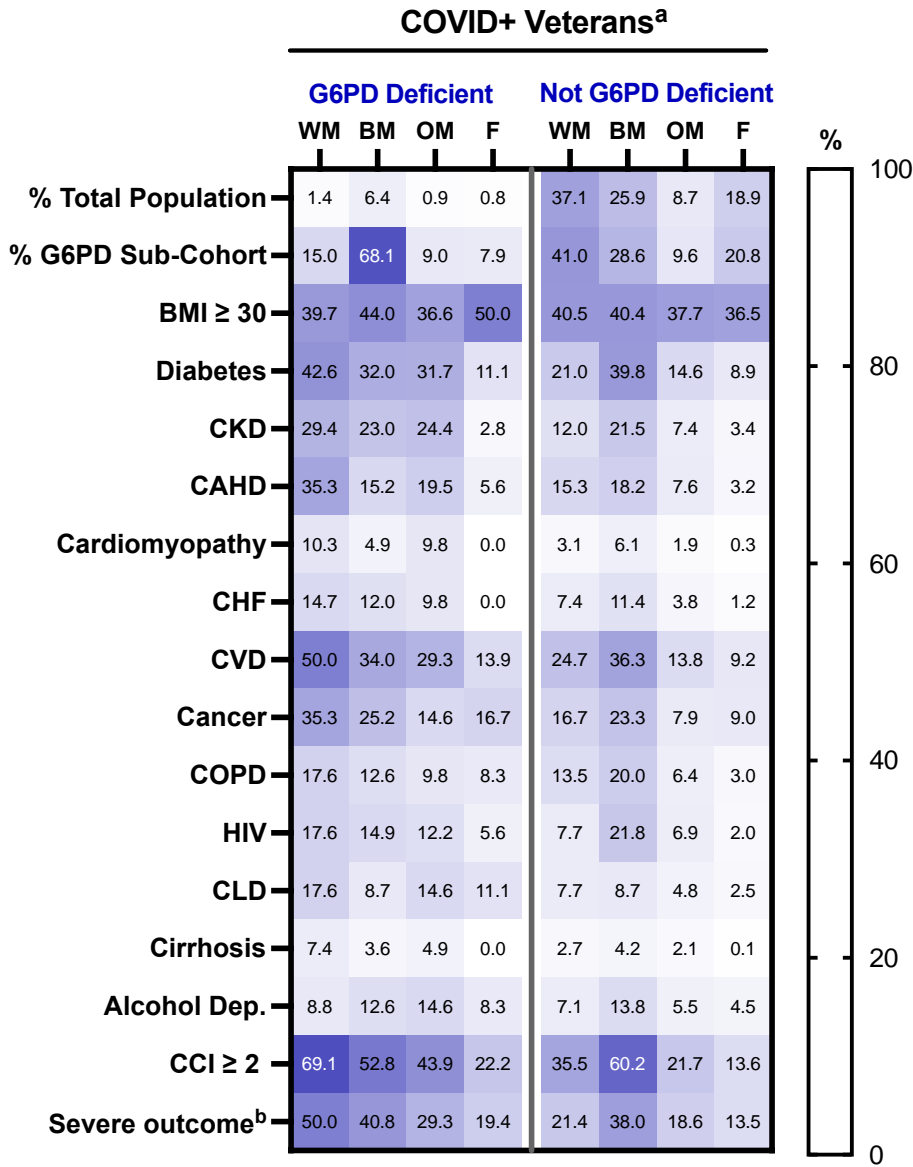
Study population was limited to patients tested for G6PD deficiency prior to January 1, 2020 and testing positive for SARS-CoV-2 between February 15, 2020 to January 1, 2021. The prevalence of comorbidities commonly associated with risk for severe outcomes due to SARS-CoV-2 infection as of April 15, 2021 are shown. Veterans are grouped by age [ $<65$  y and  $\geq 65$  y] and self-reported race and sex. The number of veterans (percentage) are shown for each comorbidity, as indicated. Data were extracted and curated from VHA EHR: age (dichotomized into  $< 65$  and  $\geq 65$  years), BMI (dichotomized into  $< 30$  and  $\geq 30$  kg/m<sup>2</sup>), Deyo-Charlson Comorbidity Index (CCI; dichotomized into  $< 2$  and  $\geq 2$ ), racial ancestry, sex, and medical history for the presence of the following: diabetes, chronic kidney disease (CKD), coronary atherosclerosis and other heart disease (CAHD), cardiomyopathy, congestive heart failure (CHF), cardiovascular disease including hypertension (CVD), cancer, chronic obstructive pulmonary disease (COPD), human immunodeficiency virus (HIV), chronic liver disease (CLD), cirrhosis, and alcohol dependency, as indicated by ICD-10 codes. See **Figure 1**, main text.

US Veterans with Historical Testing for G6PD Deficiency & Positive SARS-Co-V-2 Testing (n = 4811)								
	G6PD Deficiency n = 454				No G6PD Deficiency n = 4,357			
	White (15.0%)	Men Black (68.1%)	Other (9.0%)	Women All (7.9%)	White (41.0%)	Men Black (28.6%)	Other (9.6%)	Women All (20.8%)
n	68	309	41	36	1787	1244	419	907
BMI $\geq 30$	27(39.7)	136(44.0)	15(36.6)	18(50.0)	724(40.5)	498(40.0)	158(37.7)	331(36.5)
Diabetes	29(42.6)	99(32.0)	13(31.7)	4(11.1)	376(21.0)	495(39.8)	61(14.6)	81(8.9)
CKD	20(29.4)	71(23.0)	10(24.4)	1(2.8)	214(12.0)	267(21.5)	31(7.4)	31(3.4)
CAHD	24(35.3)	47(15.2)	8(19.5)	2(5.6)	274(15.3)	227(18.2)	32(7.6)	29(3.2)
Cardiomyopathy	7(10.3)	15(4.9)	4(9.8)	0	56(3.1)	76(6.1)	8(1.9)	3(0.3)
CHF	10(14.7)	37(12.0)	4(9.8)	0	133(7.4)	142(11.4)	16(3.8)	11(1.2)
CVD	34(50.0)	105(34.0)	12(29.3)	5(13.9)	441(24.7)	451(36.3)	58(13.8)	83(9.2)
Cancer	24(35.3)	78(25.2)	6(14.6)	6(16.7)	298(16.7)	290(23.3)	33(7.9)	82(9.0)
COPD	12(17.6)	39(12.6)	4(9.8)	3(8.3)	242(13.5)	249(20.0)	27(6.4)	27(3.0)
HIV	12(17.6)	46(14.9)	5(12.2)	2(5.6)	138(7.7)	271(21.8)	29(6.9)	18(2.0)
CLD	12(17.6)	27(8.7)	6(14.6)	4(11.1)	137(7.7)	108(8.7)	20(4.8)	23(2.5)
Cirrhosis	5(7.4)	11(3.6)	2(4.9)	0	48(2.7)	52(4.2)	9(2.1)	1(0.1)
Alcohol Dep.	6(8.8)	39(12.6)	6(14.6)	3(8.3)	127(7.1)	172(13.8)	23(5.5)	41(4.5)
CCI $\geq 2$	47(69.1)	163(52.8)	18(43.9)	8(22.2)	635(35.5)	749(60.2)	91(21.7)	123(13.6)
Severe Outcome <sup>a</sup>	34(50.0)	126(40.8)	12(29.3)	7(19.4)	375(21.0)	473(38.0)	78(18.6)	122(13.5)

Age < 65 years (n = 3,583)								
	G6PD Deficiency				No G6PD Deficiency			
	Men			Women	Men			Women
	White	Black	Other	All	White	Black	Other	All
<b>n</b>	31	205	29	33	1288	779	359	859
<b>BMI ≥ 30</b>	15(48.4)	101(49.3)	10(34.5)	18(54.5)	520(40.4)	359(46.1)	142(39.6)	312(36.3)
<b>Diabetes</b>	7(22.6)	51(24.9)	8(27.6)	3(9.1)	127(9.9)	235(30.2)	29(8.1)	55(6.4)
<b>CKD</b>	5(16.1)	30(14.6)	3(10.3)	1(3.0)	52(4.0)	104(13.4)	13(3.6)	18(2.1)
<b>CAHD</b>	3(9.7)	18(8.8)	2(6.9)	2(6.1)	55(4.3)	79(10.1)	9(2.5)	18(2.1)
<b>Cardiomyopathy</b>	0	7(3.4)	1(3.4)	0	14(1.1)	31(4.0)	4(1.1)	3(0.3)
<b>CHF</b>	0	14(6.8)	0	0	24(1.9)	44(5.6)	3(0.8)	4(0.5)
<b>CVD</b>	5(16.1)	50(24.4)	3(10.3)	5(15.2)	122(9.5)	182(23.4)	23(6.4)	61(7.1)
<b>Cancer</b>	4(12.9)	25(12.2)	2(6.9)	6(18.2)	87(6.8)	96(12.3)	14(3.9)	67(7.8)
<b>COPD</b>	2(6.5)	14(6.8)	0	3(9.1)	58(4.5)	86(11.0)	7(1.9)	15(1.7)
<b>HIV</b>	11(35.5)	32(15.6)	3(10.3)	2(6.1)	110(8.5)	191(24.5)	25(7.0)	18(2.1)
<b>CLD</b>	5(16.1)	17(8.3)	3(10.3)	4(12.1)	76(5.9)	61(7.8)	10(2.8)	19(2.2)
<b>Cirrhosis</b>	2(6.5)	7(3.4)	1(3.4)	0	13(1.0)	23(3.0)	2(0.6)	1(0.1)
<b>Alcohol Dep.</b>	2(6.5)	26(12.7)	3(10.3)	3(9.1)	83(6.4)	108(13.9)	21(5.8)	41(4.8)
<b>CCI ≥ 2</b>	13(41.9)	81(39.5)	8(27.6)	8(24.2)	230(17.9)	365(46.9)	44(12.3)	92(10.7)
<b>Severe Outcome<sup>a</sup></b>	6(19.4)	67(32.7)	5(17.2)	6(18.2)	155(12.0)	206(26.4)	50(13.9)	102(11.9)
Age ≥ 65 years (n = 1228)								
	G6PD Deficiency				No G6PD Deficiency			
	Men			Women	Men			Women
	White	Black	Other	All	White	Black	Other	All
<b>n</b>	37	104	12	3	499	465	60	48
<b>BMI ≥ 30</b>	12(32.4)	35(33.7)	5(41.7)	0	204(40.9)	139(29.9)	16(26.7)	19(39.6)
<b>Diabetes</b>	22(59.5)	48(46.2)	5(41.7)	1(33.3)	249(49.9)	260(55.9)	32(53.3)	26(54.2)
<b>CKD</b>	15(40.5)	41(39.4)	7(58.3)	0	162(32.5)	163(35.1)	18(30.0)	13(27.1)
<b>CAHD</b>	21(56.8)	29(27.9)	6(50.0)	0	219(43.9)	148(31.8)	23(38.3)	11(22.9)
<b>Cardiomyopathy</b>	7(18.9)	8(7.7)	3(25.0)	0	42(8.4)	45(9.7)	4(6.7)	0
<b>CHF</b>	10(27.0)	23(22.1)	4(33.3)	0	109(21.8)	98(21.1)	13(21.7)	7(14.6)
<b>CVD</b>	29(78.4)	55(52.9)	9(75.0)	0	319(63.9)	269(57.8)	35(58.3)	22(45.8)
<b>Cancer</b>	20(54.1)	53(51.0)	4(33.3)	0	211(42.3)	194(41.7)	19(31.7)	15(31.3)
<b>COPD</b>	10(27.0)	25(24.0)	4(33.3)	0	184(36.9)	163(35.1)	20(33.3)	12(25.0)
<b>HIV</b>	1(2.7)	14(13.5)	2(16.7)	0	28(5.6)	80(17.2)	4(6.7)	0
<b>CLD</b>	7(18.9)	10(9.6)	3(25.0)	0	61(12.2)	47(10.1)	10(16.7)	4(8.3)
<b>Cirrhosis</b>	3(8.1)	4(3.8)	1(8.3)	0	35(7.0)	29(6.2)	7(11.7)	0
<b>Alcohol Dep.</b>	4(10.8)	13(12.5)	3(25.0)	0	44(8.8)	64(13.8)	2(3.3)	0
<b>CCI ≥ 2</b>	29(78.3)	82(78.8)	10(83.3)	0	405(81.2)	384(82.6)	47(78.3)	31(64.6)
<b>Severe Outcome<sup>a</sup></b>	28(75.7)	59(56.7)	7(58.3)	1(33.3)	220(44.1)	268(57.6)	28(46.7)	20(41.7)

<sup>a</sup>Severe outcome defined as any of the following: (i) in-hospital mortality, (ii) hospitalization, (iii) intensive care unit admission or (iv) mechanical ventilation. **Abbreviations:** Other = males not self-identified as White nor Black, or self-identified as Asian, Pacific Islander or Native American; BMI = body mass index; CAHD = coronary artery heart disease; CKD = chronic kidney disease; CLD = chronic liver disease; COPD = chronic obstructive pulmonary disease; Dep=dependence; CHF = congestive heart failure; CVD = cardiovascular disease; HIV = human immunodeficiency virus; CCI = Charlson Comorbidity Index

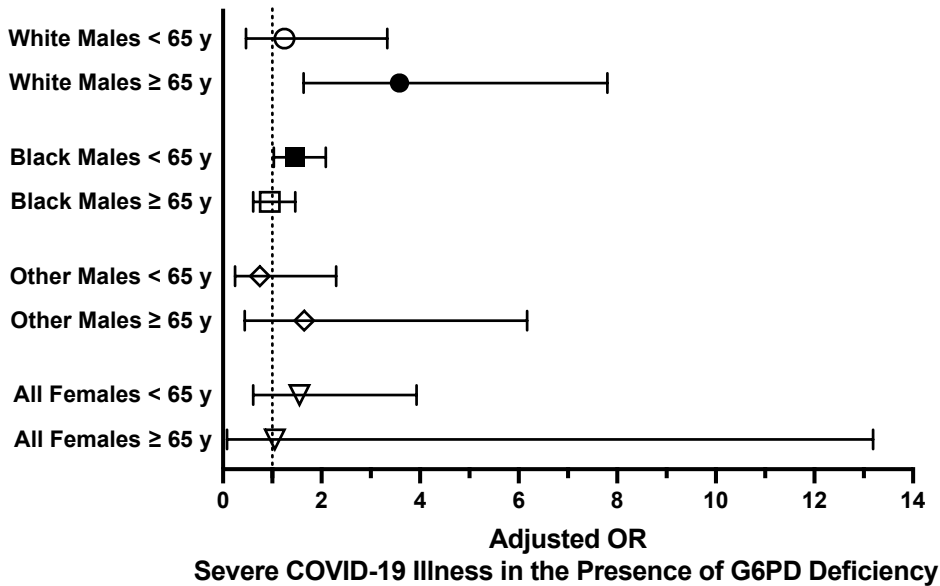
**eFigure 1. COVID+ Veterans with and without G6PD Deficiency.** Heatmap illustrates the prevalence of comorbidities commonly associated with risk for severe outcomes due to SARS-CoV-2 infection (n = 4811). Percentages for each comorbidity present in SARS-CoV-2 positive veterans with or without G6PD deficiency are shown and represented in color by the heatmap scale shown on the right. Data represent the entire cohort (n=4811) stratified by G6PD deficiency status, race, and sex. Cohort is not stratified by age in this representation.



<sup>a</sup>Study population, n=4811; <sup>b</sup>Severe outcomes include (i) in-hospital mortality, (ii) hospitalization, (iii) intensive care unit admission or (iv) mechanical ventilation; WM= White male; BM = Black male; OM = Other male not self-identified as White nor Black, or self-identified as Asian, Pacific Islander or Native American; F = All females; BMI = body mass index; CAHD = coronary artery heart disease; CKD = chronic kidney disease; CLD = chronic liver disease; COPD = chronic obstructive pulmonary disease; Dep=dependence; CHF = congestive heart failure; CVD = cardiovascular disease; HIV = human immunodeficiency virus; CCI = Charlson Comorbidity Index

**eFigure 2. Odds of Developing Severe Outcomes with SARS-CoV-2 Infection in the Presence of G6PD Deficiency.**

Adjusted odds ratios (OR) for severe disease in the presence of G6PD deficiency, stratified by self-reported race and sex, and adjusted for age, diabetes, CKD, and BMI are shown. Black men <65 years of age (black filled squares) and White men ≥65 years of age (black filled circles) have increased odds of severe outcomes, demonstrating 1.47X for young Black men and 3.56X for older White men, respectively. Significance is indicated by filled symbols. Open symbols are not significant. G6PD = glucose-6-phosphate dehydrogenase; Black males <65 years, n= 984; Black males >65 y, n=569; White males <65 y, n=1319; White males >65 y, n=536; Other males <65y, n= 388; Other males >65 y, n=72; All females <65 y, n= 892; All females >65 y, n= 51. Other = Males not self-identified as White or Black, or self-identified as Asian, Pacific Islander, or Native American.



**eTable 2. COVID-19 Outcomes in US Veterans with and without G6PD Deficiency**

Outcomes	G6PD Deficiency				No G6PD Deficiency			
	Men (n = 418)			Women (n=36)	Men (n=3450)			Women (n=907)
	White	Black	Other	All	White	Black	Other	All
<b>Hosp total (%)</b>	<b>34(50.0)</b>	<b>126(40.8)</b>	<b>12(29.3)</b>	<b>7(19.4)</b>	<b>375(21.0)</b>	<b>473(38.0)</b>	<b>78(18.6)</b>	<b>122(13.5)</b>
- ICU	18(26.5)	60(19.4)	3(7.3)	2(5.6)	185(10.4)	224(18.0)	48(11.5)	68(7.5)
- Vent	9(13.2)	23(7.4)	2(4.9)	1(2.8)	66(3.7)	98(7.9)	12(2.9)	11(1.2)
- Death	8(11.8)	14(4.5)	3(7.3)	1(2.8)	43(2.4)	81(6.5)	5(1.2)	5(0.6)
<b>age &lt; 65 years</b>								
<b>Hosp total (%)</b>	<b>6(19.4)</b>	<b>67(32.7)</b>	<b>5(17.2)</b>	<b>6(18.2)</b>	<b>155(12.0)</b>	<b>205(26.3)</b>	<b>50(13.9)</b>	<b>102(11.9)</b>
- ICU	2(6.5)	35(17.1)	0(0.0)	2(6.1)	84(6.5)	91(11.7)	31(8.6)	58(6.8)
- Vent	1(3.2)	12(5.9)	0(0.0)	1(3.0)	20(1.6)	37(4.7)	4(1.1)	7(0.8)
- Death	0(0.0)	4(2.0)	0(0.0)	1(3.0)	3(0.2)	16(2.1)	0(0.0)	1(0.1)
<b>age ≥ 65 years</b>								
<b>Hosp total (%)</b>	<b>28(75.7)</b>	<b>59(56.7)</b>	<b>7(58.3)</b>	<b>1(33.3)</b>	<b>220(44.1)</b>	<b>268(57.6)</b>	<b>28(46.7)</b>	<b>20(41.7)</b>
- ICU	16(43.2)	25(24.0)	3(25.0)	0(0.0)	101(20.2)	133(28.6)	17(28.3)	10(20.8)
- Vent	8(21.6)	11(10.6)	2(16.7)	0(0.0)	46(9.2)	61(13.1)	8(13.3)	4(8.3)
- Death	8(21.6)	10(9.6)	3(25.0)	0(0.0)	40(8.0)	65(14.0)	5(8.3)	4(8.3)

Abbreviations: Hosp = hospital; ICU – intensive care unit; Vent – ventilator; Other = Males not self-identified as White nor Black, or self-identified as Asian, Pacific Islander or Native American