Risk of Suicide-Related Outcomes After SARS-COV-2 Infection: Results from a Nationwide Observational Matched Cohort of US Veterans

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ABSTRACT

BACKGROUND: Negative mental health-related effects of SARS-COV-2 infection are increasingly evident. However, the impact on suicide-related outcomes is poorly understood, especially among populations at elevated risk.

OBJECTIVE: To determine risk of suicide attempts and other self-directed violence (SDV) after SARS-COV-2 infection in a high-risk population.

DESIGN: We employed an observational design supported by comprehensive electronic health records from the Veterans Health Administration (VHA) to examine the association of SARS-COV-2 infection with suicide attempts and other SDV within one year of infection. Veterans with SARS-COV-2 infections were matched 1:5 with non-infected comparators each month. Three periods after index were evaluated: days 1–30, days 31–365, and days 1–365.

PARTICIPANTS: VHA patients infected with SARS-COV-2 between March 1, 2020 and March 31, 2021 and matched non-infected Veteran comparators.

MAIN MEASURES: Suicide attempt and other SDV events for the COVID-19 and non-infected comparator groups were analyzed using incidence rates per 100,000 person years and hazard ratios from Cox regressions modeling time from matched index date to first event. Subgroups were also examined.

KEY RESULTS: 198,938 veterans with SARS-COV-2 (COVID-19 group) and 992,036 comparators were included. Unadjusted one-year incidence per 100,000 for suicide attempt and other SDV was higher among the COVID-19 group: 355 vs 250 and 327 vs 235, respectively. The COVID-19 group had higher risk than comparators for suicide attempts: days 1–30 hazard ratio (HR) = 2.54 (CI:2.05, 3.15), days 31–365 HR = 1.30 (CI:1.19, 1.43) and days 1–365 HR = 1.41 (CI:1.30, 1.54),

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and for other SDV: days 1–30 HR = 1.94 (CI:1.51, 2.49), days 31–365 HR = 1.32 (CI:1.20, 1.45) and days 1–365 HR = 1.38 (CI:1.26, 1.51).

CONCLUSIONS: COVID-19 patients had higher risks of both suicide attempts and other forms of SDV compared to uninfected comparators, which persisted for at least one year after infection. Results support suicide risk screening of those infected with SARS-COV-2 to identify opportunities to prevent self-harm.

KEY WORDS: COVID-19; mental health; veterans; suicide attempt; self-directed violence

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INTRODUCTION

Few studies have assessed suicide-related outcomes during the SARS-COV-2 pandemic, and results have been mixed,[1, 2] but it is clear that the effects of both SARS-COV-2 infection and the pandemic itself have contributed to poor mental health outcomes. There is evidence of psychiatric sequelae of SARS-COV-2,[3–5] although risk of suicide attempts and other forms of self-directed violence (SDV) were not evaluated. With over 100 million Americans infected with SARS-COV-2 by 2023,[6] any temporal association of SDV with SARS-COV-2 infection could help inform suicide prevention efforts.

The 9 + million U.S. Veterans—who have a higher risk of suicide at baseline—may be at especially high risk for SDV due to SARS-COV-2 infection.[7–9] Suicide prevention is a top priority of the Veterans Health Administration (VHA).[10, 11] Since suicide attempts are one of the strongest known predictors of future suicide—for up to a decade after the initial attempt—identifying Veterans who have attempted suicide or engaged in other kinds of SDV is important for risk mitigation strategies.[12] Thus while the association between SARS-COV-2 infection and suicide attempts or other SDV remains poorly understood, this gap is particularly policy relevant and urgent in VHA.

To address this gap, we utilized VHA electronic health record (EHR) data of SARS-COV-2-infected and matched uninfected comparator cohorts assembled for this study,[13] and linked with routine provider assessments of Veterans SDV data. We examined associations between suicide attempt, other SDV and time since SARS-COV-2 infection and within relevant subgroups.

METHODS

Specification of the Target Trial & Study Population

We emulated a clinical trial with randomized exposure to SARS-COV-2 infection, and one year of follow-up to record suicide attempts and other SDV outcomes among Veterans (Table ST1).[14]

Using VHA EHR data, we identified first SARS-COV-2 PCR test or documentation thereof from the VA COVID-19 Shared Data Resource (CSDR) (COVID-19) and matched similar patients without documented SARS-COV-2 infection (comparator) on or before their matched COVID-19 patient's date of infection (index date).[13] Through a previously described consensus process,[13] we identified confounders thought to be associated with SARS-COV-2 infection and clinical, functional, and economic outcomes. We used both exact and time-varying propensity score matching based on EHR-derived covariates. Briefly, we identified Veterans receiving care in the VHA system who were and were not infected with SARS-COV-2 on a rolling monthly basis -from March 2020 through March 2021. Each month, we exact-matched on index month, sex, any immunosuppressive medication use, state of residence, and COVID-19 vaccination status and then propensity-matched on 37 covariates.[15] For each infected Veteran, we selected the five comparators with the closest propensity scores. All were followed for one year after the index date through March 31, 2022.

Data Sources

We used the VHA Corporate Data Warehouse (CDW), which centralizes EHR data from all VHA facilities, and the VHA's COVID-19 Shared Data Resource (CSDR), a set of analytic variables and datasets to facilitate COVID-19 research and operations. COVID-19 vaccination, date of death, and demographic information from VHA-linked Medicare files were also used.

Suicide attempts and other forms of SDV were identified in VHA's Office of Mental Health and Suicide Prevention (OMHSP) surveillance data collected through routine clinical care.[16] Historical and recent events are reported, including date of event, method (e.g., firearms, physical, etc.), disposition (e.g., hospitalization), (e.g., VA property, home, etc.), treatment, and nature and severity of injury if any. The VHA OMHSP Program Evaluation and Resource Center (PERC) integrates this information in accordance with CDC guidelines for event classification,[16–18] and cleans and reconciles these data.

The study was approved by VHA Institutional Review Boards in Seattle, Portland, Durham, Ann Arbor, and Palo Alto.

Table 1 Baseline Characteristics of Veterans in the COVID-19 and Matched Comparator Groups, March 1, 2020 – March 31, 2021

Matching Variables*	COVID-19 N = 198,938	Comparator 5:1 N = 992,036	SMD
Sex, No. (%)			0.001
Female	20,962 (10.54)	104,294 (10.51)	
Male	177,976 (89.46)	887,742 (89.49)	
Age, No. (%)			0.072
Age 18–45	39,539 (19.88)	209,935 (21.16)	
Age 46–59	44,561 (22.40)	195,558 (19.71)	
Age 60–64	20,632 (10.37)	100,122 (10.09)	
Age 65–74	53,087 (26.69)	279,642 (28.19)	
Age 75 and older	41,119 (20.67)	206,779 (20.84)	
Race, No. (%)			0.018
American Indian/Alaska Native	1,902 (0.96)	9,217 (0.93)	
Asian	2,011 (1.01)	10,160 (1.02)	
Black	46,177 (23.21)	230,866 (23.27)	
More than one race	1,919 (0.96)	9,663 (0.97)	
Native Hawaiian/ Other Pacific Islander	1,862 (0.94)	9,287 (0.94)	
White	136,439 (68.58)	683,277 (68.88)	
Missing	8,628 (4.34)	39,566 (3.99)	
Ethnicity, No. (%)			0.007
Hispanic	19,770 (9.94)	96,476 (9.73)	
Not Hispanic	172,691 (86.81)	863,080 (87.00)	
Missing	6,477 (3.26)	32,480 (3.27)	
Smoking status, No. (%)			0.012
Never	78,233 (39.33)	391,017 (39.42)	
Current	24,830 (12.48)	124,492 (12.55)	
Former	84,471 (42.46)	422,285 (42.57)	
Missing	11,404 (5.73)	54,242 (5.47)	
CAN comorbidity score, No. (%)†			0.011
CAN Category 1, 0 – 20	32,730 (16.45)	161,966 (16.33)	
CAN Category 2, 25 – 40	30,285 (15.22)	151,792 (15.30)	
CAN Category 3, 45 – 60	36,537 (18.37)	186,013 (18.75)	
CAN Category 4, 65 – 80	44,809 (22.52)	225,878 (22.77)	
CAN Category 5, 85 – 90	29,604 (14.88)	148,012 (14.92)	
CAN Category 6, 95 – 99	21,303 (10.71)	99,436 (10.02)	
Missing	3,670 (1.84)	18,939 (1.91)	
Nosos comorbidity score, No. (%)			0.030
Nosos Category 1 [0, 0.417)	5,496 (2.76)	25,184 (2.54)	
Nosos Category 2 [0.417, 0.471)	9,048 (4.55)	42,931 (4.33)	
Nosos Category 3 [0.471, 0.534)	11,768 (5.92)	57,627 (5.81)	
Nosos Category 4 [0.534, 0.611)	14,290 (7.18)	71,628 (7.22)	
Nosos Category 5 [0.611, 0.707)	16,932 (8.51)	86,245 (8.69)	
Nosos Category 6 [0.707, 0.829)	19,446 (9.77)	100,005 (10.08)	
Nosos Category 7 [0.829, 0.998)	22,536 (11.33)	115,444 (11.64)	
Nosos Category 8 [0.998, 1.259)	25,785 (12.96)	130,916 (13.20)	
Nosos Category 9 [1.259, 1.805)	30,152 (15.16)	151,445 (15.27)	
Nosos Category 10 [1.805, 39.370)	39,154 (19.68)	187,981 (18.95)	
Missing	4,331 (2.18)	22,630 (2.28)	
Gagne comorbidity score, mean (SD)	1.45 (2.35)	1.42 (2.25)	0.016
CDC COVID-19 high risk conditions, No. (%)			
Cancer	16,549 (8.32)	87,605 (8.83)	-0.018
Pulmonary‡	40,726 (20.47)	201,112 (20.27)	0.005
Hypertension	122,027 (61.34)	608,384 (61.33)	< 0.001
Diabetes	68,266 (34.32)	337,459 (34.02)	0.006
Dementia	10,429 (5.24)	49,340 (4.97)	0.012
Coronary Heart Disease	57,533 (28.92)	283,154 (28.54)	0.008
Liver Disease	13,229 (6.65)	64,440 (6.50)	0.006
Sickle Cell	365 (0.18)	1,751 (0.18)	0.002
Transplant	649 (0.33)	3,252 (0.33)	< 0.001
Stroke/Cerebrovascular disease	12,466 (6.27)	60,648 (6.11)	0.006
Chronic Kidney Disease	45,598 (22.92)	223,090 (22.49)	0.010
Congestive Heart Failure	21,201 (10.66)	102,269 (10.31)	0.011
Substance Use Disorder	24,614 (12.37)	123,354 (12.43)	-0.002
Anxiety Diagnosis	44,891 (22.57)	223,078 (22.49)	0.002
PTSD Diagnosis	50,486 (25.38)	252,432 (25.45)	-0.002
Bipolar Diagnosis	7,593 (3.82)	37,865 (3.82)	< 0.001
Schizophrenia Diagnosis	4,548 (2.29)	22,192 (2.24)	0.003
Major depression Diagnosis	64,302 (32.32)	319,716 (32.23)	0.002
Body Mass Index (BMI), mean (SD)	31.33 (6.35)	31.27 (6.61)	0.009

Table 1 (continued)

Matching Variables*	COVID-19 N = 198,938	Comparator 5:1 N = 992,036	SMD
Immunosuppressive medication use in prior 24 months, No. (%)	19,477 (9.79)	97,088 (9.79)	< 0.001
Community Living Center resident at index date, No. (%)	2,116 (1.06)	9,344 (0.94)	0.012
# VHA inpatient admissions in prior 24 months, mean (SD)	0.35 (1.20)	0.35 (1.26)	< 0.001
# VHA primary care visits in prior 24 months, mean (SD)	16.00 (17.19)	15.33 (17.84)	0.038
# VHA specialty care visits in prior 24 months, mean (SD)	13.88 (14.14)	13.46 (15.37)	0.029
# VHA mental health care visits in prior 24 months, mean (SD)	10.60 (24.66)	10.31 (23.92)	0.012
Distance to nearest VHA medical center (miles), mean (SD)	35.62 (36.60)	35.77 (35.13)	0.004
Rurality of residence, No. (%)			0.002
Rural	59,682 (30.00)	298,485 (30.09)	
Urban	139,256 (70.00)	693,551 (69.91)	
Vaccinated for COVID-19 in January-April 2021, No. (%)			0.001
No/Missing	59,868 (30.09)	298,560 (30.10)	
Yes	1,937 (0.97)	9,530 (0.96)	
Vaccine unavailable at index date	137,133 (68.93)	683,946 (68.94)	
Other variables (not included in matching)			
Suicide attempt event in two years prior to index, No. (%)			0.008
Yes	1,496 (0.75)	6,757 (0.68)	
No	197,442 (99.25)	985,279 (99.32)	
Other SDV event in two years prior to index, No. (%)			0.008
Yes	1,212 (0.61)	5,434 (0.55)	
No	197,726 (99.39)	986,602 (99.45)	

* Pregnancy was a matching variable but was zero for all persons. State of residence was a matching variable and included 50 states and Washington D.C.; Index Month was a matching variable and spanned 14 individual months (not shown, both SMDs <0.1). † 1 year hospitalization or death CAN score. ‡ Pulmonary-related diseases: asthma, COPD, interstitial lung disease, cystic fibrosis. Abbreviations: SMD: standardized mean difference; CAN: Care Assessment Need; CDC: Centers for Disease Control and Prevention; COPD: chronic obstructive pulmonary disease; VHA: Veterans Health Administration; SDV: Self-Directed Violence; SD: Standard Deviation

Outcomes

We used OMHSP/PERC identified suicide attempts and other forms of SDV–preparatory behaviors, non-suicidal SDV, and undetermined intent SDV. We did not include suicide deaths as cause of death data were not available to us.[12, 19] When more than one event type was reported for the same date (n = 203 pre- or post-index events), the most serious event type was selected. Outcomes were assessed for short-term (days 1–30), long-term (days 31–365) and one full year (days 1–365) from index date.

Statistical Analyses

We compared COVID-19 and comparator groups using descriptive statistics and standardized mean differences (SMD).[20] We calculated event rates as per 100,000 person years. Event-free follow-up was compared between groups using cumulative incidence functions in separate models for each outcome and across pre-specified subgroups.[21]

Using an intent-to-treat (ITT) approach, we applied separate Cox regression models to estimate hazard ratios (HR) for first suicide attempt and first other SDV event, with infected vs comparator status as the independent variable. Models censored for death, used stratified baseline hazard specifications with the matched groups as the strata (i.e., each infected case was compared to his/her specific matched group of non-infected comparators), and accounted for clustering of the matched groups using robust error estimation. No regression covariates were included since all covariates were well balanced after matching (See Table 1).[22]

Since risk of suicide-related events is higher among women;[11, 23] different across age groups[23, 24] and race[24, 25] and ethnicity[26] categories; and associated with a history of prior suicide-related events,[24] we conducted subgroup analyses. We estimated HR separately by sex (male or female); age groups (18–45, 46–59, 60–64, 65–74, or 75 years or older); race groups (White, Black, and other identity/missing [the latter category included American Indian/Alaska Native, Asian, Native Hawaiian/ other Pacific Islander, Native Hawaiian/ Other Pacific Islander, more than one race, or missing]), ethnicity (Hispanic or non-Hispanic), mental health visits during 24 months before index date (yes or no), and prior SA/SDV during 24 months before index date (yes or no). We combined categories when needed for models to converge due to small numbers. As sex was one of the five exact-matched variables, the matched groups were kept intact when stratifying by sex and thus the same methods were used as the overall analyses. However, for the other subgrouping on non-exact-match variables, the matched groups were sometimes broken up, and we used robust error estimation to account for repeated observations, and no stratified baseline hazard for matched groups.

In per- protocol (PP) sensitivity analyses, we also censored individuals who either later had SARS-COV-2 infection in the comparator group (PP1) or the entire matched

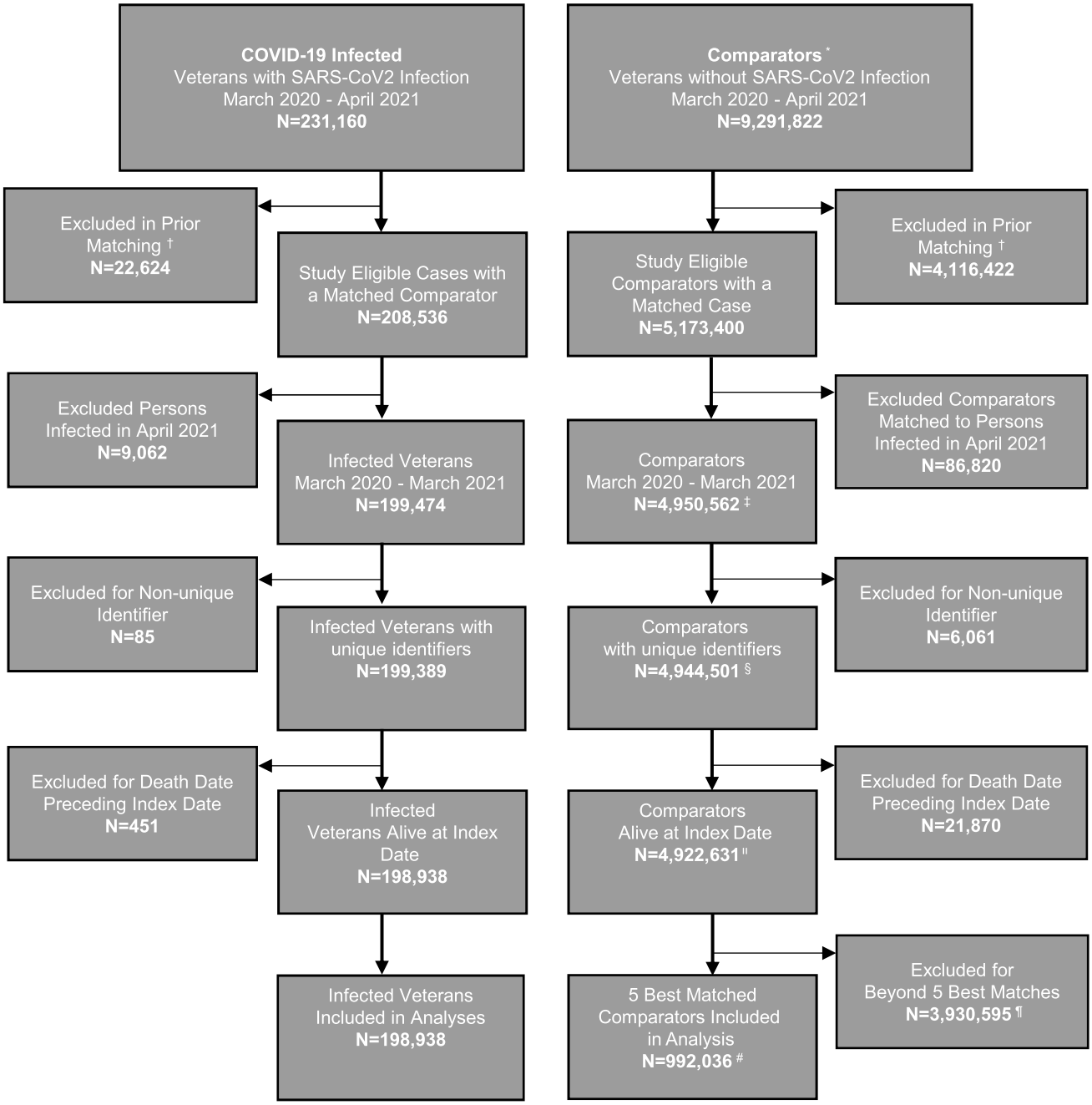

Figure 1 STROBE diagram of cohort derivation. * **There were 1,222,272 comparators matched to more than one case. In the numbers presented in this figure, comparators that were matched to more than one COVID-19 case have been counted as many times as they appeared in the dataset. The number of unique comparators at each step in the flow diagram are presented in the footnotes below.** † **Those excluded in the prior matching included: No CAN Score and no primary care, missing height, weight. or implausible value; age missing or implausible; ZIP code missing or not in DC or 50 states; had a Medicare COVID-19 diagnosis before index data; no suitable match. Additionally excluded among the comparators, those that became a "case" in the same month.[13].** ‡ **Unique number of uninfected comparators matched to a COVID-19 case N = 2,931,099.** § **Unique number of matched comparators with unique identifiers: N = 2,928,958.** ‖ **Unique number of alive matched comparators at index date: N = 2,919,231.** ¶ **Unique number of matched comparators that were dropped: N = 2,049,791.** # **Unique number of matched comparators used for analysis: N = 869,440. Of the comparators included in the analysis, 104,497 were matched to more than one COVID-19 case.**

Table 2 Description of Suicide Attempts and Other Self-Directed Violence Among COVID-19 and Matched Comparator Groups

	No. Persons	No. Suicide Attempts	% Suicide Attempts	Suicide Attempt Rate Per 100,000 PY (CI)	No. Other SDV	% Other SDV	Other SDV Rate Per 100,000 PY (CI)
Short-Term Outcomes (Days 1–30)							
Overall	1,190,974	382	0.03	393 (353, 432)	309	0.03	318 (282, 353)
COVID-19	198,938	127	0.06	798 (659, 937)	85	0.04	534 (420, 647)
Comparators	992,036	255	0.03	313 (275, 352)	224	0.02	275 (239, 311)
Difference			0.03			0.02	
Long-Term Outcomes (Days 31–365)							
Overall	1,190,974	2,778	0.23	263 (253, 272)	2,636	0.22	249 (240, 259)
COVID-19	198,938	555	0.28	328 (301, 355)	534	0.27	315 (289, 342)
Comparators	992,036	2,223	0.22	250 (240, 261)	2,102	0.21	237 (227, 247)
Difference			0.06			0.06	
One-Year Outcomes (Days 1–365)							
Overall	1,190,974	3,078	0.26	267 (257, 276)	2,887	0.24	250 (241, 259)
COVID-19	198,938	657	0.33	355 (328, 382)	606	0.31	327 (301, 353)
Comparators	992,036	2,421	0.24	250 (240, 260)	2,281	0.23	235 (226, 245)
Difference			0.09			0.08	

Abbreviations: SDV: self-directed violence; PY: person-years; CI: 95% Confidence Interval

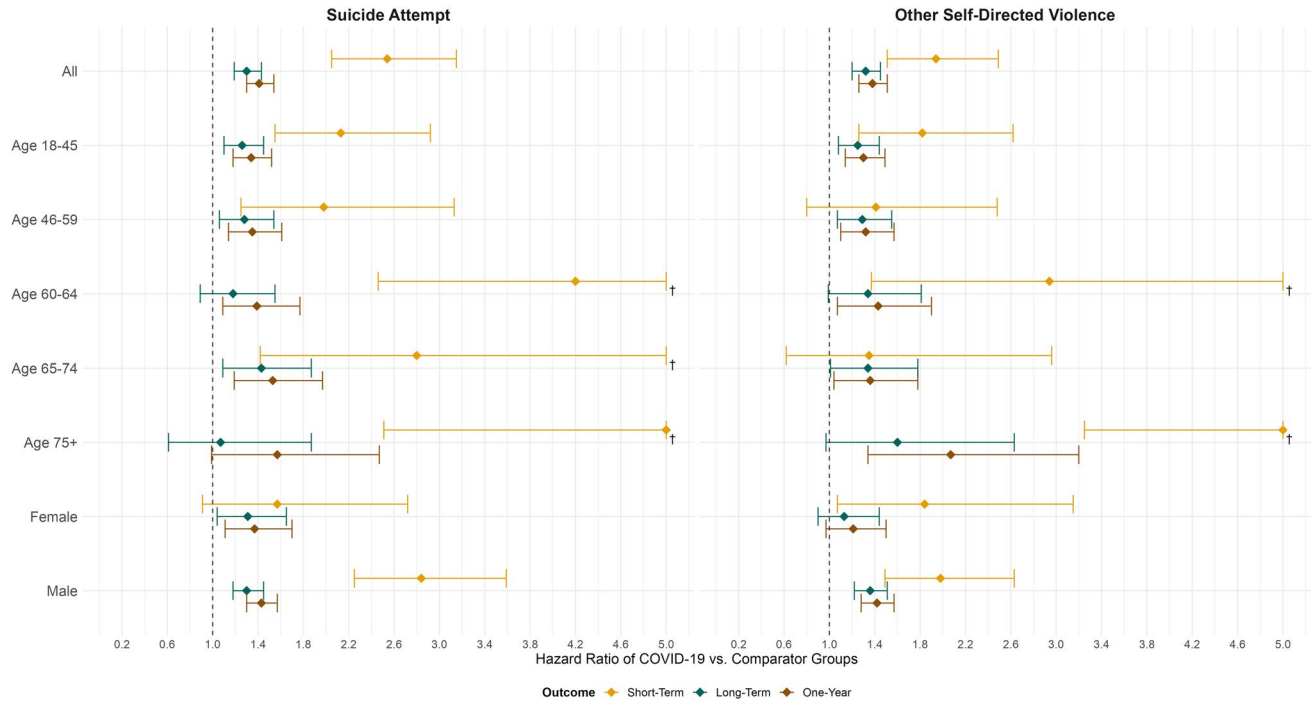

Figure 2 Intent-to-treat Cox regression model for suicide attempts & self-directed violence for Short-Term (Days 1–30), Long-Term (Days 31–365) and One Year (Days 1–365) follow-up periods after index. † 95% Confidence intervals > 5 are not shown for clarity of overall figure or would not converge where line is missing. Upper CI limits are as follows: for Suicide Attempts: Short-Term, Age 60–64: 7.16; Short-Term, Age 65 – 74: 5.52; Short-Term, Age 75 + : 18.09. For Other Self-Directed Violence: Short-Term, Age 60 – 64: 6.33; Short-Term, Age 75 + : 28.7.

group when any member of the comparator group had SARS-COV-2 infection (PP2).

Regression analyses were conducted with R version 4.1.2, and survival package version 3.4.0 for Cox regression. Level of significance was set to alpha = 0.05.

RESULTS

Characteristics of COVID-19 Versus Comparator Patients

Among the 1,190,974 Veterans in our matched cohort, 198,938 were in the COVID-19 group and 992,036 in the comparator group (Fig. 1); 475 Veterans (N = 121

COVID-19, N = 354 comparator) who experienced both events. Veteran characteristics in the two groups were similar (SMD < 0.1; Table 1), including for unmatched characteristics of prior suicide attempts and other SDV. Within the sex, age, race, ethnicity, prior mental health visits, and prior SA/SDV subgroups, characteristics were also similar.

Outcomes

Within one-year of the index date, 3,078 (0.258%) cohort members had at least one suicide attempt and 2,887 (0.242%) at least one occurrence of other SDV (Table 2), an incidence of 267 and 250 events per 100,000 person-years respectively. These unadjusted rates are substantially lower than those in the 24 months prior for suicide attempts 346 (N = 8,253, 0.693%) or other SDV 279 (N = 6,646, 0.558%). The event rates for suicide attempts and other SDV were highest in the first 30 days following the index date (393 (CI: 353, 432) and 318 (CI: 282, 353), respectively). Event rates were higher in the COVID-19 group than among comparators for suicide attempts and other SDV for all durations (Table 2 and Table ST2).

The cumulative incidence curves for the one-year follow-up period are shown in Figure SF1. Cumulative incidence for the COVID-19 group versus comparators was higher for the suicide attempts (0.33% [CI 0.31–0.36] versus 0.24% [CI 0.23–0.25], respectively) and other SDV (0.30% [CI 0.28–0.33] versus 0.23% [CI 0.22–0.24], respectively).

Suicide Attempt. In the regression analyses, the hazard of a suicide attempt in the COVID-19 infected group versus the comparators was higher in all follow-up periods: the hazard ratio was greatest days 1–30 (HR = 2.54; CI: 2.05, 3.15), and relatively lower but still elevated in days 31–365 (HR = 1.30; CI: 1.19, 1.43) and overall one-year (HR = 1.41; CI: 1.30, 1.54) (Fig. 2 and Table ST2).

In age subgroup analyses, the hazard of suicide attempt was higher among the COVID-19 group during all time periods for ages 18–45, 46–59, and 65–74 years. For these age groups HRs were highest in days 1–30, and lower, yet significant, days 31–365. For the other two age groups, 60–64 and 75 years and older, the hazard was significantly higher only days 1–30, yet greater than the other age groups, (Fig. 2 and Table ST3).

In sex subgroup analyses, the hazard of suicide attempt was significantly higher in the COVID-19 group in all time periods except for females days 1–30. The COVID-19 group males in days 1–30 had significantly higher hazard of a suicide attempt (HR = 2.84; 95% CI: 2.25, 3.59) whereas the COVID-19 group females did not (HR = 1.57; 95% CI: 0.91, 2.72) (Fig. 2 and Table ST4).

Results for other subgroups for the one-year period are shown in Tables ST5-8. Most notably, among the Black race subgroup, those with COVID-19 had the greatest hazard relative to the other race groups (HR = 1.6; 95% CI: 1.36–1.89), although the CI had overlap with the other groups. Among those with prior SA/SDV, the COVID-19 group had greater hazard of SA (HR = 1.46; 95%CI:1.24, 1.71). This was also the case among those without a prior SA/SDV, but the HR was slightly smaller (HR = 1.35; 95%CI: 1.22,1.5).

Other SDV. The hazard of other forms of SDV in the COVID-19 group versus the comparators was higher in all follow-up periods and greatest within the first 30 days: HR = 1.94 (CI: 1.51, 2.49); days 31–365 HR = 1.32 (CI: 1.20, 1.45); and one-year HR = 1.38 (CI: 1.26, 1.51) (Fig. 2 and Table ST2).

In age subgroup analyses, the hazard of SDV was significantly higher for the COVID-19 group in the one-year period for all age groups. Amongst 18–45 year-olds, the hazard of other SDV was higher for the COVID-19 group in all three time periods, while those 60–64 and age 75 and older the hazard was higher among the COVID-19 group only in the days 1–30 (age 60–64: HR = 2.94 [CI: 1.37, 6.33]; age 75 and older: HR = 9.65 [CI: 3.25, 28.70]), and these rates attenuated yet remained significant in the overall one-year period. Among those 46–59 and 65–74 years, the COVID-19 group had significantly higher hazard for days 31–365, which were similar in the one-year follow-up period. (Fig. 2 and Table ST3).

In sex subgroup analyses, the hazard of other SDV was significantly higher for the COVID-19 group in all time periods in the male subgroup, but only significantly higher in the female subgroup in days 1–30 (HR = 1.84, CI: 1.07, 3.15) (Fig. 2 and Table ST3).

Results for other subgroups for the one-year period for other SDV are shown in Table ST5-8. Most notably, the White race subgroup had the greatest hazard ratio (HR = 1.47; CI: 1.32, 1.65), although the CI had overlap with those of the other race groups. Among those without a prior SA/SDV, the COVID-19 group had 1.39 times the hazard of those in the uninfected comparator group, which was slightly greater than the HR of 1.26 among those with a prior SA/SDV.

Sensitivity analyses were largely like those of the primary analyses (Tables ST2-8).

DISCUSSION

We found that Veterans infected with SARS-COV-2 had more attempted suicide and other SDV than matched comparators: the COVID-19 group had a 41% higher risk of a suicide attempt and 38% higher risk of other SDV over one year. This is among the first reports of the incidence of suicide attempts and other forms of SDV during the pandemic in Veterans and among the first to compare the incidence of

these outcomes among patients infected with SARS-COV-2 to contemporaneous, well-matched controls. Comparisons between infected persons and contemporaneous controls can help to disentangle the effects of SARS-COV-2 infection on mental health outcomes from those of the multiple other stressors of the pandemic.

We found that one-year cumulative incidence for the COVID-19 group versus the comparator group was 0.33% versus 0.24%. This is higher than the 0.05% 9-month rate reported for self-harm for those who had SARS-COV-2 in Denmark.[27] While it is not surprising that rates in a low-risk general population are lower than in higher-risk US Veterans, the dramatic difference points to a need to look across sub-populations.

In our sex subgroup analyses, we found that the risk of suicide attempt was significantly higher among those in the COVID-19 group versus the comparators in all periods in both the male and female subgroups except for the first 30 days for the female subgroup. Yet for other SDV the pattern for the female subgroup was the opposite: the risk was higher only in the first 30 days after index date. Prior work has shown that women Veterans are more likely than men to have their SDV events classified according to the CDC as "undetermined intent", rather than "with intent", which in turn may put them at risk for less follow-up care in the VHA.[28] It is noteworthy that the suicide rate among women Veterans increased at a higher rate compared to their male counterparts: 61% (from 10.4 to 16.8 per 100,000) versus 43% increase (from 27.3 to 39.1 per 100,000), respectively from 2005 to 2017.[11, 23] Past research finds that female sex is associated with higher rates of long-term SARS-COV-2 sequelae.[29] With potential for down-classifying of suicide risk for women Veterans in general as well as differential impacts of SARS-COV-2 infection, these trends highlight the importance of thorough clinical assessments to better elicit intent of SDV during periods of such illness to ensure women Veterans receive needed, equitable SDV preventive care and treatment.

In age subgroup analyses (separating 18–45, 46–59, and 65–74 years), suicide attempts were more common among those with SARS-COV-2 infection in all time periods. We also found that both suicide attempts and other SDV decreased as age increased, consistent with a meta-analysis conducted early in the pandemic.[30] Although earlier studies were mostly cross-sectional with younger samples, our results over a longer period with a broad age range also show that the risk of suicide attempts as well as other SDV decreased as age increased—yet the risk was higher in the COVID group in both younger and older adults.

We found that the risk of suicide attempts and other forms of SDV were greatest during the first 30 days after infection, and the subsequent period of increased risk seemed to vary across subgroups. Whether the elevated short term versus longer term risk of suicide attempts and other forms of SDV observed in our study reflects sudden disruption in care versus the underlying biology of infection and associated inflammatory response,[31] or others aspects, is unknown. Our findings raise the question of whether bolstering social connectedness and protective psychosocial characteristics may help mitigate risk of suicide attempts and other forms of SDV,[32, 33] and suggest that the timing of such actions, including pivoting to alternative care delivery options and providing resources (e.g., suicide hotline, information on mental health services, access to virtual care support) and/or outreach as early as possible may be important.

Although suicide attempts and other forms of SDV were rare (0.258% had suicide attempt, 0.244% had other SDV), these are important risk factors for future occurrences as well as suicide completion.[12, 34] While these unadjusted rates are substantially lower than those reported for the Veteran population during the two-year period preceding the pandemic among cohort members, it is possible that the lower rates during the pandemic resulted from care disruption and limited access to other routine health visits that provide an opportunity to uncover these events.[35, 36]

Our findings align with the national VA suicide prevention strategy indicating the need for an increased focus on suicide risk among at-risk populations such as those infected with SARS-COV-2.[37] To facilitate such efforts, VA has implemented tiered, universal suicide risk screening. For example, nurses and medical assistants can complete the initial screening instrument and direct appropriate patients to a licensed independent provider -only a small proportion of patients require further evaluation (0.4–2.1%) suggesting such screenings have had limited impact on capacity.[38] Further, among those identified who were not previously in care, those who had a positive suicide screen were more likely to have mental health care follow-up, suggesting screening may increase mental healthcare.[38, 39]

There are limitations to our study. First, although we used data that differentiated between current and historical events, we cannot rule out outcome ascertainment bias related to increased access to healthcare among SARS-COV-2-infected patients during the pandemic. Second, lack of cause of death data prevented inclusion of deaths caused by suicide as a separate outcome. Third, although we included both VHA and Medicare claims data to capture documentation of SARS-COV-2 infection, some misclassification of infected Veterans is inevitable, particularly with greater home testing, or where patients did not know they were infected.[40] The attenuating association of SARS-COV-2 infection with study outcomes could reflect undetected infections in comparators. Fourth, although we achieved close matching and/or good balance on available covariates, our results may still be subject to unobserved confounding.

CONCLUSIONS

This study employed an emulated trial design to assess the risk of attempted suicide and other SDV among patients with SARS-COV-2 infection compared to a contemporaneous matched uninfected comparator group. Our findings demonstrate that Veterans infected with SARS-COV-2 were at greater risk for suicide attempts and other SDV compared to similar patients who were not infected, and that the risks were especially elevated during the first 30 days after infection and persisted for at least a year after infection. Our findings highlight the importance of assessing the experiences of patients at elevated risk for suicide attempts and other forms of SDV beginning early after SARS-COV-2 infection and over at least the following year to identify opportunities for prevention and treatment.

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Data Availability *The datasets generated and/or analyzed during the current study are not publicly available due to US Department of Veterans Affairs data restrictions prohibiting sharing. Contact the corresponding author, Dr. Hynes for data requests.*

Declarations

Conflict of Interest *The authors report no conflicts.*

REFERENCES

1. **Rudenstine S, Schulder T, Bhatt KJ, McNeal K, Ettman CK, Galea S.** Suicidal ideation during COVID-19: The contribution of unique and cumulative stressors. Psychiatry Res. 2022;310:114475. doi:https://doi.org/10.1016/j.psychres.2022.114475
2. **Nichter B, Hill ML, Na PJ, et al.** Prevalence and trends in suicidal behavior among US Military Veterans during the COVID-19 Pandemic. JAMA Psychiatry. 2021;78(11):1218. doi:https://doi.org/10.1001/jamapsychiatry.2021.2332
3. **Taquet M, Geddes JR, Husain M, Luciano S, Harrison PJ.** 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. Lancet Psychiatry. 2021;8(5):416-427. doi:https://doi.org/10.1016/S2215-0366(21)00084-5
4. **Taquet M, Sillett R, Zhu L, et al.** Neurological and psychiatric risk trajectories after SARS-CoV-2 infection: an analysis of 2-year retrospective cohort studies including 1 284 437 patients. Lancet Psychiatry. 2022;9(10):815-827. doi:https://doi.org/10.1016/S2215-0366(22)00260-7
5. **Xie Y, Xu E, Al-Aly Z.** Risks of mental health outcomes in people with covid-19: cohort study. BMJ. Published online February 16, 2022:e068993. https://doi.org/10.1136/bmj-2021-068993
6. U.S. Centers for disease control and prevention. COVID data tracker. Accessed December 23, 2022. https://covid.cdc.gov/covid-data-tracker
7. **McCarthy JF, Bossarte RM, Katz IR, et al.** Predictive modeling and concentration of the risk of suicide: implications for preventive interventions in the US department of Veterans affairs. Am J Public Health. 2015;105(9):1935-1942. doi:https://doi.org/10.2105/AJPH.2015.302737
8. **Bullman T, Schneiderman A**. Risk of suicide among U.S. Veterans who deployed as part of operation enduring freedom, operation iraqi freedom, and operation new dawn. Inj Epidemiol. 2021;8(1):40. doi:https://doi.org/10.1186/s40621-021-00332-y
9. **Veazie S, Lafavor B, Vela K, et al.** Mental health outcomes of adults hospitalized for COVID-19: A systematic review. J Affect Disord Rep. 2022;8:100312. doi:https://doi.org/10.1016/j.jadr.2022.100312
10. U.S. Department of Veterans Affairs. Veterans Health Administration. Accessed December 23, 2022. https://www.va.gov/health/
11. U.S. Department of Veterans Affairs. 2021 National veteran suicide prevention annual report. Office of mental health and suicide prevention; 2021:17. https://www.mentalhealth.va.gov/docs/data-sheets/2021/2021-National-Veteran-Suicide-Prevention-Annual-Report-FINAL-9-8-21.pdf
12. **Hein T, Cooper SA, McCarthy JF.** Mortality following non-fatal suicide attempts by Veterans in Veterans Health. Suicide Life Threat Behav. 2022;52(2):222-230. doi:https://doi.org/10.1111/sltb.12811
13. **Smith VA, Berkowitz TSZ, Hebert P, et al.** Design and analysis of outcomes following SARS-CoV-2 infection in Veterans. BMC Med Res Methodol. 2023;23(1):81. doi:https://doi.org/10.1186/s12874-023-01882-z
14. **Hernán MA, Robins JM.** Using big data to emulate a target trial when a randomized trial is not available: Table 1. Am J Epidemiol. 2016;183(8):758-764. doi:https://doi.org/10.1093/aje/kwv254

15. **Smith VA, Berkowitz TSZ, Hebert P, et al.** Correction: Design and analysis of outcomes following SARS-CoV-2 infection in Veterans. BMC Med Res Methodol. 2023;23:194. doi:https://doi.org/10.1186/s12874-023-02021-4
16. The assessment and management of suicide risk work group. VA/DoD Clinical practice guideline for assessment and management of patients at risk for suicide.U.S. Department of Veterans Affairs, Department of Defense; 2019.
17. **Crosby A, Ortega L, Melanson C.** Self-directed violence surveillance; uniform definitions and recommended data elements. Centers for Disease Control and Prevention; 2011.
18. **Hoffmire C, Stephens B, Morley S, Thompson C, Kemp J, Bossarte RM.** VA suicide prevention applications network: A national health care system–based suicide event tracking system. Public Health Rep. 2016;131(6):816-821. doi:https://doi.org/10.1177/0033354916670133
19. **Palframan KM, Szymanski BR, McCarthy JF.** Ascertainment of patient suicides by veterans affairs facilities and associations with Veteran, Clinical, and suicide characteristics. Am J Public Health. 2021;111(S2):S116-S125. doi:https://doi.org/10.2105/AJPH.2021.306262
20. **Austin PC.** Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. Commun Stat - Simul Comput. 2009;38(6):1228-1234. doi:https://doi.org/10.1080/03610910902859574
21. **Austin PC, Lee DS, Fine JP.** Introduction to the analysis of survival data in the presence of competing risks. Circulation. 2016;133(6):601-609. doi:https://doi.org/10.1161/CIRCULATIONAHA.115.017719
22. **Nguyen TL, Collins GS, Spence J, et al.** Double-adjustment in propensity score matching analysis: choosing a threshold for considering residual imbalance. BMC Med Res Methodol. 2017;17(1):78. doi:https://doi.org/10.1186/s12874-017-0338-0
23. **Hedegaard H.** Suicide rates in the United States continue to increase. NCHS Data Brief. 2018;(309).
24. Centers for disease control and prevention, National center for injury prevention and control. Suicide data and statistics. Centers for Disease Control and Prevention. Published August 10, 2023. Accessed September 13, 2023. https://www.cdc.gov/suicide/suicide-data-statistics.html
25. **Rockett IRH, Caine ED, Connery HS, et al.** Unrecognised self-injury mortality (SIM) trends among racial/ethnic minorities and women in the USA. Inj Prev. 2020;26(5):439-447. doi:https://doi.org/10.1136/injuryprev-2019-043371
26. **Thomeer MB, Moody MD, Yahirun J.** Racial and ethnic disparities in mental health and mental health care during the COVID-19 Pandemic. J Racial Ethn Health Disparities. 2023;10(2):961-976. doi:https://doi.org/10.1007/s40615-022-01284-9
27. **Erlangsen A, Qin P, Madsen T, et al.** Association between SARS-CoV-2 infection and self-harm: Danish nationwide register-based cohort study. Br J Psychiatry. 2023;222(4):167-174. doi:https://doi.org/10.1192/bjp.2022.194
28. **Chen JI, Cameron DC, Laliberte AZ, Hooker ER, Niederhausen M, Denneson LM.** Assessment of suicidal intent in self-directed violence and subsequent care received among military Veterans: A National Study of Gender Differences. Med Care. 2021;59:S17-S22. doi:https://doi.org/10.1097/MLR.0000000000001455
29. **Fernández-de-las-Peñas C, Martín-Guerrero JD, Pellicer-Valero ÓJ, et al.** Female sex is a risk factor associated with long-term post-COVID related-symptoms but not with COVID-19 symptoms: The LONG-COVID-EXP-CM Multicenter Study. J Clin Med. 2022;11(2):413. doi:https://doi.org/10.3390/jcm11020413
30 **Dubé JP, Smith MM, Sherry SB, Hewitt PL, Stewart SH.** Suicide behaviors during the COVID-19 pandemic: A meta-analysis of 54 studies. Psychiatry Res. 2021;301. doi:https://doi.org/10.1016/j.psychres.2021.113998
31. **Costanza A, Amerio A, Aguglia A, et al.** Hyper/neuroinflammation in COVID-19 and suicide etiopathogenesis: Hypothesis for a nefarious collision? Neurosci Biobehav Rev. 2022;136:104606. doi:https://doi.org/10.1016/j.neubiorev.2022.104606
32. **Herzog S, Tsai J, Nichter B, Kachadourian L, Harpaz-Rotem I, Pietrzak R.** Longitudinal courses of suicidal ideation in U.S. military Veterans: a 7-year population-based, prospective cohort study [published online ahead of print. Psychol Med. Published online February 19, 2021:1–10. https://doi.org/10.1017/S0033291721000301
33. **Cui R, Gujral S, Galfalvy H, Szanto K.** The Role of perceived and objective social connectedness on risk for suicidal thoughts and behavior in late-life and their moderating effect on cognitive deficits. Am J Geriatr Psychiatry. 2022;30(4):527-532. doi:https://doi.org/10.1016/j.jagp.2021.08.014
34. **Gradus JL, Street AE, Suvak MK, Resick PA.** Predictors of suicidal ideation in a gender-stratified sample of OEF OIF. Suicide Life Threat Behav. 2013;43(5):574-588. doi:https://doi.org/10.1111/sltb.12040
35. **Czeisler MÉ, Marynak K, Clarke KEN, et al**. Delay or Avoidance of medical care because of COVID-19–Related Concerns - United States, June 2020. Morb Mortal Wkly Rep. 2020;69(36):8.
36. **Allameh SF, Shateri Amiri B, Zarei Jalalabadi N.** Disruption in medical care of non-COVID Patients in COVID-19 Pandemic. Adv J Emerg Med. 2020;4(2s):e45. doi:https://doi.org/10.22114/ajem.v4i2s.394
37. U.S. Department of Veterans Affairs. 2022 National Veteran Suicide Prevention Annual Report. Office of Mental Health and Suicide Prevention; 2022:43.
38. **Bahraini N, Brenner LA, Barry C, et al.** Assessment of Rates of Suicide Risk Screening and Prevalence of Positive Screening Results Among US Veterans After Implementation of the Veterans Affairs Suicide Risk Identification Strategy. JAMA Netw Open. 2020;3(10):e2022531. doi:https://doi.org/10.1001/jamanetworkopen.2020.22531
39. **Bahraini N, Reis DJ, Matarazzo BB, Hostetter T, Wade C, Brenner LA.** Mental health follow-up and treatment engagement following suicide risk screening in the Veterans Health Administration. Doran N, ed. PLOS ONE. 2022;17(3):e0265474. doi:https://doi.org/10.1371/journal.pone.0265474
40. **Ferguson JM, Abdel Magid HS, Purnell AL, Kiang MV, Osborne TF.** Differences in COVID-19 testing and test positivity among veterans, United States, 2020. Public Health Rep. 2021;136(4):483-492. doi:https://doi.org/10.1177/00333549211009498