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Associations between Post Traumatic Stress Disorder, Combat Exposure, and COVID-19 Post Acute Sequalae among War Veterans

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B.S.
William & Mary
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2024

Abstract

Associations between Post Traumatic Stress Disorder, Combat Exposure, and COVID-19 Post Acute Sequalae among War Veterans

By Thomas Hess

Objectives: In this analysis, we sought to determine whether PTSD could increase the risk of Post Acute Sequelae of COVID-19 (PASC) outcomes and whether combat exposure and number of deployments had a modifying effect on this association for individuals who served in Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn (OEF/OIF/OND).

Design: This was a secondary analysis of electronic health record data contained in the Corporate Data Warehouse (CDW) and DaVINCI databases in the VA national health delivery system.

Methods: Veterans diagnosed with COVID-19 were included in the analyses. Demographic and clinical data were compared using the Chi-squared test for categorical data and Mann-Whitney-Wilcoxon for continuous data. The logistic regression analysis was conducted using a Poisson distribution. Models were adjusted for covariates based on previous research and subject matter recommendations.

Results: More than 116,000 OEF/OIF/OND Veterans with COVID-19 were analyzed; most were men, white and an average age of 44 years. Additionally, more than 50% had a diagnosis of PTSD prior to their COVID-19 diagnosis and 4% were diagnosed with PASC. Veterans with PTSD were more than three times as likely to have PASC outcomes compared to those without PTSD (incidence rate (IR) of 3.58 (95% Confidence Interval (CI) 3.54, 3.61, p-value < 0.01). When number of deployments was considered as an effect modifier, Veterans with PTSD who were deployed 2 times or more were 62% more likely to have PASC compared to those with PTSD who deployed 1 time (IR 1.62, 95% CI 1.34, 1.95, $p < 0.001$).

Conclusion: This research shows the importance of conducting observational epidemiological research on populations with increased rates of PTSD such as Veterans. Interventions targeting Veterans who have PTSD and/or were exposed to a higher number of deployments should have special considerations regarding their PASC risk.

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1. Introduction

1.1 Overview

The Coronavirus-19 (COVID-19) global pandemic caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) was one of the largest public health crises in history. Its scale was, and still is, global and continues to influence societal spheres. Systemic issues and vulnerabilities before the pandemic were put under greater strain thereafter through physical, social, and psychological burdens. Vulnerable populations such as individuals suffering from Post Traumatic Stress Disorder (PTSD) were susceptible to worse outcomes[1]. This analysis is focused on the relationship between PTSD and post-acute sequelae of COVID-19 (PASC) among Veterans who have had COVID-19.

The SARS-CoV-2 virus is a single-stranded positive-sense RNA virus that infects an individual after it is inhaled into the respiratory system. Other forms of coronaviruses previously had human transmission such as SARS-CoV-1 in 2002 and MERS-CoV in 2012. Comparatively, SARS-CoV-2 shares many structural and genetic similarities, specifically with a 94.6% amino acid and 80% nucleotide base pairing to SARS-CoV-1[2]. After entering the respiratory tract, the viral spike protein binds the angiotensin-converting enzyme (ACE2) receptor on the surface of host epithelial cells. For this binding and subsequent fusion to occur, the spike protein is cleaved into active components by the host transmembrane protease serine two protein (TMPRSS2) ultimately permitting the virus to enter and consequently infect the host cell[3,4]. After entering the cell, mutations in the spike protein are also responsible for variability in the infectivity of viral variants.

PASC is a complication of COVID-19, and is defined as continuous, remerging, or the emergence of COVID-19 like symptoms after the acute stage of a SARS-CoV-2 infection[4]. As

defined by the CDC, PASC is a form of Long COVID[5]. Long COVID is the lasting health effects that occur after a SARS-CoV-2 infection. The term was first used in public health discourse after May 2020 in Lombardy Italy[6]. An international standard to identify different chronic and communicable disease diagnosis provided by the World Health Organization (WHO) are International Classification of Diseases (ICD) codes[7]. PASC was issued a corresponding ICD-10 code on October 2021, 17 months after the term was first used in Italy[8]. Long COVID was not a clinical diagnosis early in the pandemic but rather was defined by patients who began suffering from this complication. Therefore, the late emergence of the ICD-10 codes, the varied presentation, and the lack of care resources may undercount the true burden of PASC in the general population. To complicate matters further; there are different subtypes (endotypes) of PASC. For example, Deer et. al. used Human Phenotype Ontology to determine that there could be as many as 287 unique phenotypic abnormalities. Some of these unique abnormalities could include memory impairment, insomnia, and other physical and psychological factors[9].

1.2 Combat Related PTSD

According to the Veterans Affairs, combat-related PTSD is defined as traumatic events during war specifically with deployment to a combat zone involving life-threatening situations where the individual has experienced injury or death, had a serious accident, or handled human remains[10]. These experiences eventually lead to post traumatic stress symptoms (PTSS) which can include nightmares, insomnia, hypervigilance, and the evasion of psychological triggers[11]. Different risk factors for combat-related PTSD increase over deployment time, physical trauma, for those serving with a lower military rank, education level, and unit morale[10]. Veterans Affairs research has found that 10 to 18% of all troops returning from Operation Enduring Freedom or Operation Iraqi Freedom (OEF/OIF) are likely to have PTSD after their deployment[10].

This study is focused on Veterans from the most recent conflict in US history Iraq and Afghanistan Wars. This was one of the longest armed conflicts in modern history, that lasted 20 years in scale. The longevity of this war means that it also had substantial impacts across the Millennial generation. Combat exposure and respiratory illness risk have been investigated by the Veteran's Affairs. Burn pits, as defined by the burning of trash outside, can lead to the inhalation of large particles or hazardous chemicals[12]. General respiratory risk regarding burn pit exposure is highly variable depending on the location of military camp or the self-reported radius around the burn pit[13]. Despite the evidence for general respiratory risk, there has been no research regarding the risk of COVID-19 or PASC risk after burn pit exposure.

1.3 PTSD and PASC

The overall field of PASC research is still nascent, especially regarding the relationship to PTSD. Most of the literature has investigated COVID-19 outcomes in addition to PASC. Nishimi et. al. examined the relationship between COVID-19 and PTSD regarding hospitalizations and deaths due to complications such as comorbidities, health behaviors, and immune disorders[1]. The researchers determined that among those that were not diagnosed with psychiatric conditions, Veterans Administration patients with PTSD were at higher risk for hospitalization and death following a COVID-19 infection[1]. They also found that individuals older than 65 years and those with bipolar disorder, substance abuse, and alcoholism were more likely to be hospitalized. One study, during the initial emergence of PASC, determined that the primary barriers for these groups were economic, geographical, housing, and occupational disparities[14]. Studies conducted within the Veterans Health Administration found that these social determinants of health play an important role in Veteran PASC incidence[15].

1.4 Preventing PASC

One method to protect against PASC is through vaccination which helps prevent transmission of COVID-19 and reduces the overall severity of the infection. Tenforde et. al. determined that mRNA vaccines, Moderna (mRNA-1273) and Pfizer (BNT162b2), are associated with better outcomes even among those hospitalized including less mortality and a lower need for mechanical ventilation. Beyond vaccinations, treatment of COVID-19 with monoclonal antibodies has been shown to reduce the risk of and complications from PASC[16]. However, among US Veterans, research showed an overall decline in the proportion receiving pharmacotherapy after August 2022, though the investigator hypothesized this may be due to more asymptomatic infections and higher rates of mild COVID-19 cases that are not commonly treated with monoclonal antibodies[17].

2. Methods

2.1 Specific Aims

This study's main aim was to determine the association between combated-related PTSD and separate outcomes defined as the incidence of PASC among Veterans deployed for OEF/OIF/OND operations. The study was approved by the Emory University Institutional Review Board and the Atlanta VA Medical Center Research and Development Committee. A waiver of consent was obtained for this analysis.

2.2 Data Sources

This analysis was done using electronic health record data that were prospectively entered for Veterans deployed for OEF/OIF/OND operations across the VA healthcare system using two different data sources. The Corporate Data Warehouse (CDW) is a database used by the VA national healthcare delivery system to store patient health information across the entire network. There are nearly 20 million patients recorded within this dataset, which is continuously updated. The Department of Defense (DoD) and VA Infrastructure for Clinical Intelligence (DaVINCI) is an electronic database that pulls data through the DoD and the VA. This provides an important pipeline of information that provides different key characteristics regarding Veterans.

2.3 Study design and model specification

This study characterized the association between PTSD and PASC among Veterans that previously been deployed during OEF/OIF/OND military operations after 9/11 who had an inpatient or outpatient ICD10 code of COVID-19. This study included individuals that were deployed to both combat and non-combat zones and included individuals enrolled in any of the

171 VA medical centers or the 1,112 VA outpatient clinics across the United States[18]. Data were first extracted from the VINCI network and was imported into Statistical Analysis Software (SAS) to conduct analysis. Veterans without a COVID-19 associated ICD10 code and Veterans without service dates associated with OEF/OIF/OND military operations were excluded from this analysis. After this initial filtering of data, the data was then cleaned to allow for input into regression models. The variables used in this study are specified in Table 1. Variables such as age at VA COVID diagnosis, age at military separation, and number of deployments were calculated from the extracted dates. The final dataset contained 116,547 Veterans.

PTSD is the exposure of interest in this study and data were collected for all diagnoses that occurred after US involvement in Afghanistan in 2002. The variables and corresponding definitions are summarized in Table 1. Demographic and clinical characteristics, such as age, sex, income, and race, that could have an impact on the incidence of PTSD and COVID-19 were organized into a directed acyclic graph as shown in Figure 1. PTSD was defined as the exposure of interest and was defined using the corresponding ICD9 and ICD10 codes. To be included, the occurrence of PTSD had to happen after the OEF/OIF/OND deployment date. The related outcome of interest of PASC was defined using the corresponding ICD-10 codes. The linear regression model was adjusted for these variables. Additionally, depression and anxiety metrics were adjusted for logistic regression models. Confounding variables included military related factors, such as military rank, branch, the number of tours, and length of service. This analysis was performed using Poisson models to incorporate PTSD onset time and for modeling the outcome of PASC.

Poisson model for PASC:

Poisson function: $\ln(\lambda_{ij}) = \ln(\frac{E(Y_{ij})}{l})$

Poisson model: $\ln(\lambda_{ij}) = \alpha + \beta_1 PTSD + \gamma_1 AGE + \gamma_2 RACE_1 + \gamma_3 RACE_2 + \gamma_4 RACE_3 + \gamma_5 RACE_4 + \gamma_6 EDUCATION + \gamma_7 INCOME + \gamma_8 ANXIETY + \gamma_9 DEPRESSION$

$Where\ \alpha = intercept$

$\beta_i = regression\ coefficent\ for\ exposure$

Poisson model for PASC with Combat as an Effect Measure Modifier (EMM):

Poisson function: $\ln(\lambda_{ij}) = \ln(\frac{E(Y_{ij})}{l})$

Poisson model: $\ln(\lambda_{ij}) = \alpha + \beta_1 PTSD + \gamma_1 AGE + \gamma_2 RACE_1 + \gamma_3 RACE_2 + \gamma_4 RACE_3 + \gamma_5 RACE_4 + \gamma_6 EDUCATION + \gamma_7 INCOME + \gamma_8 ANXIETY + \gamma_9 DEPRESSION + \delta_1 PTSD * COMBAT$

$Where\ \alpha = intercept$

$\beta_i = regression\ coefficent\ for\ exposure$

$\gamma_i = regression\ coefficient\ for\ confounder$

$\delta_i = regression\ coefficient\ for\ effect\ measure\ modifier$

Poisson model for PASC with Combat and Deployment as an EMM:

Poisson function: $\ln(\lambda_{ij}) = \ln(\frac{E(Y_{ij})}{l})$

Poisson model: $\ln(\lambda_{ij}) = \alpha + \beta_1 PTSD + \gamma_1 AGE + \gamma_2 RACE_1 + \gamma_3 RACE_2 + \gamma_4 RACE_3 + \gamma_5 RACE_4 + \gamma_6 EDUCATION + \gamma_7 INCOME + \gamma_8 ANXIETY + \gamma_9 DEPRESSION + \delta_1 PTSD * COMBAT + \delta_2 PTSD * DEPLOYMENT$

$Where\ \alpha = intercept$

$\beta_i = regression\ coefficent\ for\ exposure$

$\gamma_i = regression\ coefficient\ for\ confounder$

$\delta_i = regression\ coefficient\ for\ effect\ measure\ modifier$

$\gamma_i = regression\ coefficient\ for\ confounder$

2.4 Bias Considerations

The exposure of combat-related PTSD is likely to have bias in the form of non-differential misclassification of the exposure. In this situation the true cause of PTSD cannot be determined. PTSD can vary in severity, and by the number of PTSS. However, properly recording this level of detail is not possible with the current dataset. Previous research conducted by Vyas et. al. discovered that only 64% of Veterans who were deployed to a combat zone during OEF/OIF/OND reported combat exposure[18]. This problem can make it difficult for researchers to properly ascertain the reason for PTSD within a study population. Additionally, COVID-19 was a highly stressful event which has had psychosocial implications for many individuals and has led to an increase in the number of PTSD cases reported[19]. To account for this issue, the study included individuals who had combat-related service for their deployment during OEF/OIF/OND.

Table 2 provides the current counts or medians of the data, with the column percentage for the overall total, and row percentages for those with the outcome of PASC or not. Household income was set to quartiles, to allow for a more direct comparison using the Chi-squared test. Data about military rank and form of service (active, reserve, or national guard) were categorized. The underlying assumption of the Chi-squared test was a non-parametric statistic, which was appropriate for categorical data where the underlying distribution is unknown. This test also assumed that the sample sizes were unequal. Mann-Whitney-Wilcoxon (MWW) test were used for continuous data, which also assumes a non-parametric distribution as well. This test works through the calculation of weighted sums, which is then used to explain variation group to group. When creating the table, some variables had more missing data such as

education, which was missing for 28,049 patients. The dataset included all Veterans that were involved with the OEF/OIF/OND operations and were censored on December 31, 2023.

3. Results

More than half of the cohort had a diagnosis of PTSD (52.05%), 53.07% were diagnosed with anxiety, and 37.87% with depression (Table 2). Four percent of Veterans were diagnosed with PASC using the ICD10 codes in this analysis, and of these, 57.11% had a previous diagnosis of PTSD. Of the veterans without PASC, 43% of them had a previous PTSD diagnosis. There were differences in PTSD incidence among individuals with anxiety (36.48%) having PTSD compared to those who were not diagnosed with anxiety ($p < 0.001$). More than 40% of the veterans with PTSD also had depression (43.58%) and Veterans who had one deployment (versus two) were more likely to have PTSD (76.00% versus 24.00%).

Most of the patients were biologically male (83.22%), high school educated (63.90%), and had an annual income between $40,000 and $74,999 (38.88%). Veterans across all education levels had differing PASC incidence ($p = 0.003$), with the highest burden being for individuals who received a high school education (61.44%). Across all income levels, there were differences in PASC status with the most PASC seen in the upper income levels ($p = 0.008$). Though the cohort was primarily male, females were disproportionately more like to have PASC ($p < 0.001$).

Regarding military characteristics, most of the patients were in the Army (58.33%), on active duty 81.20%, and with the rank grades of E5 through E9 (61.50%). There were differences in the burden of PASC across all branches within the military ($p < 0.001$), with those in the Army having a higher burden of PASC. For military rank there were meaningful differences in PASC risk, with the greatest burden being among enlisted members ranked E1-E4 (56.31%). The average age for service withdrawal among the sample was 31 years of age (IQR: 16). Only 18%

of the veterans in this cohort had seen combat but more than 76% had been deployed at least two times.

Veterans with PTSD were more than three times as likely to have PASC outcomes than those without PTSD (IR 3.58, 95% CI 3.54, 3.61, p-value < 0.001) after controlling for biological sex, branch, age at COVID diagnosis, age at service, education, race, and household income (Table 3). Combat and the number of deployments were used as effect measure modifiers within the Poisson regression models and were tested for interaction. When combat was considered as an effect measure modifier, no association was found between PTSD and PASC (IR 0.945, 95% CI 0.81-1.10, p-value = 0.46) after controlling for biological sex, branch, age at COVID diagnosis, age at service, education, race, and household income. When the number of deployments was considered as an effect modifier, Veterans with PTSD were 62% more likely to have PASC compared to those without PTSD (IR 1.62; 95% CI 1.34-1.95, p < 0.001 after controlling for the same variables.

4. Discussion

Four percent of the patients in this analysis of more than 117,000 Veterans had PASC, and 52% had a history of PTSD diagnosed since 2001. In an adjusted model examining the relationship between PTSD and PASC in Veterans who had had a documented case of COVID-19, Veterans with PTSD were more than three times as likely to have PASC outcomes than those without PTSD. Previous literature has found that Veterans had higher rates of COVID-19 has been related hospitalization and death compared to Veterans without PTSD[1]. This analysis adds long-term complications from COVID-19 to the list of increased risk for veterans and further describes how large the burden of COVID-19 is on our Veteran population. The relationship between PTSD and PASC is not well understood but a possible explanation is the psychological and biochemical abnormalities in the endocrine system and increases in an individual's allostatic load associated with PTSD are also associated with, or increasing the risk of, PASC, possibly due through to the sustained alterations of the immunologic pathways[20].

When combat was considered as an effect measure modifier, no association was found between PTSD and PASC (IR 0.945, 95% CI, 0.81, 1.10, p-value = 0.46). This null result may be due to issues regarding information bias with combat exposures. The number of individuals exposed to combat were more predisposed to get PTSD. Therefore, there is not an issue of directionality regarding combat and exposure. Additional information regarding combat, such as the province of deployment, or hours of exposure may be important in determining the level of severity of combat. While the results for combat were not statistically significant, it should be noted that there may be issues regarding the self-reporting of combat. Combat exposure can vary in length and severity, which can be difficult to quantify, and we dichotomized this variable and included all combat together. Other research has included more combat related characteristics

such as deployment climate, large particulate matter exposure, and closeness of living quarters to determine the effect of combat related service more accurately on respiratory illnesses[21]. A more qualitative approach regarding combat experience may be required to investigate this variable properly.

The number of deployments is more quantifiable and can be used to determine the burden of service for Veterans. When the number of deployments was considered as an effect modifier, Veterans with PTSD who were deployed 2 times or more were 62% more likely to have PASC compared to those with PTSD who deployed 1 time. These models help describe the burden PTSD and number of deployments can have on Veterans who have served within the OEF/OIF/OND operations. Increased deployment count may be related to an increased risk in more general exposures during military service. Prior research on Veterans who have served in OEF/OIF/OND as well as other operations in the Middle East were more likely to have experienced airborne hazards such oil-well fire smoke, burn pit emissions, and airborne sand or dust particles[22].

This is the first to examine the relationship between PTSD in Veterans and the long term sequalae of COVID-19. Additionally, this study used data from the robust VA datasets and included many covariates to describe social aspects of PTSD and PASC. This study also has limitations. The definition of PASC is ever evolving and in this analysis, we limited this to two previously used ICD-10 codes, which may not fully represent the full nature of PASC. Additionally, different characteristics of a COVID-19 may be important to the risk of PASC, such as SARS-CoV-2 viral load, inflammatory biomarkers, or antibody titers, but they were not available for this analysis. This analysis also examined PTSD from operations that concluded many years ago, thus allowing for a long length of time from the onset of PTSD and the COVID-

10 pandemic. The deployments considered in this analysis ended at different dates, Operation Iraqi Freedom in 2003, Operation New Dawn in 2011, and Operation Enduring Freedom in 2014. Combat PTSD can affect individuals for the rest of their lives, but it also may be more acute with closer time proximity to serviceI[23]. Additionally, the level of combat severity for individuals can vary substantially and this analysis examined combat exposure as a dichotomous variable, which may miss the amount of time in combat[24]. Other important psychological implications of PTSD such as insomnia or nightmares were not accounted for with the data. Many aspects of this condition are highly individualistic and would require more qualitative data to reflect on individual experiences more accurately.

Future studies should continue to explore the relationship between PTSD and long-term sequelae of COVID-19 in Veterans or other people who have experienced PTSD. Additionally, the underlying mechanisms for how PTSD might increase the risk of PASC should be examined. This study shows that PTSD was observed to increase the risk of PASC for OEF/OIF/OND Veterans. This study was conducted in the US Veterans population that served in OEF/OIF/OND operations and shows the importance of conducting observational epidemiological research on populations with increased rates of PTSD such as Veterans. PTSD reduction programs, such as the VHA's primary care mental health integration (PCMHI) program or similar initiatives, help individuals seek PTSD-related care[25]. These programs are important to reduce the burden on our Veterans. Interventions targeting Veterans who have PTSD and/or were exposed to a higher number of deployments should consider the increased risk of long-term complications when a veteran has COVID-19. Reducing the social, economic, and health burdens of veterans through interventions can help ease the disparities caused by the COVID-19 pandemic. The effect that

COVID-19 has had on our Veterans is important for policymakers to consider as they push for efforts that continue to provide medical support to this vulnerable population.

5. List of Abbreviations

CDW Corporate Data Warehouse

CI Confidence interval

DAG Directed acyclic graph

DaVINCI DoD and VA Infrastructure for Clinical Intelligence

DF Degrees of freedom

DoD Department of Defense

HR Hazard ratio

IED Improvised explosive device

International Classification of Diseases

MMW Mann-Whitney-Wilcoxon

OEF/OIF/OND Operations Enduring Freedom, Iraqi Freedom, and New Dawn

OR Odds ratio

(PCMHI) Primary care mental health integration

PTSD Posttraumatic stress disorder

PTSS Posttraumatic stress symptoms

SAS Statistical Analysis Software

VA Veterans Affairs

VINCI VA Informatics and Computing Infrastructure

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7. Tables

Table 1. Definitions of Study Covariates

	Variable	Definition	Source
Confounders (time-independent)	Sex	Biologically assigned at birth male or female	CDW
	Age	Calculated from date of birth (DOB) and date of VA eligibility (DOE)	
	Race	(1) White (2) Black (3) Asian (4) Native American and Pacific Islander	
Confounders (time-dependent)	Depression	Clinical-diagnosis with codes: (ICD-9: 296.3; ICD-10: F33) after the Veteran ended their deployment and before PTSD diagnosis.	CDW
	Anxiety	Clinical-diagnosis with codes: (ICD-9: 300.00, 300.02, 300.09) (ICD-10: F41.1, F41.3, F41.8, F41.9) after the Veteran ended their deployment and before PTSD diagnosis.	
	Branch	Branch of service, to include Army, Air Force, Marines, Navy, and Coast Guard	DaVINCI
	Length	Length of military service	
	Rank	Military rank: Enlisted: E1-E4; Non-commissioned officers: E4-E9 Warrant officers: W1-W5; Commissioned officers: O1-O-10	
Effect Measure Modifiers	Combat	Combat or combat-related service defined by Veteran VA eligibility, determined through if an individual that experienced combat or had combat-related service	DaVINCI
	Deployment number	The number of deployments calculated from the OEF/OIF/OND start and end dates among individuals that were in support of OEF/OIF/OND	
	Date of Birth (DOB)	Date where patient was born	CDW
	Date of Eligibility (DOE)	Date where patient was eligible for VA care	
	Date of Death (DOD)	Date where patient died (general mortality that can include deaths outside COVID-19).	
	Last Visit	Date where patient last visited the VA for any reason	
	COVID-19	Clinical-diagnosis with codes: (U07.1, J12.89, J20.8, J22, J80, Z86.16, Z28.310, Z28.311)	

Table 2. Characteristics of OEF/OIF/OND Veterans by PASC diagnosis (2001-2024)

	N=117,362	PASC n=4,989	No PASC n=112,373	
	n (%)	n (%)	n (%)	P-value
Outcome				
PTSD	61,082 (52.05)	2,849 (57.11)	58,233 (42.89)	<0.001
Sociodemographic factors				
Age at COVID diagnosis (years), median (IQR)	44 (14)	46 (14)	44 (15)	0.024
Biological sex				<0.001
Male	97,666 (83.22)	3,980 (79.78)	93,686 (83.37)	
Female	19,696 (16.78)	1,009 (20.22)	18,687 (16.63)	
Race/ethnicity				<0.001
White	74,760 (72.08)	3,261 (75.12)	71,499 (71.95)	
Black	23,742 (22.89)	863 (19.88)	22,879 (23.02)	
Asian	3,378 (3.26)	124 (2.86)	3,254 (3.27)	
Native American or Pacific Islander	1,835 (1.77)	93 (2.14)	1,742 (1.75)	
Educational attainment				0.003
High school	54,485 (63.90)	2,353 (61.44)	54,485 (64.01)	
Vocational/technical	699 (0.82)	28 (0.73)	699 (0.82)	
College/university	29,939 (35.29)	1,449 (37.83)	29,939 (35.17)	
Household income (USD, annual)				0.008
<20,000	12,680 (11.06)	569 (11.66)	12,111 (11.03)	
20,000-39,999	22,986 (20.05)	1056 (21.65)	21,930 (19.98)	
40,000-74,999	44,571 (38.88)	1843 (37.78)	42,728 (38.92)	
≥75,000	34,414 (30.02)	1410 (28.91)	33,004 (30.07)	
Military history				
Age Service (years), median (IQR)	31 (16)	33 (16)	31 (16)	<0.001
Branch				<0.001
Air Force	18,992 (15.30)	913 (18.30)	18,079 (16.09)	
Army	68,459 (55.94)	2,999 (60.11)	65,460 (58.25)	
Coast Guard	326 (0.26)	11 (0.22)	315 (0.28)	
Marines	16,937 (13.64)	630 (14.51)	16,307 (12.63)	
Navy	19,452 (15.67)	785 (15.73)	18,667 (16.61)	
Component				<0.001
Active duty	72,022 (64.45)	3,052 (61.58)	72,022 (64.58)	
Guard	20,420 (18.32)	919 (18.54)	20,420 (18.31)	
Reserve	19,086 (17.23)	985 (19.87)	19,086 (17.11)	
Rank/grade				<0.001
Enlisted, E1-E4	66,567 (61.50)	2,590 (56.51)	63,977 (61.72)	
Enlisted, E5-E9	32,314 (29.85)	1,565 (34.15)	30,749 (29.66)	

Officer, O1-O9	9,364 (8.65)	428 (9.34)	8,936 (8.62)	
Number of deployments				0.008
1	27,626 (23.54)	1,273 (25.52)	26,353 (23.45)	
≥2	89,736 (76.46)	3,716 (74.48)	86,020 (76.55)	
Combat exposure				<0.001
Combat	21,481 (18.30)	520 (18.25)	12,546 (21.56)	
Noncombat	95,881 (81.70)	2329 (81.75)	45,687 (78.46)	
Mental health history				
Anxiety	62,286 (53.07)	3,056 (61.25)	59,230 (38.75)	<0.001
Depression	44,445 (37.87)	2,174 (43.58)	42,271 (56.42)	<0.001

CI, confidence interval; PASC, Post Acute Sequalae; IR, incidence rate; OEF/OIF/OND, Operations Enduring Freedom, Iraqi Freedom, and New Dawn; PTSD, posttraumatic stress disorder; VA, United States Department of Veterans Affairs. Includes all OEF/OIF/OND Veterans who enrolled in the VA between 7 October 2001 and 31 December 2020, and censored on 31 December 2023. Marginal structural Poisson models with generalized estimating equations, as appropriate, with a time-dependent exposure (PTSD), adjusted for time-independent confounders (age at military separation, sex, race/ethnicity, marital status, education, income) and time-dependent confounders (anxiety disorder, depressive disorder). Meets VA combat Veteran eligibility requirements.

Table 3. Associations between PTSD and PASC among OEF/OIF/OND Veterans with COVID-19

	PASC n=56,280 IR (95% CI)	P-value
PTSD		
Overall Model	3.58 (3.54, 3.61)	<0.001
PTSD with Combat as Effect Measure Modification		
Combat Exposure		
Yes	0.945 (0.81, 1.10)	0.46
No	1.168 (1.10, 1.24)	<0.001
PTSD with Deployments as Effect Measure Modification		
Deployments		
1	1.15 (1.03, 1.28)	0.012
≥2	1.62 (1.34, 1.95)	<0.001

CI, confidence interval; PASC, Post Acute Sequalae; IR, incidence rate; OEF/OIF/OND, Operations Enduring Freedom, Iraqi Freedom, and New Dawn; PTSD, posttraumatic stress disorder; VA, United States Department of Veterans Affairs, adjusted for time-independent confounders (age at military separation, sex, race/ethnicity, marital status, education, income) and time-dependent confounders (anxiety disorder, depressive disorder).

8. Figures

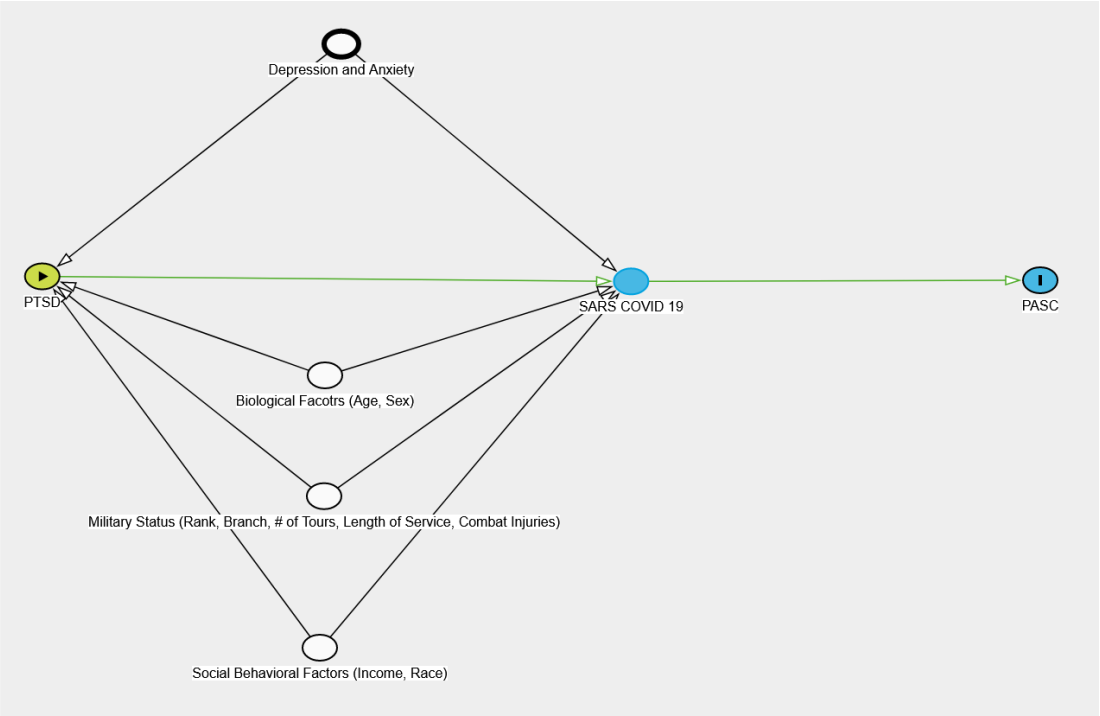

Figure 1. This directed acyclic graph (DAG) included covariates of interest listed in Table 1. This diagram was created using Daggity (https://dagitty.net/). PTSD was set as the exposure with PASC Incidence set as the outcome. Depression, anxiety, age, sex, income, race, rank, branch, number of tours, and length of service were determined to be confounders. Effect measure modifiers such as combat, and deployment were not included.