Military Population Health Outcomes Associated with Hospitalization for COVID-19 infection between 1 March 2020 and 31 December 2022

Karla Vega Colon

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Committee:
Luke Mease
Marissa Baker
Debra Cherry

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University of Washington

Abstract

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Karla Vega Colon

Chair of the Supervisory Committee:

Luke Mease

Department of Environmental and Occupational Health Sciences

BACKGROUND: Coronavirus Disease 2019 (COVID-19) has been shown to increase certain health outcomes including death, respiratory, and other conditions. It has increased the overall demand on the Military Health System (MHS). There are limited studies that measure the association between demographics and health risk factors and COVID-19 related adverse health outcomes for Department of Defense (DoD) beneficiaries.

METHODS: A retrospective cohort study was conducted to assess the associations between COVID-19 hospitalization and adverse health outcomes for MHS beneficiary population adjusting for demographics and risk factors using the DoD Joint Trauma Registry (JTR) COVID-19 Registry database.

RESULTS: 8,769 cases were included in this study. Among those who died after hospitalization from COVID-19 illness, the majority were 65 years and older (63%). Male sex assigned at birth

appeared be a significant predictor for being in a higher risk disposition group. Race appeared to be a minimal predictor of being in a higher risk disposition group. Burn pit exposure did not appear to be a significant predictor of being in a higher risk disposition group.

CONCLUSIONS: The results of this study suggest that those who were 65 years of age and older with more risk factors for severe disease had the highest odds of death and requiring ongoing care at time of hospital discharge when compared to those under 65 with fewer risk factors after adjusting for sex assigned at birth, race, rank/grade, burn pit registry status, and smoking status.

SPECIFIC AIMS

Respiratory illness caused by COVID-19 continue to be a threat not only to the military but also public health on a global scale. However, the impact of COVID-19 and related conditions on military readiness of its service members, personnel, and the dependents of the U.S. Armed Forces is not yet fully characterized. COVID-19 has been shown to increase the occurrence of certain health outcomes including mortality, as well as morbidity from cardiovascular, respiratory, psychiatric, and neurologic sequalae. The purpose of this study is to test for the presence of potential association between demographic factors, military factors, and pre-existing health conditions in our hospitalized military population within the MHS with COVID-19 illness and specific adverse outcomes to include death. The hypothesis of the study postulates that there are differences in COVID-19 health outcomes by demographic data (i.e., age, sex assigned at birth, race, rank/grade), military status (i.e., military and non-military dependent children and spouse) and pre-existing conditions (i.e., risk factors) affecting susceptibility and disease severity. The primary question of interest is how age, sex assigned at birth, race, rank/grade, military status, and pre-existing conditions are associated with the risk of COVID-19 adverse outcomes among hospitalized MHS beneficiaries. This study also focuses on assessing potential differences by military status including severity of illness and common risk factors, if any, among Service Members with significant disease (e.g., severe disease and/or deaths). Using de-identified DoD COVID-19 repository data, this study will capture the volume of cases that required hospitalization including those with severe disease requiring significant hospital resources and the impact on the military population.

Specific aim: To determine the characteristics of the U.S. Armed Forces service members and beneficiaries hospitalized with COVID-19 experiencing adverse health outcomes such as death or severe disease requiring ongoing care after hospitalization.

Sub aim 1.1: To characterize adverse health outcomes associated with hospitalization for COVID-19 by demographics within the Military Health System (MHS). Determine the odds and statistical significance of adverse health outcomes by demographics.

Sub aim 1.2: To characterize adverse health outcomes associated with hospitalization for COVID-19 by military specific risk factors. Determine the odds and statistical significance of adverse health outcomes by military risk factors.

Sub aim 1.3: To characterize adverse health outcomes associated with hospitalization for COVID-19 by previously defined (non-military) risk factors for severe disease within the MHS. Determine the odds and statistical significance of adverse health outcomes by number of risk factors.

RESEARCH STUDY

BACKGROUND AND SIGNIFICANCE:

Coronavirus Disease 2019 (COVID-19) has been shown to increase the occurrence of certain health outcomes including death and other sequelae including cardiovascular, respiratory, psychiatric, and neurologic conditions. Recent studies indicate that a patient's first infection with SARS-CoV-2 is associated with an increased risk of acute and post-acute sequelae, as well as death from injury to the pulmonary and broad array of extrapulmonary organ systems.[1] Although attenuated by vaccination, risk of these outcomes is present for all infected with SARS-CoV-2.[1] The risk of severe complications has been shown to increase after each reoccurring infection, as shown in a retrospective cohort study conducted by the Clinical Epidemiology Center for the

Veteran Affairs (VA) Saint Louis Health Care System. In this study, survival models showed a hazard ratio of 2.17 risk of death post-reinfection versus no reinfection after adjusting for demographic factors, diagnoses, prescription records, geographic region, and COVID-19 vaccination status.[1]

COVID-19 has also had a significant impact on military readiness and the MHS. A study published in September 2021, used surveillance modeling to show the impacts of quarantine length alone on military readiness by approximating lost duty days from a single COVID-19 case. This study demonstrated that from the 226,510 cases (as of August 25, 2021) the total DoD impact ranged from 5.4 to 13.4 million lost duty days for 7-day quarantine and 8.6 to 24.5 million lost duty days for 14-day quarantine depending on number of contacts per case (i.e., 2, 4, or 7).[2] Burden due to demands on the healthcare system caused by the increased healthcare response redirected towards the COVID-19 pandemic has reduced the MHS' ability to provide routine preventive medical services including childhood vaccinations, cancer screenings, and occupational health exams similar to U.S. Healthcare System.[3,4] Furthermore, U.S. Armed Forces had to mobilize medical resources to help support the overwhelmed civilian hospital systems[5,6] while still having the task of maintaining operations and readiness to deploy.[7,8]

Since the onset of the pandemic in early 2020 the VA has conducted active COVID-19 surveillance using the "Surveillance Platform for Enteric and Respiratory Infectious Organisms in the Veteran Affairs population," or "SUPERNOVA," where information was gathered on cases of 400,000 veterans with acute gastroenteritis and respiratory illnesses across five VA hospitals.[9] This study concluded that Black and Hispanic veterans were more likely to test positive for COVID-19 and have a higher risk for sepsis and respiratory, neurologic, and renal in-hospital complications when compared to White veterans.[9] Age was also a predictor, where veterans over 65 years old had a

4.5-fold rate of hospitalization and veterans over 85 years old had a 14-fold rate of hospitalization compared to those 18-29 years of age.[9] Demographic information from another nationwide cohort study conducted by the VA Connecticut Healthcare System noticed that Black and Hispanic veterans were experiencing an excess burden of COVID-19.[10] This study used the electronic health records from the largest integrated healthcare system in the U.S. to investigate racial and ethnic disparities in testing and subsequent COVID-19 mortality.

While the VA has analyzed the impact of COVID-19 among more than 9,000,000 its beneficiaries, the impact of COVID-19 and related outcomes on military missions, readiness, service members and their dependents are not fully characterized. [10] Patients acutely infected by SARS-CoV-2 may continue to have sequelae that last for many months after resolution of initial infection as shown by a study conducted by Adams et. al. in which over 150,000 DoD service members have recovered or are still recovering from acute COVID-19. [11] After two years post-illness, 50% of patients have reported poorer exercise capacity compared to those who never had the disease, and 40% of those recovering from COVID-19 still had chronic fatigue syndrome (CFS), including neurological, mental health, cardiovascular, pulmonary, and exercise intolerance complications.[11]

There have been limited studies that measure the association between demographics and health risk factors and related adverse outcomes for service members within the MHS. The purpose of this research is to study how demographic factors, military status, and pre-existing health conditions in our hospitalized COVID-19 patient population are associated with risk of COVID-related adverse outcomes within the MHS to include need for ongoing care or death after hospitalization.

GAPS

Though all the U.S. Armed Forces have been impacted by COVID-19 there's a paucity of published literature on how it has impacted military community including service members, retirees, and their families. There is also insufficient data on how burn pit emissions exposure history is associated with risk of COVID-19 related adverse health outcomes within the MHS. Additionally, there's limited data on how race has played a role in the risk of COVID-19 adverse outcomes since theoretically we have equal access to care within the MHS. It is imperative that we bridge this gap with innovative research to evaluate and mitigate the impact of COVID-19 and any future highly contagious emerging diseases on DoD personnel. The purpose of this research is to use existing data in the Department of Defense Joint Trauma Registry's (DoD JTR) COVID-19 Registry database, a centralized data collection platform for clinical research across Defense Health Agency (DHA), to study to study how demographic factors, military status, and number of pre-existing health conditions in our hospitalized COVID-19 patient population are associated with risk of COVID-related adverse outcomes within the MHS. The study seeks to evaluate the impact of COVID-19 on the service members, DoD personnel, and the dependents of the U.S. Armed Forces within the MHS.

METHODS

STUDY DESIGN

This is a retrospective cohort study using the DoD JTR COVID-19 Registry database to answer the above specific aims. The relevant clinical data was extracted by the study team from the database. The data was de-identified and subsequently analyzed using descriptive and comparative statistics outlined in the data analysis section. The primary aim is to assess if any

association exists between COVID-19 and adverse health outcomes for our military population hospitalized with COVID-19 adjusting for demographics (i.e., age, sex assigned at birth, race, and grade/rank). The sub-aims are to characterize adverse health outcomes by military specific risk factors such as military status (military vs non-military) and burn pit registry status, and by number of pre-existing conditions previously identified as risk factors to severe disease. The goal is that the information garnered from this study protocol will inform military operational and treatment facility preparation for current and future pandemics or other emerging infectious diseases.

STUDY SETTING

The DoD JTR contains records from across the geographical footprint of the DoD,[12] the data analysis comprising this study was conducted at a single site. This study was limited to use of existing records in the DoD JTR COVID-19 Registry from 1 March 2020 to 31 December 2022 and conducted at Madigan Army Medical Center (MAMC). Only protocol-identified and approved study personnel had access to the electronic data. The data was stored on a secure server in a user restricted directory, in a password protected file, and accessible only through common access card (CAC) credentialed staff. Access to Protected Health Information (PHI, non-deidentified data) was limited to Principal Investigator (PI) who utilized PHI only as necessary to merge data from other sources such as electronic medical record (to include AHLTA, MHS genesis, Essentris, Joint Legacy Viewer, and MDR). The data will be maintained in accordance with the protocol and Defense Health Agency (DHA) Data Sharing Agreement (DSA).

STUDY SUBJECTS

The target population for this study is the military community, to include service members, retirees, and their dependents who were hospitalized for COVID-19 between March 1, 2020, and 31 December 2022, to allow for stratification by types of participants. Data access was obtained for 18,468 individuals. Study subject age ranges from 0-85+ and includes both female and male sex assigned at birth. Based on existing age range definitions reflecting the stages of development and aging in the context of COVID-19 disease, age in this study was classified into five groups: 0-14 (children and young teens), 15-44 (adolescents and adult), 45-64 (middle aged adults), 65-84 (older adults), and 85+ (oldest adults).[12,13,14] For rank and grade, participants were classified into non-military, junior enlisted (E1-E4), senior enlisted (E5-E9), warrant officer (W1-W5), junior officer (O1-O3), and senior officer (O4-O10) based on military rank and pay grade scale. The final sample population was driven by the number and category of subjects that existed within the DoD JTR COVID-19 Registry at the time of data extraction. Special category of subjects identified by the JTR for inclusion included minors/children, students, DoD employees (Civilian and Contractors), Residents/trainee, Cadets/Midshipmen, Active-Duty Military Personnel, Wounded Warriors, economically disadvantaged persons, educationally disadvantaged persons, physically challenged to include visual and auditory impairment, persons with impaired decisional capacity, pregnant women, fetuses, neonates, and non-English Speakers. The defined exclusion criteria are subjects whose data was not available within the DoD JTR COVID-19 Registry such as individuals with incomplete records (i.e., unknown disposition status, n = 9,986, or unknown military status, n =10), and those admitted in calendar year 2023 (n = 3). The defined inclusion criteria are individual's whose record and corresponding data existed within the DoD Joint Trauma Registry's (DoD JTR) COVID-19

Registry. The DoD JTR specifically extracted data from medical records into their database of beneficiaries who were hospitalized for COVID-19. Extracting data from medical records was performed by case (e.g., when a case was identified for inclusion in the DoD JTR database), and all available pertinent data was then abstracted into the DoD JTR database. All known active duty were included, and records were extracted from non-active-duty hospitalizations in such a way as to provide a representative sample. Data abstraction priorities for the DoD JTR pandemic registry included inpatient, burn pit emissions exposure, convalescent plasma recipient, vaccine breakthrough, multisystem inflammatory syndrome in children (MIS-C), monoclonal antibody recipient, persistent COVID-19 illness, reinfection, and lastly outpatient; however, the data available at the time of extraction for our study only contained those that had COVID-19 positive polymerase-chain reaction (PCR) and were hospitalized for COVID-19 disease. Where applicable, those hospitalized with COVID-19 were identified as having burn pit exposure by cross referencing with the VA airborne hazards and open burn pit registry from 1 March 2020 to 31 December 2022. Those who were not hospitalized were not included.

DATA COLLECTION

The investigators did not have contact with any study subjects to include recruitment of subjects as the source of the data was the existing data in the DoD JTR Pandemic (COVID-19) Registry. The registry was from a centralized data collection platform which captures approximately 270 unique data points that include demographics, symptoms, past medical history, lab, and radiology tests, contact with known infected patients, treatments, outcomes, and complications related to COVID-19. All participants included in the data extraction protocol for this study had been hospitalized with diagnosis of COVID-19 disease, had a positive SARS-CoV-2 polymerase chain reaction (PCR) test, and if applicable, had documentation of burn pit exposure. This study

protocol was considered human research, therefore, it was submitted for review and approved by the Madigan Institutional Review Board (IRB), as well as the University of Washington (UW) IRB. In addition, the study protocol was reviewed and approved by the DHA by way of completion of a DSA, which governs the use of the data.

DATA ANALYSIS

First, we reviewed the data and coded it for all outcomes (i.e., disposition groups - home, skilled nursing facility (SNF), rehabilitation center, long-term acute care (LTAC), and death), demographics, military status, smoking status, burn pit registry status, pre-existing risk factors for severe disease, and presence of severe disease. For severe disease, we reviewed the data for common indicators for severe illness to produce a composite. For our study, all symptomatic cases not mild or moderate (i.e., severe and critical) were termed as severe: Severe illness: dyspnea, respiratory frequency ≥30/min, blood oxygen saturation ≤93%, partial pressure of arterial oxygen to fraction of inspired oxygen ratio <300, and/or lung infiltrates >50% within 24 to 48 hours; Critical Illness: respiratory failure, septic shock, and/or multiple organ dysfunction or failure.[15] A subject was counted as having had severe disease if they experienced an occurrence of any of several indicators or symptoms (i.e., dyspnea, hypoxemia, viral pneumonia, Acute Respiratory Distress Syndrome (ARDS), respiratory failure, viral sepsis/shock, multiple organ dysfunction, renal failure/injury, coagulopathy, intensive care unit admission, intubation, mechanical ventilation, non-invasive ventilation, extracorporeal membrane oxygenation (ECMO), vasopressors, prone position, immune modulator use and/or remdesivir use).[16,17] Then we used descriptive statistics to categorize demographic data. We assessed the descriptive findings using either Chi-Squared or Fisher's Exact tests, where applicable (i.e., large sample > 5 vs small sample sizes < 5, respectively), when checking differences between categorical

variables of interest. For continuous variables, we used mean and standard deviation or median and interquartile range (IQR) to summarize.

Finally, ordinal regression was used to assess relationships between predictors and dependent variables adjusted for potential confounders. Demographic and previously defined predictors of interest were chosen a priori based on already published data in the literature of U.S. and VA population (i.e., age, sex assigned at birth, race, pre-existing conditions/risk factors for severe disease, smoking). Burn pit registry was chosen a priori based on biological plausibility of worse COVID-19 related health outcomes given the presence of evidence of associations between adverse cardiorespiratory outcomes and burn pit emissions exposure[18, 19, 20] and paucity of published literature about the health impact on military population hospitalized with COVID-19 within the MHS. Other military specific predictors of interest included rank/grade and military status given the association between serving in the officer ranks and better veteran health outcomes when compared to serving in the enlisted ranks during their military career.[21] Primary outcome disposition groups (dependent variables) were ranked from least severe to most severe (home, nursing home/rehabilitation center/Long Term Acute Care (LTAC), and death, respectively). We chose the home disposition group as the reference group and ranked it the least severe category for our comparison given our assumption that they were the lowest risk (i.e., healthier) group due to majority having younger age and fewer risk factors for severe disease (see Table 3). We evaluated association of each predictor with our ordinal dependent variable adjusting for all others. We used odds ratio (OR) as the measure of association. A p-value of less than or equal to 0.05 was defined as statistically significant for all tests. All analysis was conducted using R and R Studio Statistical Software.[22]

STUDY POWER AND SAMPLE SIZE

Published data has shown mortality rate for COVID-19 to be between 2 to 4% compared to seasonal influenza of less than 1%.[23, 24, 25] Based on global estimates, the proportion of severe to critically ill cases in the general population were estimated to be 5%[23,26,27] Based on these estimates, proportions chosen as reasonable estimates to calculate required sample sizes for the primary outcome of death and for severe disease were 3% and 5%, respectively. Using the one sample, dichotomous outcome sample size calculation formula[28] to detect a 1% increase in outcomes, the required sample sizes were: 1118 for death and 1825 for severe disease. The number of subjects and corresponding data points within the DoD JTR COVID-19 Registry at the time of data extraction determined the sample size available and specific variables to be compared as the data input into the registry is ongoing. We ran two different models for regression analysis and given our population of 18,468 we were sufficiently powered to detect a statistically significant result for the outcome of death and severe disease at a p-value of 0.05 and consistent power of 80% with 7 predictors (i.e., age, sex assigned at birth, race, grade/rank, smoking status, burn pit exposure, and risk factor count).

ANALYSIS RESULTS:

DEMOGRAPHICS DESCRIPTIVE STATISTICS

Descriptive statistics for demographic and military factors are presented in Tables 1 and 2. A total of 18,468 participants were reviewed. They ranged from 0 to 104 years of age with mean age of 42.29 (SD of 22.21) and median age of 37 years (IQR of 37 years). Overall, the age distribution is right skewed with majority of participants falling in the 15-44 age range. Among those who died after hospitalization from COVID-19 disease, the majority were 65 years and

older (63%) with mean of 3.23 risk factors (SD 1.84), White (58%), male (76%), non-military (92%), a large proportion had severe disease (99 %), slightly less than half were ever smokers (48%), and none had documented burn pit exposure.

Among those whose disposition was to a nursing home, rehabilitation center, or LTAC after hospitalization from COVID-19 disease, majority were 65 years and older (67%) with mean of 3.2 risk factors (SD 1.91), White (59%), male (67%), non-military (94%), 40% were ever smokers, 80% had severe disease and less than 1% had documented burn pit exposure.

Among those whose disposition was to home after hospitalization from COVID-19 disease, majority were 15 to 64 years of age (72%) with a mean of 1.82 risk factors (SD 1.78), White (51%), male (57%), non-military (78%), one-third ever smokers (33%), 76% had severe disease and less than 1% had documented burn pit exposure. Among those whose disposition was unknown after hospitalization from COVID-19 disease, majority were 15 to 64 years of age (92%) with a mean of 0.48 risk factors (SD 0.97), White (55%), male (67%), enlisted in the military (52%), 20% were ever smokers, 31% had severe disease, and 2.3% had documented burn pit exposure.

ORDINAL REGRESSION ANALYSIS:

The likelihood of being in a high-risk disposition group after hospitalization for COVID-19 disease within the MHS from 1 March 2020 to 31 December 2022 is presented in Table 3 and Figure 1. This regression analysis contains 8,769 eligible participants from the initial total of 18,468. Individuals who had an unknown disposition outcome status (n=9,686), admitted in 2023 (n=3), and unknown grade/rank (n=10) were excluded from the analysis.

For risk factor count, one risk factor was selected as the reference because it accounted for the minimum number of risk factors for severe illness in the cohort included for the analysis. This study found that for those with greater than 1 risk factor for severe disease, the odds of being in a higher risk disposition group (i.e., nursing home, rehabilitation center, LTAC, or death) after hospitalization for COVID-19 disease was almost 1.5 times higher than the odds of patients with fewer than 1 risk factor after adjusting for age, race, sex assigned at birth, rank/grade, burn pit registry status, and smoking status (OR 1.46, p-value < 0.05, 95% CI: 1.28, 1.67). For sex assigned at birth, male sex was selected as the reference group because it accounted for the largest proportion of hospitalizations for COVID-19 compared to female sex. Those with female sex assigned at birth had 0.62 times the odds of being in a higher risk disposition group comparing those with male sex assigned at birth, after adjusting for risk factor count, age, race, rank/grade, burn pit registry status, and smoking status (p-value < 0.05, 95% CI: 0.54, 0.72).

For age, the 15 to 44 years of age group was selected as the reference group because it accounted for the largest proportion of participants hospitalized for COVID-19 compared to other age groups. There were no significant differences in the odds of being in a higher risk disposition group after hospitalization with COVID-19 disease comparing those who were 0 to 14 years of age and those 15 to 44 years of age after adjusting for risk factor count, race, sex assigned at birth, rank/grade, burn pit registry status, and smoking status (OR 0.68, p-value > 0.05, 95% CI: 0.24, 1.92). Among those who were 45 to 64 years of age, the odds of being in a higher risk disposition group after hospitalization for COVID-19 disease was 2.2 times higher when compared to those among 15 to 44 years of age (p-value < 0.05, 95% CI: 1.67, 2.90). Among those who were 65 to 84 years of age, the odds of being in a higher risk disposition group after hospitalization for COVID-19 disease was 5-fold higher than the odds of patients 15 to 44 years

of age (OR 5.01, p-value < 0.05, 95% CI: 3.71, 6.77). Among those who were 85 years and older, the odds of being in a higher risk disposition group after hospitalization for COVID-19 disease was almost 11-fold higher than the odds of patients 15 to 44 years of age (OR 10.60, p-value < 0.05, 95% CI: 7.64, 14.71).

For race, those who identified as White were selected as the reference group because it accounted for the largest proportion of participants hospitalized for COVID-19 compared to other groups. Race did not appear to be a significant predictor of being in a higher risk disposition group after hospitalization for COVID-19 disease among those who were of unknown race (OR 0.96, p-value > 0.05, 95% CI: 0.81, 1.13), identified as Asian (OR 1.01, p-value > 0.05, 95% CI: 0.77, 1.32), Native Hawaiian or Other Pacific Islander (OR 1.35, p-value > 0.05, 95% CI: 0.88, 2.08), or American Indian (OR 1.48, p-value > 0.05, 95% CI: 0.65, 3.37) when compared to those who identified as White after adjusting for risk factor count, age, sex assigned at birth, rank/grade, burn pit registry status, and smoking status. For those who identified as Black or African American the odds of being in a higher risk disposition group was 0.70 times the odds when compared to those who identified as White and it was statistically significant (p-value < 0.05, 95% CI: 0.60, 0.81).

For rank/grade, the non-military was selected as the reference group because it accounted for the largest proportion of hospitalizations for COVID-19 compared to other groups. There were ten participants that were not included in the analysis given unknown status. All ten of the participants came from the home disposition group and accounted for only 0.1% of the total participants in this disposition group (N=7256). Rank/grade did not appear to be a significant predictor of being in a higher risk disposition group after hospitalization for COVID-19 disease when comparing those in the senior enlisted category (E5-E9) (OR 1.23, p-value > 0.05, 95% CI:

0.86, 1.75), junior officer category (O1-O4) (OR 0.75, p-value > 0.05, 95% CI: 0.23, 2.45), and senior officer category (O4-O10) (OR 0.83, p-value > 0.05, 95% CI: 0.40, 1.74) to those in the non-military category after adjusting for risk factor count, age, sex assigned at birth, race, burn pit registry status, and smoking status. Those in the grade of junior enlisted category (E1-E4) had 0.75 times the odds of being in a higher risk disposition group after hospitalization for COVID-19 disease compared to those in the non-military category (p-value = 0.05, 95% CI: 0.43, 1.19). Among those in the rank/grade of warrant officer (W1-W5), the odds of being in a higher risk disposition group were the highest at 4-fold the odds when compared to those in the non-military category (OR 4.12, p-value < 0.05, 95% CI: 1.80, 9.43).

For burn pit exposure, we used Veterans Affairs (VA) Airborne Hazards and Open Burn Pit Registry registration as a surrogate for exposure. Those who were in Veterans Affairs (VA) Airborne Hazards and Open Burn Pit Registry had an odds of being in a higher risk disposition group after hospitalization for COVID-19 disease of 0.24 times the odds compared to those who were not in the Veterans Affairs (VA) Airborne Hazards and Open Burn Pit Registry after adjusting for risk factor count, age, sex assigned at birth, race, rank/grade, and smoking status, however, this was not statistically significant (p-value > 0.05, 95% CI: 0.032, 1.78). Smoking status did not appear to be a significant predictor of being in a higher risk disposition group after hospitalization for COVID-19 disease when comparing those who were ever smokers (i.e., current or former smoker) and those who were non-smokers after adjusting for risk factor count, age, sex assigned at birth, race, rank/grade, and burn pit registry status (OR 1.05, p-value > 0.05, 95% CI: 0.91, 1.20).

For admission by calendar year (CY), CY 2021 was selected as the reference group because it accounted for the largest proportion of hospitalizations for COVID-19 compared to the other CY

year groups. CY 2023 was not included given variable only contained 3 participants all of which died. There were no significant differences in the odds of being in a higher risk disposition group after hospitalization with COVID-19 disease comparing those who were hospitalized in CY 2020 and those hospitalized in CY 2021 after adjusting for risk factor count, age, race, sex assigned at birth, rank/grade, burn pit registry status, and smoking status (OR 0.92, p-value > 0.05, 95% CI 0.80, 1.06). Those hospitalized for COVID-19 in CY 2022 had lower odds of being in a higher risk disposition group compared to those hospitalized in CY 2021 (OR 0.79, p-value < 0.05, 95% CI: 0.66, 0.96).

DISCUSSION:

This study provides valuable data about health outcomes in hospitalized MHS beneficiaries. Some of these findings are consistent with published literature, while others, particularly involving race are different than what has been found previously. The results of this study suggest that those who were 65 years of age and older with more risk factor for severe disease had the highest odds of death and requiring ongoing care at a nursing home, rehabilitation center, or LTAC at the time of hospital discharge when compared to those under 65 years of age with fewer risk factors after adjusting for sex assigned at birth, race, rank/grade, burn pit registry status, and smoking status. This is consistent with current literature regarding pre-existing health conditions previously identified as risk factors associated with severe disease and COVID-19 related poor health outcomes.[16-17, 24-25] This highlights that prevention and mitigation strategies are imperative in this vulnerable population especially for future pandemics or other infectious disease outbreaks.

Female sex assigned at birth appeared to be negatively correlated with death or the requirement of ongoing care at a nursing home, rehabilitation center, or LTAC after hospitalization with

COVID-19 disease which is consistent with what has been found in the literature showing that men have worse COVID-19 related health outcomes compared to women.[29, 30] A study conducted by Fabiao et. al comparing men and women health outcomes related to COVID-19 illness showed that men had a higher relative risk of severity of disease and mortality regardless of age (1.29 and 1.36, respectively).[30] This study also suggests that burn pit emissions exposure is negatively correlated with death or requirement of ongoing care which is different than what other studies have found about particulate matter adverse health associations such as cardiovascular and respiratory disease.[18-20] However, this was not statistically significant. More studies are required with respect to burn pit emission exposure and its association with risk of adverse COVID-19 related health outcomes given the limited number of participants in this study with documented history of exposure.

Studies on social determinants of health have shown that social and economic factors (40%), individual health behaviors (30%), in addition to physical environment (10%) make up 80% of the major impacts on health outcomes and 20% is affected by the healthcare environment including access and quality.[31, 32] The study hypothesis postulated that increasing rank and grade, a surrogate for higher socioeconomic status, would lead to decreased risk of COVID-19 related adverse outcomes. This study suggests that having economic stability (i.e., employment and steady income from active service or retirement) and healthcare (i.e., healthcare coverage and access) may lead to more equitable outcomes given overall military grade/rank and race did not appear to be a significant predictors with risk of death or requirement of ongoing care. Lastly, this study suggests that ever smoker status was not a significant predictor for death or requirement of ongoing care which is also not consistent with published data by the Centers of

Disease Control and Prevention regarding smoking and poor health outcomes related to COVID-19 illness (i.e., severe disease, hospitalization, and death).[33, 34, 35]

Overall, the largest number of individuals hospitalized for COVID-19 occurred in calendar year (CY) 2021. The proportion of participants of unknown disposition decreased for CY2021 to 2023 (80 to < 0.1 %) suggesting that over time medical record documentation may have improved. When all participants who had an unknown disposition and the three participants in CY 2023 who died were excluded, the proportions of hospitalizations for COVID-19 from 1 March 2020 to 31 December 2022 were similar across all disposition groups (i.e., home, nursing home/Rehab/LTAC, and death). This study suggests that the rates of hospitalizations for COVID-19 decreased overtime which could be a product of increasing knowledge, improved treatment protocols, prevention strategies (i.e., vaccinations, ventilation, mask wearing), containment strategies (i.e., early detection, isolation, quarantine of close contacts), and mitigation strategies (i.e., social distancing, society lockdowns).[36, 37]

SCOPE

Data abstraction priorities for the DoD JTR pandemic registry were inpatient, burn pit exposure, convalescent plasma recipient, vaccine breakthrough, multisystem inflammatory syndrome in children (MIS-C), monoclonal antibody recipient, persistent COVID-19 illness, reinfection, and lastly outpatient. Given the large incursion of positive tests during each wave of COVID-19 (i.e., delta and omicron variants), the data available at the time of extraction only contained those that had COVID-19 positive PCR and were hospitalized for COVID-19 disease, thus, we did not have access to the records of patient with less severe disease that were treated on outpatient basis.

STRENGTHS

As before mentioned this research study is a retrospective cohort study and useful for accessing temporal relationship between exposure and outcomes, allowing us to investigate common exposures such as risk factors for COVID-19 disease severity outcomes. Other strengths include that it is a unique study that is highly relevant to the military, it used a high-quality data set, and had a large sample size.

LIMITATIONS

This study shares limitations common to cohort studies. For example, the existing data may not have data on all potential confounders particularly for data recorded in the past. Also, we may be missing information on part of the affected population for which data is not available in the registry due to incomplete documentation. Examples of missing data include ethnicity and disposition outcome, access to home testing kits, utilization of non-MHS emergency department or urgent care facility instead of military training facility, or less severe disease that did not seek medical attention. Another limitation of cohort study design is that it may not be useful if disease outcome or associated complications are very rare. To mitigate this, we made a composite of severe disease, however, this brings to into question whether each of the different components are equal in value regarding clinical impact.

Misclassification may have played a role particularly for burn pit registry analysis results. Over half the participants within the DoD JTR pandemic registry were excluded from the analysis due to unknown disposition and contained the highest proportion of participants in the VA Airborne Hazards and Open Burn Pit Registry. We suspect we did not have enough participants that were registered in the VA Airborne Hazards and Open Burn Pit Registry overall which resulted in not

having an accurate list of burn pit registrants to cross reference to show the true relationship. This may explain the unanticipated result with burn pit registrants having lower odds of being in the higher risk disposition groups for COVID-19 adverse health outcome which differed from what was hypothesized and was not statistically significant.

Selection bias may have also played a role given that we don't have access to all the existing records in the DoD JTR pandemic registry just the ones that were available to us at the time of extraction and from over half of participants excluded due to unknown disposition status. If records available to us were systematically different in characteristics and differential to those who were more likely to have the outcomes of interest, there may be an overestimation of association or vice versa. There is also a potential for healthy worker effect which falls under selection bias resulting from the improper selection of a comparison group (i.e., general population). In contrast to the general population, the military workforce tends to have fewer sick people given that the U.S. Armed Forces have specific accession standards and individuals must undergo physical examinations to assess their physical health before they are allowed to enter the service. Thus, comparisons between military group and the general population will be biased. We tried to mitigate this in our study by also including family members of active-duty service members and retirees who would be a heterogeneous mixture consisting of healthy and unhealthy people representative of the general population (i.e., children, elderly, medically retired people, as well as people who left the military after a short period of service such as spouses from dual-military service members).

Lastly, generalizability may be a concern as we cannot extrapolate to the current state of the pandemic as rates of hospitalization changed overtime and may only be generalizable to military beneficiary population. Additionally, data in the registry was skewed towards younger age, a

large proportion of participants that went home, and were more likely to be hospitalized earlier in the pandemic. A theory about why the data was skewed towards younger age and earlier dates of COVID-19 pandemic time frame was due to the abstraction priorities in which inpatient (i.e., hospitalization) and burn pit registry status took precedence during different waves of COVID-19.

CONCLUSIONS:

As the study hypotheses postulated, those who were 65 years of age and older and those who had more risk factors for severe disease had the highest odds of being in the higher risk disposition groups after hospitalization for COVID-19 disease especially disposition to nursing home, rehabilitation center, LTAC or death when compared to those who were 64 years of age and younger and those who had fewer risk factors. Female sex assigned at birth was negatively correlated with being in the higher risk disposition category after hospitalization for COVID-19 disease when compared to those with male sex assigned at birth. However, smoking did not appear to be a significant predictor being in the higher risk disposition group after hospitalization for COVID-19 disease.

Contrary to our hypothesis regarding race, those that identified as Black or African American had lower odds of being in the higher risk disposition groups after hospitalization for COVID-19 disease when compared to those who identified as White. As mentioned above, race did not appear to be a significant predictor of being in a higher risk disposition group after hospitalization for COVID-19 disease among those who were of unknown race, identified as Native Hawaiian or Other Pacific Islander, Asian, or American Indian when compared to those who identified as White. Notably, this differs from what other studies have found in the general U.S. population and VA population which showed that those who identified as Black or African

American and Hispanic had the highest burden of COVID-19 disease and associated mortality.[9-10, 31-33, 38] This may suggest that more equitable access to care within the MHS may lead to more equivalent outcomes. It is important to note that this study looked at race but excluded consideration of ethnicity, including Hispanic ethnicity. This may be due to the way data was abstracted for the registry or a consequence of a lack of data completeness.

Overall, military rank/grade did not appear to be a significant predictor of being in a higher risk disposition group compared to non-military within the MHS. Measuring socioeconomic status (SES) is complex and usually encompasses a combination of economic, social, and work status measured by education level attained, total family income or wealth, and current occupation. Military pay grade is the best our data allows as a surrogate to measure SES.[21,39] It appears that there may be a slight suggestion that higher SES such as being in the grade of commissioned officer may be protective, but generally, at least for those young enough to be on active duty, SES is not a significant predictor for being in a higher risk disposition group. This also suggests that more equitable access to healthcare leads to more equal outcomes. Those in the grade of junior enlisted category had the lowest odds of being in the higher risk disposition groups after hospitalization for COVID-19 disease when compared to non-military category and those in the grade of warrant officer category had the highest odds. This may be a consequence of residual collinearity as age and rank/grade are correlated with one another. If the degree of correlation between these two predictors is high enough a change in one variable can affect the other as they tend to change in unison, which may explain why, after adjusting for age, junior enlisted had the lowest odds and warrant officers had the highest odds given that junior enlisted tend to be younger and warrant officers much older.[40, 41]

For those in the VA airborne hazards and open burn pit registry, the odds were lower for being in the higher risk disposition group after hospitalization for COVID-19 disease when compared to those not in the registry, however, this was not statistically significant. Given what is known about associated adverse outcomes of burn pit emissions exposures, it was hypothesized that those with burn pit exposure would suffer more severe disease or have more severe outcomes. Burn pit emissions exposure (especially particulate matter) is associated with multiple adverse health outcomes (i.e., chronic multisystem illness including chronic fatigue, impaired cognition, respiratory disease, cardiovascular disease).[18-20, 42]

A lot changed from CY 2020 to CY 2023 in terms of circulating variants, prevention strategies including vaccination, knowledge, indications for hospitalization, and treatment protocols.[36,37] Although there was a slight uptick in hospitalizations from CY 2020 to CY 2021, overall, the number of participants hospitalized for COVID-19 decreased by CY from March 1, 2020, to February 10, 2023. There were also improvements in documentation of disposition in the medical record overtime suggested by the decrease in the proportion of participants of unknown disposition from CY2021 to 2023 (80 to < 0.1 %). Later in the pandemic, excluding the three participants who died in CY 2023, those who were hospitalized in CY 2022 had lower odds of being in a higher risk disposition group after hospitalization for COVID-19 disease compared to those hospitalized in CY 2021, however, there were no significant differences in the odds comparing those who were hospitalized in CY 2020 and those hospitalized in CY 2021.

TABLES AND FIGURES

Table 1: Demographic characteristics of persons hospitalized with COVID-19 disease, Department of Defense Military Health System, 1 March 2020 to 10 February 2023

Characteristic[1]	
Sex assigned at birth	
Female	6721 (36%)
Male	11747 (64%)
Age (yrs.)	
0-14	399 (2.2%)
15-44	10236 (55%)
45-64	4625 (25%)
65-84	2650 (14%)
85+	558 (3.0%)
Grade/Rank	
Non-Military	10674 (58%)

Table 1: Demographic characteristics of persons hospitalized with COVID-19 disease, Department of Defense Military Health System, 1 March 2020 to 10 February 2023

Characteristic[1]	
Junior enlisted (E1-E4)	3460 (19%)
Senior enlisted (E5-E9)	3016 (16%)
Junior officer (O1-O3)	688 (3.7%)
Senior officer (O4-O10)	465 (2.5%)
Warrant officer (W1-W5)	120 (0.6%)
Unknown	45 (0.2%)
Race	
Unknown	3331 (18%)
White	9893 (54%)
Black or African American	4111 (22%)
Asian	780 (4.2%)

Table 1: Demographic characteristics of persons hospitalized with COVID-19 disease, Department of Defense Military Health System, 1 March 2020 to 10 February 2023

Characteristic[1]	
Native Hawaiian or Other Pacific Islander	240 (1.3%)
American Indian	113 (0.6%)
Burn Pit Exposure (i.e., in the VA Burn Pit Registry)	
	258 (1.4%)
Ever Smoker Status	
	4969 (27%)
Beneficiary Status	
Active Duty	7311 (40%)
Dependent	5152 (28%)
Foreign Civilian	14 (<0.1%)
Non-U.S. Military	81 (0.4%)
Other	45 (0.2%)

Table 1: Demographic characteristics of persons hospitalized with COVID-19 disease, Department of Defense Military Health System, 1 March 2020 to 10 February 2023

Characteristic[1]	
Retiree	4681 (25%)
Trainee	503 (2.7%)
U.S. Civilian	680 (3.7%)
Branch of Service	
Air Force	1589 (8.6%)
Army	3359 (18%)
Civilian/National Guard/Other	10635 (58%)
Coast Guard	66 (0.4%)
Marines	898 (4.9%)
Navy	1921 (10%)
Region	

Table 1: Demographic characteristics of persons hospitalized with COVID-19 disease, Department of Defense Military Health System, 1 March 2020 to 10 February 2023

Characteristic[1]	
Continental United States (CONUS)	16717 (91%)
Outside the Continental United States (OCONUS)	1715 (9.3%)
Unknown	36 (0.2%)

[1] Statistics presented: n (%), Total (N)= 18468

Table 2. Demographic characteristics and exposures of persons hospitalized with COVID-19 disease, stratified by disposition group, Department of Defense Military Health System, 1 March 2020 to 10 February 2023

Characteristic	**Unknown**, N = 9686	**Home**, N = 7256	**Nursing Home / Rehab / LTAC**, N = 726	**Death**, N = 800
No. Risk Factor[1]				
	0.48 (0.97)	1.82 (1.78)	3.20 (1.91)	3.23 (1.84)
Age (yrs.)[2]				
0-14	226 (2.3%)	168 (2.3%)	4 (0.6%)	1 (0.1%)
15-44	7307 (75%)	2771 (38%)	90 (12%)	68 (8.5%)
45-64	1797 (19%)	2459 (34%)	142 (20%)	227 (28%)
65-84	333 (3.4%)	1603 (22%)	336 (46%)	378 (47%)
85+	23 (0.2%)	255 (3.5%)	154 (21%)	126 (16%)
Race[2]				
Unknown	1783 (18%)	1313 (18%)	113 (16%)	122 (15%)
White	5308 (55%)	3690 (51%)	431 (59%)	464 (58%)
Black or African American	2051 (21%)	1782 (25%)	134 (18%)	144 (18%)

Table 2. Demographic characteristics and exposures of persons hospitalized with COVID-19 disease, stratified by disposition group, Department of Defense Military Health System, 1 March 2020 to 10 February 2023

Characteristic	**Unknown**, N = 9686	**Home**, N = 7256	**Nursing Home / Rehab / LTAC**, N = 726	**Death**, N = 800
Asian	371 (3.8%)	330 (4.5%)	36 (5.0%)	43 (5.4%)
Native Hawaiian or Other Pacific Islander	104 (1.1%)	105 (1.4%)	9 (1.2%)	22 (2.8%)
American Indian	69 (0.7%)	36 (0.5%)	3 (0.4%)	5 (0.6%)
Sex assigned at birth[2]				
Female	3197 (33%)	3091 (43%)	243 (33%)	190 (24%)
Male	6489 (67%)	4165 (57%)	483 (67%)	610 (76%)
Grade/Rank[2]				
Non-Military	3609 (37%)	5647 (78%)	685 (94%)	733 (92%)
Junior enlisted (E1-E4)	2725 (28%)	705 (9.7%)	21 (2.9%)	9 (1.1%)
Senior enlisted (E5-E9)	2284 (24%)	673 (9.3%)	17 (2.3%)	42 (5.2%)
Junior officer (O1-O3)	613 (6.3%)	72 (1.0%)	0 (0%)	3 (0.4%)

Table 2. Demographic characteristics and exposures of persons hospitalized with COVID-19 disease, stratified by disposition group, Department of Defense Military Health System, 1 March 2020 to 10 February 2023

Characteristic	**Unknown**, N = 9686	**Home**, N = 7256	**Nursing Home / Rehab / LTAC**, N = 726	**Death**, N = 800
Senior officer (O4-O10)	337 (3.5%)	120 (1.7%)	1 (0.1%)	7 (0.9%)
Warrant officer (W1-W5)	83 (0.9%)	29 (0.4%)	2 (0.3%)	6 (0.8%)
Unknown	35 (0.4%)	10 (0.1%)	0 (0%)	0 (0%)
Burn Pit[2]				
	224 (2.3%)	33 (0.5%)	1 (0.1%)	0 (0%)
Ever Smoker Status[2]				
	1898 (20%)	2394 (33%)	294 (40%)	383 (48%)
Admission by Calendar Year (CY)[2]				
CY 2020	7718 (80%)	2957 (41%)	334 (46%)	309 (39%)
CY 2021	1747 (18%)	3144 (43%)	286 (39%)	373 (47%)
CY 2022	220 (2.3%)	1155 (16%)	106 (15%)	115 (14%)
CY 2023	1 (<0.1%)	0	0	3 (0.4%)

Table 2. Demographic characteristics and exposures of persons hospitalized with COVID-19 disease, stratified by disposition group, Department of Defense Military Health System, 1 March 2020 to 10 February 2023

Characteristic	**Unknown**, N = 9686	**Home**, N = 7256	**Nursing Home / Rehab / LTAC**, N = 726	**Death**, N = 800
Severe Disease Noted[2]				
	3014 (31%)	5501 (76%)	583 (80%)	789 (99%)

[1] Statistics presented as Mean (SD)
[2] Statistics presented as n (%)

Table 3. Likelihood of being in a high-risk disposition group after hospitalization for COVID-19 disease, Department of Defense Military Health System, 1 March 2020 to 31 December 2022

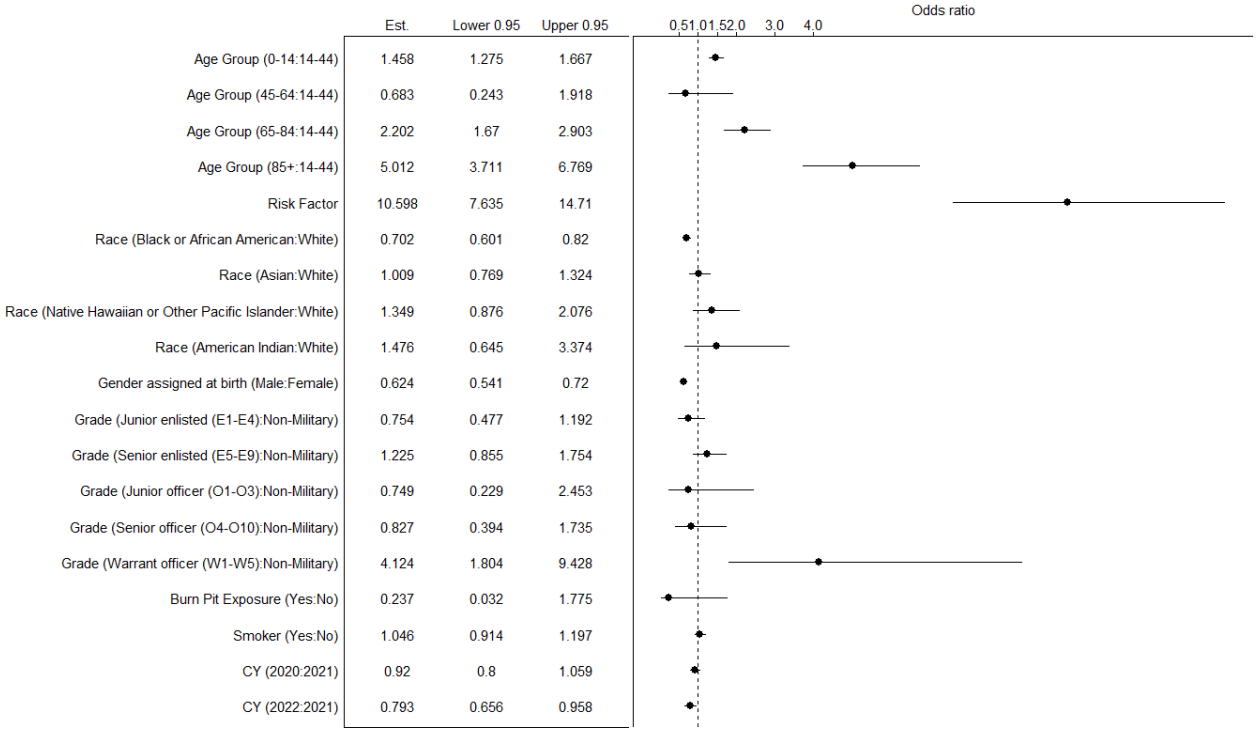
Variable[2]	Odds ratios	L 95% CI, H 95% CI	p-value[1]
Age Group			
0-14	0.68	0.24, 1.92	0.134
15-44	Reference	-	-
45-64	2.20	1.67, 2.90	< **0.0001**
65-84	5.01	3.71, 6.77	< **0.0001**
85+	10.60	7.64, 14.71	< **0.0001**
No. Risk Factor			
	1.46	1.28, 1.67	< **0.0001**
Race			
Unknown	0.96	0.81, 1.13	0.603
White	Reference	-	-
Black/African American	0.70	0.60, 0.82	< **0.0001**
Asian	1.01	0.77, 1.32	0.914
Native Hawaiian/Pacific Islander	1.35	0.88, 2.08	0.180
American Indian	1.48	0.65, 3.37	0.349
Sex assigned at birth			
Male	Reference	-	-
Female	0.62	0.54, 0.72	< **0.0001**
Grade/Rank			

Non-Military	Reference	-	-
Junior Enlisted (E1-E4)	0.75	0.48, 1.19	**0.050**
Senior Enlisted (E5-E9)	1.23	0.86, 1.75	0.620
Junior Officer (O1-O3)	0.75	0.23, 2.45	0.365
Senior Officer (O4-O10)	0.83	0.40, 1.74	0.164
Warrant Officer (W1-W5)	4.12	1.80, 9.43	**0.004**
Burn Pit YES			
	0.24	0.032, 1.78	0.092
Ever Smoker YES			
	1.05	0.91, 1.20	0.759
Admission by Calendar Year (CY)			
CY 2020	0.92	0.80, 1.06	0.115
CY 2021	Reference	-	-
CY 2022	0.79	0.66, 0.96	**0.003**

[1] Not significant; p-values less than or equal to 0.05 are considered significant

[2] Reference groups: *Age* – 15-44 age group was selected as the reference group because it accounted for the largest proportion of participants hospitalized for COVID-19 compared to the other age groups; *Risk Factor Count* – 1 risk factor was selected as the reference because it accounted for the a minimum number of risk factors for severe COVID-19 illness in the cohort included in the analysis; *Race* – White was selected as the reference group because it accounted for the largest proportion of participants hospitalized for COVID-19 compared to other groups; *Sex assigned at birth* – Male was selected as the reference group because it accounted for the largest proportion of participants hospitalized for COVID-19 compared to Female; *Grade/Rank* – Non-Military was selected as the reference group because it accounted for largest proportion of participants hospitalized for COVID-19 compared to those in the other rank/grade groups; grade unknown was not included given unknown status and contained only 10 participants all of which were in the home disposition outcome; *Burn pit YES* (in the burn pit registry) – NO (not in the burn pit registry); *Ever Smoker YES* (ever smokers)- NO (non-smokers); *Admission by CY* – 2021 was selected as the reference group because it accounted for the largest proportion of hospitalizations for COVID-19 compared to the other CY year groups; CY 2023 was not assessed given variable only contained 3 participants all of which died

Figure 1. Forest plot – Adjusted Odds ratio, odds of being in the higher risk disposition group after hospitalization for COVID-19 disease, Department of Defense Military Health System, 1 March 2020 to 31 December 2022



	Est.	Lower 0.95	Upper 0.95
Age Group (0-14:14-44)	1.458	1.275	1.667
Age Group (45-64:14-44)	0.683	0.243	1.918
Age Group (65-84:14-44)	2.202	1.67	2.903
Age Group (85+:14-44)	5.012	3.711	6.769
Risk Factor	10.598	7.635	14.71
Race (Black or African American:White)	0.702	0.601	0.82
Race (Asian:White)	1.009	0.769	1.324
Race (Native Hawaiian or Other Pacific Islander:White)	1.349	0.876	2.076
Race (American Indian:White)	1.476	0.645	3.374
Gender assigned at birth (Male:Female)	0.624	0.541	0.72
Grade (Junior enlisted (E1-E4):Non-Military)	0.754	0.477	1.192
Grade (Senior enlisted (E5-E9):Non-Military)	1.225	0.855	1.754
Grade (Junior officer (O1-O3):Non-Military)	0.749	0.229	2.453
Grade (Senior officer (O4-O10):Non-Military)	0.827	0.394	1.735
Grade (Warrant officer (W1-W5):Non-Military)	4.124	1.804	9.428
Burn Pit Exposure (Yes:No)	0.237	0.032	1.775
Smoker (Yes:No)	1.046	0.914	1.197
CY (2020:2021)	0.92	0.8	1.059
CY (2022:2021)	0.793	0.656	0.958

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