Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Correlates of death among SARS-CoV-2 positive veterans: The contribution of lifetime tobacco use

Amanda M. Raines a,b,c,*, Jamie L. Tock a,b,d, Shelby J. McGrew a, Chelsea R. Ennis a,b, Jessa Derania a,b,e, Christina L. Jardak a,b,e, Jennifer H. Lim a,e, Joseph W. Boffa a,b, Claire Houtsma a,b, Kenneth R. Jones a,e, Caitlin Martin-Klinger a,e, Kyle Widmer a,f, Ralph Schapira a, Michael J. Zvolensky g,h, Michael Hoerger g,i, Joseph I. Constans a,b,c,e, C. Laurel Franklin a,b,e

a Southeast Louisiana Veterans Health Care System (SLVHCS), New Orleans, LA 70119, USA
b South Central Mental Illness Research, Education and Clinical Center (MIRECC), New Orleans, LA 70119, USA
c Department of Psychiatry, School of Medicine, Louisiana State University, New Orleans, LA 70112, USA
d Florida State University Reading Research Center, Tallahassee, FL 32310, USA
e Department of Psychiatry and Behavioral Sciences, School of Medicine, Tulane University, New Orleans, LA 70112, USA
f Department of General Internal Medicine, School of Medicine, Tulane University, New Orleans, LA 70112, USA

ABSTRACT

Despite a growing body of research examining correlates and consequences of COVID-19, few findings have been published among military veterans. This limitation is particularly concerning as preliminary data indicate that veterans may experience a higher rate of mortality compared to their civilian counterparts. One factor that may contribute to increased rates of death among veterans with COVID-19 is tobacco use. Indeed, findings from a recent meta-analysis highlight the association between lifetime smoking status and COVID-19 progression to more severe or critical conditions including death. Notably, prevalence rates of tobacco use are higher among veterans than civilians. Thus, the purpose of the current study was to examine demographic and medical variables that may contribute to likelihood of death among veterans testing positive for SARS-CoV-2. Additionally, we examined the unique influence of lifetime tobacco use on veteran mortality when added to the complete model. Retrospective chart reviews were conducted on 440 veterans (80.5% African American/Black) who tested positive for SARS-CoV-2 (7.3% deceased) at a large, southeastern Veterans Affairs (VA) hospital between March 11, 2020 and April 23, 2020, with data analysis occurring from May 26, 2020 to June 5, 2020. Older age, male gender, immunodeficiency, endocrine, and pulmonary diseases were positively related to the relative risk of death among SARS-CoV-2 positive veterans, with lifetime tobacco use predicting veteran mortality above and beyond these variables. Findings highlight the importance of assessing for lifetime tobacco use among SARS-CoV-2 positive patients and the relative importance of lifetime tobacco use as a risk factor for increased mortality.

ARTICLE INFO

Keywords:
SARS-CoV-2
COVID-19
Lifetime tobacco use
Veterans
Mortality

1. Introduction

First identified amid an outbreak of respiratory illness in Wuhan, China, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes the Coronavirus Disease 2019 (COVID-19), has been identified as a pandemic. Despite a growing body of research examining correlates and consequences of this disease (Chow et al., 2020; Richardson et al., 2020; Xu et al., 2020; Zhou et al., 2020), only one study to date has been published examining such factors among military veterans. Using a large retrospective cohort of COVID-19 positive...
patients receiving care within the Department of Veterans Affairs (VA), Rentsch et al. (2020) found that older age as well as renal, pulmonary, endocrine, and cardiovascular diseases were associated with hospitalization and intensive care. Although informative, this study did not examine correlates of death. This limitation is particularly concerning as preliminary data indicate that veterans may experience a higher rate of mortality compared to their civilian counterparts due to COVID-19 complications. Indeed, as of September 14, 2020 there have been a total of 48,932 COVID-19 cases within the VA, including 3,158 deaths (U.S. Department of Veterans Affairs, 2020). Whereas veterans are known to have overall poorer health status and more medical conditions than the general patient population (Agha, Loefgren, VanRuiswyk, & Layde, 2000; Hoerster et al., 2012), it is unclear if these factors alone account for discrepancies in COVID-19 mortality rates.

One factor that may contribute to increased rates of death among veterans with COVID-19 is tobacco use. A recent meta-analysis of 19 published papers primarily examining hospitalized patients in China (N = 11,590) indicated a significant association between lifetime smoking status and COVID-19 progression to more severe or critical conditions including death (AOR = 1.91) (Patanavanich & Glantz, 2020). Notably, prevalence rates of tobacco use are higher among military veterans than civilians (Centers for Disease Control and Prevention, March 23, 2020) and thus may be one factor contributing to higher rates of mortality among veterans. To this end, the purpose of the current study was to examine factors, both demographic and medical, that may contribute to likelihood of death among veterans testing for positive for SARS-CoV-2. Additionally, we examined the influence of lifetime tobacco use (i.e., use of tobacco at any point in one’s life), above and beyond the role of demographic and medical variables, on veteran mortality. To our knowledge, this is the first study to examine retrospective risk factors for COVID-19 related deaths among veterans, including the unique contribution of lifetime tobacco use.

2. Method

2.1. Sample and procedures

Demographic, medical, and lifetime tobacco use data were extracted from the electronic medical records of 453 veterans who tested positive for SARS-CoV-2 (polymerise chain reaction [PCR] test) at a large southeastern VA hospital between March 11, 2020 and April 23, 2020. All demographic and lifetime tobacco use data were culled by a group of licensed clinical psychologists, pre-doctoral clinical psychology interns, and a research coordinator. Lifetime tobacco use was ascertained from the veteran’s annual tobacco use screening, which assesses for lifetime use of tobacco including cigarettes, cigars, pipe smoking, snuff, dip, or chewing tobacco. Lifetime tobacco use was coded as “1” if the veteran endorsed being a current or former user or “0” if the veteran denied being a current or former user of tobacco. Medical data were culled by a group of physicians and medical students. A full list of medical variables and search terms can be found in Table 1. All medical data were computed by an independent reviewer and entered into a de-identified database. Informed consent was not required given the data were collected retrospectively, but all use of these data for research purposes was approved by the VA Institutional Review Board.

2.2. Statistical analysis

Descriptive statistics were reported for the complete sample by variable and veteran outcome status. Difference tests on outcome status were performed with independent samples t-tests for continuous variables and chi-square difference tests for categorical variables. The p-values for chi-square difference tests were computed by Monte Carlo simulation with 5000 replicates. Both tests were computed via the R base package stats (Team, 2013).

A hierarchical logistic regression approach was selected to examine the contribution of lifetime tobacco use to COVID-19 mortality after determining the role of relevant demographic and medical variables. First, an initial model (Model 1) was composed with veteran outcome regressed on four demographic variables (age, gender, race, body mass index [BMI]) and nine medical categories (immunodeficiency syndromes, pulmonary diseases, oncological diseases, gastrointestinal diseases, renal diseases, hematologic diseases, endocrine diseases, cardiovascular diseases, and neurological problems). A second model (Model 2) was then composed to 1) determine whether the addition of lifetime tobacco use was statistically significantly associated with a unique contribution to veteran mortality, 2) determine whether the addition of lifetime tobacco use contributed to a statistically significant improvement in model fit relative to Model 1, and 3) examine the change in classification quality of the outcome variable when compared to Model 1.

Prior to estimating the regression models, a sampling procedure was performed to address the severe class imbalance of the outcome variable (92.7% survived). Class imbalance has been shown to degrade accurate model estimation (King & Zeng, 2001) and classification quality for logistic regression models (Cramer, 1999), especially as class imbalances become severe (>90% in the majority class) (Brown & Mues, 2012). Notably, this issue is more prominent for logistic regression models when compared to other non-parametric models (e.g. gradient boosting and random forest models) (Brown & Mues, 2012). A package in R called ROSE (random over sampling examples) was utilized to address class imbalance by generating artificial samples from the feature space neighborhood of the minority class (Lunardon, Menardi, & Torelli, 2014). The ROSE sampling procedure has been shown to be related to

### Table 1

| Medical Categories |
|--------------------|
| Relevant Conditions |

| Immunodeficiency Syndromes | Human Immunodeficiency Virus (HIV); Acquired Immunodeficiency Syndrome (AIDS); Transplant history; Neutropenia |
|----------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| Gastrointestinal (GI) Diseases | End Stage Liver Disease; Alcoholic Liver Disease; Non-Alcoholic Steatohepatitis (NASH); Cirrhosis; Hepatitis B; Hepatitis C; Ulcerative Colitis; Crohn’s Disease; History of GI Bleed; Pancreatitis |
| Pulmonary Diseases | Chronic Obstructive Pulmonary Disease (COPD)/ Emphysema; Asthma; Obstructive Sleep Apnea (OSA); Intestinal Lung Disease; Pulmonary Hypertension; Asbestos Exposure; Cystic Fibrosis; Pulmonary Scleroderma; Bronchiitis |
| Renal Diseases | End Stage Renal Disease (ESRD); Dialysis; Chronic Kidney Disease (CKD) |
| Hematologic Diseases | Deep Vein Thrombosis (DVT); Pulmonary Embolus (PE); Anemia |
| Oncologic Diseases | Chemotherapy; Malignancy; Leukemia; Myeloma; Neoplasm; Carcinoma; Lymphoma; Tumor; Cancer |
| Endocrine Diseases | Thyroid Disorder; Diabetes Mellitus Type 1 (DM1); Diabetes Mellitus Type 2 (DM2) |
| Cardiovascular Diseases | Congestive Heart Failure; Hyperlipidemia; Hypertension (HTN); Atrial Fibrillation; Atrial Flutter; Ventricular Tachycardia; Supraventricular Tachycardia; Pacemaker; Bradycardia; Coronary Artery Disease; Valvular Heart Disease; Peripheral Vascular Disease; Myocardial Infarction (STEMI) |
| Neurologic Problems | Stroke; Seizure Disorder; Dementia; Parkinson’s; Multiple Sclerosis; Neuruphoty |

---

1 Of note, these numbers do not include non-veteran employees, active duty military, or civilians admitted to VA hospitals as humanitarian cases.
consistent improvements in model performance especially when it is applied to the data prior to model estimation (Menardi & Torelli, 2014).

After addressing class imbalance, Model 1 was estimated with the glm function in the stats package (Team, 2013) via the caret package wrapper which was selected for its ability to implement the ROSE balanced method. Model performance was assessed with McFadden glm function in the applied to the data prior to model estimation (Menardi & Torelli, 2013), with models exceeding R² values of 0.20 indicative of excellent fit (McFadden, Hensher, & Stephen, 1979). Additionally, classification accuracy of veteran outcome was indicated by prediction accuracy (i.e., correctly classified outcomes/total outcomes), area under the curve (AUC; the overall performance of the classifier), kappa (an indication of model performance above random chance), sensitivity (percentage of positive instances correctly predicted/observed total number of positive instances), specificity (percentage of negative instances correctly predicted/observed total number of negative instances), and precision (total number of positive instances correctly predicted/total number of instances predicted) (Agresti, 2003) AUC was calculated with the pROC package in R (Robin et al., 2011), while kappa, sensitivity, specificity, and precision were calculated via the confusionMatrix function in the caret package (Kuhn, 2015).

To estimate Model 2, lifetime tobacco use was added to the complete list of variables from Model 1. RR ratios were reported, and a chi-square difference test was performed to provide evidence for judging the relative improvement in model fit associated with the more complex model. Classification indices for Models 2 were then compared to the indices for Model 1 to make conclusions about improvement in classification quality. Data were analyzed from May 26, 2020 to June 5, 2020.

3. Results

From the 453 veterans in the total study sample, 440 patients (Male = 393, Female = 47) with a mean age of 60.80 (SD = 14.07) had complete data for those variables included in the model and thus were included in data analyses (see Table 2 for sample descriptives). The racial/ethnic breakdown was as follows: 80.5% African American/Black; 17.0% Caucasian/White; and 2.5% Other (i.e., Asian, Pacific Islander, American Indian/Alaskan Native) with 98.0% identifying as Non-Hispanic/Latino. The largest sample group was married (48.4%), followed by divorced/separated (25.9%), single/never married (16.6%), widowed (5.9%) and other/missing (3.2%). In terms of military characteristics, the largest sample group served in the Army (48.2%), followed by the Navy (17.7%), Marine Corps (11.8%), Air Force (11.8%), National Guard (2.7%), Coast Guard (0.7%), and multiple branches (3.4%), with a small percentage missing (3.6%).

Of the demographic variables entered into the regression models, the group of veterans who died from COVID-19 were statistically significantly older than those who lived, 73.00 (SD = 2.02) years, p < .001, while race, gender, and BMI indicated no group differences by veteran outcome (Table 2). For the medical variables, veterans from the sample who were significantly more likely to die from COVID-19: immunodeficiency syndromes, X²(440) = 11.70, p < .01, pulmonary diseases, X²(440) = 9.53, p < .01, renal diseases, X²(440) = 6.15, p < .05, hematologic diseases, X²(440) = 9.22, p < .01, and neurologic problems, X²(440) = 8.95, p < .01, while there were no group differences for the remaining four medical categories (i.e., gastrointestinal, oncologic, endocrine, and cardiovascular diseases).

3.1. Hierarchical regression analysis

For Model 1, two of the four demographic variables including age and gender, and three of the nine medical variables, including immunodeficiency, pulmonary, and renal diseases, were associated with statistically significant positive changes in the likelihood of death, while race, BMI, and the six remaining medical conditions were unrelated to veteran outcome (eTable 1 in the Supplement). A ten year increase in age was associated with being 1.65 times as likely to die by COVID-19 (Wald = 5.95; RR = 1.65, 95% RR CI = [1.34, 2.58], p < .001), while females were 0.26 times as likely to die than males, (Wald = 2.69; RR = 0.26, 95% RR CI = [0.09, 0.66], p < .01), veterans identified as having immunodeficiency diseases were 3.42 times as likely to die by COVID-19 (Wald = 3.63; RR = 3.42, 95% RR CI = [1.82, 5.70], p < .001), those identified as having pulmonary diseases were 1.89 times as likely to die by COVID-19 (Wald = 2.40; RR = 1.89, 95% RR CI = [1.14, 3.03], p < .05), and those identified as having renal diseases were 1.75 times as likely to die by COVID-19 than those who were not identified as having these diseases (Wald = 2.52; RR = 1.75, 95% RR CI = [1.14, 2.58], p < .05). The complete Model 1 had a R²MF of 0.22, indicative of an excellent fitting model.

When lifetime tobacco use was added into Model 2, the association between veteran outcome and age, gender, immunodeficiency, and pulmonary diseases remained statistically significant and comparable in the size of their association with outcome status as Model 1 (Table 3). In contrast, the effect of renal diseases on patient outcome became non-significant while the association between having endocrine diseases

### Table 2: Descriptives and difference tests for variables included in regression models (N = 440).

| Variable                  | Group     | Outcome          | Alive (SD) | Deceased (SD) | t-test    |
|---------------------------|-----------|------------------|------------|---------------|-----------|
| **Continuous Variables**  |           |                  |            |               |           |
| Demographics              |           |                  |            |               |           |
| Age                       |           |                  | 59.80      | 73.00         | 6.85 **   |
| BMI                       |           |                  | 30.5       | 28.00         | 2.02      |
| **Categorical Variables**|           |                  |            |               |           |
| Demographics              |           |                  |            |               |           |
| Gender                    |           |                  | Male 361   | Female 32     | 3.01      |
| Race                      |           |                  | White 71   | Non-White 337 | 0.50      |
| Smoking                   |           |                  | No 186     | Yes 222       | 13.24 **  |
| **Medical Categories**    |           |                  |            |               |           |
| Immunodeficiency Syndromes|           |                  | Absent 395 | Present 357   | 11.70 **  |
| Pulmonary Diseases        |           |                  | Absent 387 | Present 375   | 9.53 **   |
| Oncologic Diseases        |           |                  | Absent 71  | Present 51    | 2.29      |
| Gastrointestinal Diseases |           |                  | Absent 357 | Present 51    | 1.03      |
| Renal Diseases            |           |                  | Absent 357 | Present 51    | 6.15      |
| Hematologic Diseases      |           |                  | Absent 305 | Present 103   | 9.22 **   |
| Endocrine Diseases        |           |                  | Absent 245 | Present 163   | 1.24      |
| Cardiovascular Diseases   |           |                  | Absent 73  | Present 335   | 1.51      |
| Neurologic Problems       |           |                  | Absent 341 | Present 67    | 8.95 **   |

Note: BMI = Body Mass Index; Chi-square tests were performed with p-values computed by Monte Carlo simulation with 5000 replicates.

** p < .05.
*** p < .001.
and veteran outcome became statistically significant, with those who had an endocrine disorder being 1.77 times as likely to die of COVID-19 than those who did not (Wald = 3.09; RR = 1.77, 95% RR CI = [1.23, 2.40], p < .01) in Model 2. Importantly, lifetime tobacco use was statistically significantly associated with the likelihood of death by COVID-19 (Wald = 3.42; RR = 2.25, 95% RR CI = [1.39, 3.10], p < .001), with patients who endorsed lifetime tobacco use being 2.25 times as likely to die from COVID-19 than those who did not endorse lifetime tobacco use. The complete Model 2 had a $R^2_{AOM}$ of 0.25, indicative of an excellent fitting model.

Compared to Model 1, the addition of lifetime tobacco use in Model 2 resulted in a statistically significantly better fit for the more complex model, $\Delta \chi^2 = 16.49, p < .001$, and a positive change ($\Delta R^2_{AOM} = 0.03$) in relative model fit (Table 3). As indicated in the model comparison for the classification statistics listed in Table 4, the more complex model also indicated better classification quality with an overall prediction accuracy of 77 percent, indicating a positive change in accuracy of 0.04 over the simpler model, an AUC of 0.76, ($M2 - M1 = 0.04$), Kappa of 0.53 ($M2 - M1 = 0.07$), sensitivity of 0.74 ($M2 - M1 = 0.04$), specificity of 0.79 ($M2 - M1 = 0.03$), and precision of 0.75 ($M2 - M1 = 0.04$).

4. Discussion

Despite a growing body of research examining correlates and consequences of COVID-19 (Chow et al., 2020; Richardson et al., 2020; Xu et al., 2020; Zhou et al., 2020), few studies have been published examining such factors among military veterans. To this end, the current study was designed to specifically examine the role of lifetime tobacco use on death from COVID-19, while controlling for demographic and medical factors that have been found to influence patient mortality among patients testing positive for SARS-CoV-2. We found that older age, male gender, immunodeficiency, endocrine, and pulmonary diseases were associated with higher risk of death among COVID-19 patients. These findings are consistent with currently available information indicating that older adults, individuals with chronic lung disease, diabetes, and those who are immunocompromised may be at higher risk for severe illness within the context of COVID-19 (Centers for Disease Control and Prevention, June 15, 2020). Additionally, these findings are consistent with the limited information available among veterans which highlight the association between various medical conditions, namely pulmonary and endocrine diseases, and COVID-19 positive status (Rentsch et al., 2020).

Notably, we also found that lifetime tobacco use was statistically significantly associated with the likelihood of COVID-19 mortality, above and beyond the included demographic and medical conditions. Indeed, the introduction of lifetime tobacco use in Model 2 was associated with an improved overall model fit and an improved ability to identify veteran outcomes. Such findings are consistent with recent research demonstrating a significant association between lifetime smoking status and progression of COVID-19 to more severe or critical conditions including death and extend upon this research by examining the relative contribution of lifetime tobacco use above and beyond demographic and medical conditions (Patanavanich & Glantz, 2020). The current findings, coupled with the well-known negative health consequences of tobacco use, underscore the need for continued research in this area.

To our knowledge, this is the first study to examine retrospective risk factors for COVID-19 related deaths among veterans including lifetime tobacco use. Additional strengths of the current study include a racially unique patient population (80.5% African American/Black), a comprehensive description of patient medical status (i.e., medical variables), the selection of a modelling approach to isolate the contribution of lifetime tobacco use, and the use of a contemporary statistical technique to address class imbalance in veteran outcomes. However, the current

Table 3
Model 2 logistic regression with adjusted odds ratios, model summary, and model comparison statistics ($N = 440$).

| Coefficient | B     | SE    | Wald   | RR    | 95% RR Odds CI | AOR   | 95% AOR Odds CI |
|-------------|-------|-------|--------|-------|----------------|-------|-----------------|
| Age         | 0.06  | 0.01  | 5.80   | 1.66  | [1.55, 2.24]   | 1.75  | [1.46, 2.12]    |
| Gender      | -1.41 | 0.54  | -2.60  | 0.26  | [0.08, 0.68]   | 0.25  | [0.08, 0.66]    |
| Race        | 0.09  | 0.28  | -0.81  | 0.91  | [0.54, 1.52]   | 0.91  | [0.53, 1.58]    |
| BMI         | 0.01  | 0.02  | 0.94   | 1.77  | [0.80, 1.10]   | 0.94  | [0.81, 1.09]    |
| Immunodeficiency Syndromes | 1.49  | 0.36  | 3.67   | 2.00  | [1.18, 3.29]   | 2.14  | [1.19, 3.59]    |
| Pulmonary Diseases | 0.76  | 0.31  | 0.04   | 0.96  | [0.64, 1.46]   | 0.97  | [0.62, 1.52]    |
| Oncologic Diseases | -0.03 | 0.23  | -0.13  | 0.97  | [0.49, 1.58]   | 0.81  | [0.47, 1.39]    |
| Gastrointestinal Diseases | -0.21 | 0.28  | -0.76  | 0.82  | [0.49, 1.35]   | 0.81  | [0.47, 1.39]    |
| Renal Diseases | 0.39  | 0.24  | 1.45   | 1.45  | [0.93, 2.18]   | 1.48  | [0.92, 2.39]    |
| Hematologic Diseases | 0.06  | 0.21  | 0.27   | 1.06  | [0.72, 1.53]   | 1.06  | [0.70, 1.59]    |
| Endocrine Diseases | 0.60  | 0.19  | 3.09   | 1.77  | [1.23, 2.40]   | 1.83  | [1.25, 2.69]    |
| Cardiovascular Diseases | -0.10 | 0.33  | -0.31  | 0.91  | [0.49, 1.64]   | 0.90  | [0.47, 1.73]    |
| Neurologic Problems | 0.20  | 0.22  | 1.21   | 1.21  | [0.80, 1.79]   | 1.22  | [0.79, 1.90]    |
| Lifetime Tobacco User | 0.82  | 0.24  | 3.42   | 2.25  | [1.39, 3.10]   | 2.28  | [1.43, 3.68]    |

Note. RR = Relative Risk; AOR = Adjusted Odds Ratio; Gender (0 = Male, 1 = Female); Race (0 = White, 1 = Non-White); BMI = Body Mass Index.

Pseudo r-square (1 - (Residual Deviance/Null Deviance)); R$^2_{AOM}$ = Change in R$^2$ between Model 1 and Model 2; ΔR$^2$ = Chi-Square.

Difference test for comparison of model fit for Model 2 compared to Model 1.

Δ = corresponds to a 10-year increase in age.

Δ = corresponds to a 5 unit increase in BMI; R$^2_{AOM}$ = McFadden’s.

p < .05.

p < .01.

p < .001.

Table 4
Classification Quality Indices and Differences for Model 1 and Model 2 ($N = 440$).

| Classification Index | Model 1 | Model 2 | Difference |
|----------------------|---------|---------|------------|
| AUC                  | 0.728   | 0.764   | 0.036      |
| Accuracy             | 0.730   | 0.766   | 0.036      |
| Kappa                | 0.454   | 0.528   | 0.074      |
| Sensitivity          | 0.693   | 0.737   | 0.044      |
| Specificity          | 0.761   | 0.790   | 0.029      |
| Precision            | 0.711   | 0.749   | 0.038      |

Note. AUC = Area Under Curve [95% Confidence Interval for AUC].
study was also limited by the retrospective study design meaning inferences regarding causality cannot be made. Although most medical conditions were present prior to the patient’s death, we cannot conclude that these conditions led to death from COVID-19. Authors of future research should use longitudinal designs to establish a prospective relationship between these variables and COVID-19 mortality. Further, although the model fit was strong and the classification metrics indicated good classification quality, caution should be taken in interpreting these values given the issue with overfitting associated with predicting outcomes on the same dataset with which the model was trained (Babyak, 2004). Additionally, the sample was comprised primarily of male veterans which may affect the generalizability of our findings. Whereas men comprise 85% of our armed forces, the number of female military personnel has increased in recent years (Patten & Parker, 2011). Indeed, women are now the fastest growing cohort in the military, with the number of women enrolling in the VA recently increasing by 90% (Department of Veterans Affairs, 2017, February). As such, authors of future investigations should attempt to replicate these findings in larger, more gender diverse samples.

In addition, this paper was focused specifically on the impact of lifetime tobacco history on veteran mortality among patients testing positive for SARS-CoV-2 and was not designed to test the controverted issue of whether tobacco use protects against disease acquisition. Indeed, nicotine has been found to protect against a number of inflammatory diseases including acute respiratory distress symptoms (Mabley, Gordon, & Pacher, 2011). As such, authors of future investigations should seek to determine the therapeutic benefits of nicotine replacement products among SARS-CoV-2 patients, as such products have been used in the treatment of other medical conditions in smokers and non-smokers alike (Villafane et al., 2018). Relatedly, given our method of data collection, we were unable to determine the relative importance of the type of tobacco used or differentiate between those who were lifetime tobacco users and have maintained current use versus lifetime tobacco users who have ceased use. However, results from a recent meta-analysis highlight the association between former rather than current smoking status and COVID-19 severity (Lippi & Henry, 2020), further highlighting the potential role of nicotine replacement therapy in the treatment of COVID-19.

Findings from the current study indicated that older age, male gender, immunodeficiency, endocrine, and pulmonary diseases were associated with higher risk of death among SARS-CoV-2 positive veterans. Consistent with findings from a recent meta-analysis (Patanavanich & Glantz, 2020), lifetime tobacco use was significantly associated with the likelihood of death among veterans testing positive for SARS-CoV-2. Notably, our findings expanded upon this work by demonstrating the relative contribution of lifetime tobacco use above and beyond relevant demographic and medical conditions. Such findings highlight the importance of assessing for lifetime tobacco use among SARS-CoV-2 positive patients and the significance of tobacco use as a risk factor for increased mortality.

5. Contributors

Author one conceptualized the research idea, drafted the introduction, method, and discussion sections. Author two conducted the formal analyses and wrote the data analytic plan and results sections. Author three assisted with project administration and led the data curation efforts. Author four assisted with drafting the introduction, methods, and discussion sections as well as data curation. Authors five through nine assisted with data curation. Authors ten through thirteen provided supervision. Authors fourteen and fifteen reviewed and edited. Authors sixteen and seventeen provided supervision. All authors reviewed and edited the manuscript.

Role of Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors report no conflict of interest.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This material is the result of work supported with resources and the use of facilities at the Southeast Louisiana Veterans Health Care System in New Orleans, Louisiana. The contents of this article do not represent the views of the Department of Veterans Affairs (VA) or the United States Government.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.addbeh.2020.106692.

References

Agha, Z., Lofgren, R. P., VanRuiswyk, J. V., & Layde, P. M. (2000). Are patients at Veterans Affairs medical centers sicker?: A comparative analysis of health status and medical resource use. Archives of Internal Medicine, 160(21), 3252-3257.
Agresti, A. (2003). Categorical data analysis (Vol. 482). John Wiley & Sons. Babylon, M. A. (2004). What you see may not be what you get: A brief, nontechnical introduction to overfitting in regression-type models. Psychosomatic Medicine, 66(3), 411-421.
Brown, L., & Mues, C. (2012). An experimental comparison of classification algorithms for imbalanced credit scoring data sets. Expert Systems with Applications, 39(3), 3446-3453.
Centers for Disease Control and Prevention. (March 23, 2020). Burden of Cigarette Use in the United States. Retrieved from https://www.cdc.gov/tobacco/campaign/tips/resources/data/cigarette-smoking-in-united-states.html#twelve.
Centers for Disease Control and Prevention. (June 15, 2020). Cases in the United States. Retrieved from https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html.
Chow, N., Fleming-Dutra, K., Giereke, R., Hall, A., Hughes, M., Pilishvili, T., & Ritchie, M. (2020). Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019—United States, February 12–March 28, 2020. Morbidity and Mortality Weekly Report, 69(13), 362.
Cramer, J. S. (1999). Predictive performance of the binary logit model in unbalanced samples. Journal of the Royal Statistical Society: Series D (The Statistician), 48(1), 85-94.
Department of Veterans Affairs. (2017, February). Women veterans report: The past, present, and future of women veterans. Retrieved from Washington, DC: https://www.va.gov/vetdata/docs/specialreports/women_veterans_2015_final.pdf.
Hoerster, K. D., Leavato, K., Simpson, T., McFall, M., Reiber, G., & Nelson, K. M. (2012). Health and health behavior differences: US Military, veteran, and civilian men. American Journal of Preventive Medicine, 43(5), 483-489.
King, G., & Zeng, L. (2001). Logistic regression in rare events data. Political Analysis, 9(2), 137-163.
Kuh, M. (2015). Caret: Classification and regression training. R package version 6.1-18.
Kuhn, M. (2015). Caret: Classification and regression training. R package version 6.1-18.
Mabley, J., Gordon, S., & Pacher, P. (2011). Nicotine exerts an anti-inflammatory effect in a murine model of acute lung injury. Inflammation, 34(4), 231–237.
McFadden, D., Henninger, D. A., & Stephe, P. F. (1979). Behavioural travel modelling (pp. 279-318). London: Croom Helm.
Menardi, G., & Torelli, N. (2014). ROSE: A package for binary imbalanced learning. R Journal, 6(1).
Mabley, J., Gordon, S., & Pacher, P. (2011). Nicotine exerts an anti-inflammatory effect in a murine model of acute lung injury. Inflammation, 34(4), 231–237.
Patten, E., & Parker, K. (2011). Women in the US military: Growing share, distinctive profile: Pew Research Center Washington, DC.
Rentsch, C. T., Kidwai-Khan, F., Tate, J. P., Park, L. S., King, J. T., Skanderson, M., … Holodniy, M. (2020). Covid-19 testing, hospital admission, and intensive care among 2,026,227 United States veterans aged 54–75 years. MedRxiv.

Richardson, S., Hirsch, J. S., Narasimhan, M., Crawford, J. M., McGinn, T., Davidson, K. W., … Cohen, S. L. (2020). Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA.

Robin, X., Turck, N., Hainard, A., Tiberti, N., Lisacek, F., Sanchez, J.-C., & Müller, M. (2011). pROC: An open-source package for R and S+ to analyze and compare ROC curves. BMC Bioinformatics, 12(1), 77.

Smith, T. J., & McKenna, C. M. (2013). A comparison of logistic regression pseudo R2 indices. Multiple Linear Regression Viewpoints, 39(2), 17–26.

Team, R. C. (2013). R: A language and environment for statistical computing.

U.S. Department of Veterans Affairs. (September 14, 2020). Department of Veterans Affairs COVID-19 national summary. Retrieved from https://www.accesstocare.va.gov/Healthcare/COVID19NationalSummary.

Villafane, G., Thiriez, C., Audureau, E., Straczek, C., Kerschen, P., Cormier-Degrauair, F., … Evangelista, E. (2018). High-dose transdermal nicotine in Parkinson’s disease patients: A randomized, open-label, blinded-endpoint evaluation phase 2 study. European Journal of Neurology, 25(1), 120–127.

Xu, Z., Shi, L., Wang, Y., Zhang, J., Huang, L., Zhang, C., … Zhu, L. (2020). Pathological findings of COVID-19 associated with acute respiratory distress syndrome. The Lancet Respiratory Medicine, 8(4), 420–422.

Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., … Gu, X. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. The Lancet.