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GENDER AND DEPRESSION AMONG VETERANS OF OPERATION ENDURING
FREEDOM, IRAQI FREEDOM, AND NEW DAWN

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ABSTRACT

The Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn (OEF/OIF/OND) Veterans utilizing Veterans Affairs (VA) services are medically and psychosocially complex, diverse, and rapidly growing. A significant portion of women Veterans seek out mental health services and they are more likely to be diagnosed with major depression than men, however the majority of prior studies informing Veteran mental health services have been done with predominantly male study populations (16,18,19). Our objectives were 1) to identify characteristics associated with a major depression diagnosis among OEF/OIF/OND men and women Veterans after stratifying by gender and 2) to identify gender differences in the nature of depressive symptoms among these Veterans. We identified 493,747 OEF/OIF/OND personnel—via the VA OEF/OIF/OND roster—who were discharged from the U.S. military from 2001-2010, utilized VA health care services, and met study criteria. Descriptive statistics and multivariable logistic regression models were used to determine how selected demographic characteristics and medical conditions were associated with a major depression diagnosis among women and men. Also, a PHQ-9 in the baseline Women Veterans Cohort Study (WVCS) survey of 644 male and women OEF/OIF/OND Veterans in the Midwest and Northeast U.S. was used to assess depressive symptoms. Among the 493,747 Veterans studied, 5.6% had a major depression diagnosis (8.7% of women vs. 5.1% of men). Hispanic ethnicity (OR=1.26 (1.14, 1.40) was associated with a depression diagnosis in women while older age (OR=1.06 (1.04, 1.09)) and "Other" race/ethnicity (OR=1.14 (1.05, 1.25) was associated with a depression diagnosis in men. Black race was no longer a protective factor for women when the cohort was stratified by gender (OR=0.94 (0.90, 0.97) → OR=1.03 (0.95, 1.11)). Unmarried status was protective against a depression diagnosis in both men (OR=0.94 (0.90, 0.97) and women (OR=0.92 (0.86, 0.94)). All

comorbid conditions—psychiatric illnesses, alcohol abuse, substance abuse, hypertension, and unspecified joint or back disorders—were associated with a depression diagnosis in both men and women and having another psychiatric illness was the strongest correlate in both groups. Military service-connected disability was associated with depression in both men and women, but there was a stronger correlation between service-connected disability rating and a depression diagnosis in women. Depressive symptoms were prevalent among this cohort, the most frequent of which was fatigue. Women were more likely to endorse appetite changes while men were more likely to endorse suicidal ideation. It can be concluded that there are differences between women and men OEF/OIF/OND Veterans with major depression. Further research disentangling the intersection of gender and depression in this medically and psychosocially complex population of Veterans is needed. As the women Veteran population utilizing VA care continues to grow, increasing our understanding of major depression and its risk factors, symptomology, and its comorbidities is crucial to improving overall health outcomes.

ACKNOWLEDGMENTS

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INTRODUCTION

Veterans of Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn who use VA health care

The Veterans that have returned from Operation Enduring Freedom/ Operation Iraqi Freedom/ Operation New Dawn (OEF/OIF/OND) are diverse and are as characteristically unique as the wars in which they served. The U.S. launched Operation Enduring Freedom (OEF) in October of 2001 in response to the September 11, 2001 terrorist attacks as a part of the General War on Terror (GWOT) and ended the war in 2014 (1). Military recruits were primarily deployed to Afghanistan as well as several smaller subordinate operations with a stated focus on counterterrorism (1). Operation Iraqi Freedom/Operation New Dawn (OIF/OND) began in 2003 with the asserted goal of quelling the threat of the Iraqi government and securing weapons of mass destruction (WMDs) (2). The operation was renamed Operation New Dawn in 2010 and officially withdrew combat troops in 2011 (1).

These operations have notably been distinctive for their warfare characteristics. Unlike previous wars in which more traditional methods were utilized, enemy combatants employed insurgency and guerilla warfare tactics that presented novel challenges. The use of improvised explosive devices (IEDs) accounted for 75% of casualties (3). All of these developments, along with improved military body armor that decreased mortality and artificially increased morbidity, have resulted in a greater number of returning seriously injured Veterans and concomitant mental health issues (4). Although 2014 marked the official end of those operations, learning how to best address the high rate of

both mental and physical illnesses amongst this cohort of Veterans will be of interest to the Veterans Health Administration for several years (5-7).

As of June 2014, 60% (1,089,668) of OEF/OIF/OND Veterans had utilized Veterans Affairs (VA) health care (8). The most common diagnostic categories for these Veterans include musculoskeletal problems (60.5%), mental disorders (56.5%), and "ill-defined" conditions (56.4%) (8). In particular, Post Traumatic Stress Disorder (PTSD) and Traumatic Brain Injury (TBI) have been considered the signature wounds of OEF/OIF/OND (9). Mental and behavioral health issues as a result of serving in these conflicts are expected to have a continuing impact for years to come (9). Illnesses impacting the respiratory and nervous system are expected to rise as a result of added exposure to chemical and biological weapons as well as other hazardous materials (9). Of particular interest are individuals who use VA services because they represent particularly vulnerable Veterans, they are typically of lower socioeconomic status, and they have more service-connected disability (10). They also tend to have higher levels of mental illness (6,7).

The growing incidence of these ailments among military Veterans who utilize VA health care services has prompted the VA to expand programs and resources in recent years. In particular, the high prevalence of chronic pain, mental illness, and psychosomatic conditions have spurred efforts attempting to better serve the growing number of Veterans seeking mental health care. (5-7,9). A major component of one of the VA strategic goals outlined for 2014-2020 involves improving cost effective and efficient care for Veterans (9). Addressing mental illnesses especially in their comorbid state with other ailments in an integrated model has been shown to significantly improve both

health outcomes and costs (11,12). Although VA healthcare generally already relies on a relatively integrated model of care, the approach to mental health care especially for women Veterans varies widely nationally (13).

Women's participation in the U.S military increased significantly with OEF/OIF/OND (14). As of September 2014, there were over 2 million women Veterans (14). They are also utilizing VA resources more than ever before; 44% of women Veterans returning from Iraq and Afghanistan elect to enroll in the VA system compared to 11% in past eras (15). Consequently, the number of women Veterans utilizing services has doubled in recent years (16). In addition to the increasing population of women Veterans, the nature of their roles, their social demographics, and their level of exposure to combat has also evolved over time. Women also have higher disease burdens than they did in past years (16). Of the women Veterans who used VA outpatient services in 2009, 40% used mental health services. A recent study seeking to identify medical priorities among women Veterans found depression to be a main concern. The study also concluded that women Veterans' preferences for mental health services differ by both demographic and clinical characteristics (17).

Women Veterans in the OEF/OIF/OND cohort are more likely to be of Black or Hispanic race/ethnicity when compared to women in the general population and men. In a study of OEF/OIF/OND Veterans who used VA services within 1 year of their last deployment, Black and Hispanic women were found to make up almost half of women Veterans seeking VA health care; this figure is much higher than the percentage of Black and Hispanic men (41% vs. 25%) (18). Previous studies found that women Veterans are also more likely to be educated, older, and unmarried (19). Women are more likely to

suffer from major depression and it has a significant effect on overall quality of life and health outcomes (5,11,20,21). Naturally, profiling major depression—a disease with far reaching impacts—is a vital portion of understanding morbidity in this cohort of Veterans (11).

Depression epidemiology and disease comorbidity

Major depression is a significant public health issue affecting 17% of American adults in their lifetime. (22). It serves as the leading cause of disability among adults 15 to 44 years old and is slated to be the overall leading cause of disability among high income countries in the next 20 years (23,24). Per employee with depression, it is estimated that twenty seven productive work days are lost annually (25,26). Depression may significantly impact one's ability to maintain employment and—in the case of Veterans—reintegrate with society. In addition, depressive symptoms are the strongest predictors of suicidal ideation and addressing modifiable risk factors for suicide among Veterans has been a significant and ongoing issue (27,28).

In the general population, despite its major impact on morbidity, quality of life, and cost, only one third of those with depression are diagnosed and only half of those diagnosed with depression receive any treatment (24,29). The USPSTF, recommends screening all individuals during routine primary care visits as long supports are in place to accurately diagnosis and treat depression. The PHQ-2 or PHQ-9 (Patient Health Questionnaire) are commonly used instruments and are widely considered to be the most accurate publically available screens (30-33).

Our understanding of the etiology of depression relies heavily on the

biopsychosocial model of disease. It is commonly believed to be multifactorial with several potential genetic and psychosocial contributing factors (34). There are multiple known risk factors for depression in the community dwelling general population including female gender, young adult age, and obesity (35-37). The point prevalence of depression decreases significantly with increasing age and the lowest rates are among older adults above sixty five years old (38). However, depression is more common in older adults with high burdens of medical illness and those in assisted living/nursing facilities (36,39-42). Individuals with less education and those of lower socioeconomic status are also more likely to experience depression (43).

The association between race/ethnicity and depression in the United States is somewhat complicated. Major depression has often been found to be less prevalent among racial minority groups after controlling for socioeconomic status (44). A study on race and the differential vulnerability hypothesis suggested that when exposed to the same stressors White individuals were more vulnerable to major depression than Black and Hispanic minority groups in the U.S. (45). There is a greater lifetime prevalence of depression among White Americans (18%) than African Americans (10%) (46). Though, the same study found that African Americans with depression were less likely to receive treatment and experienced greater chronicity and greater overall functional impairment (46). Another study examining lifetime prevalence of depression reported a rate of 6.52% among whites, 4.57% among blacks, and 5.17% among Hispanics. Hispanic Americans also experience disparities in access to adequate mental health care (47). In the VA healthcare system, when utilization and access disparities are accounted for, the association between race/ethnicity and depression diagnoses may be different from what

is normally seen in the general population.

In addition, depression is intricately correlated with chronic illness. Via a variety of causal pathways, depression is significantly associated with conditions that are characterized by pain, inflammation, and/or have high symptom burdens (11). It is also strongly associated with other psychiatric illnesses and substance abuse disorders. (11,48) Depression may contribute to and complicate the progression of illness (11,49). Addressing co-morbid issues may improve major depression outcomes. Likewise, it has been shown that treating depression can help improve coexisting illness(es) (50). Addressing major depression may be key to alleviating overall disease burden and disability. Common diseases specifically linked to depression include stroke, cancer, HIV/AIDS, diabetes, heart disease, Parkinson's, thyroid disorders, substance abuse, PTSD, and multiple sclerosis (51). "Vascular depression" is also a phenomenon in older adults thought to be linked directly to small vessel cerebral ischemia (52). A significant demonstration of outcome improvement through depression treatment has been shown in congestive heart failure (CHF) patients (53).

Veterans often present with multiple health conditions that affect and ultimately impact the treatment of each other. In particular, TBI and painful injury sequelae are highly associated with major depression (54,55). Accurately characterizing and ultimately better addressing depression in this cohort can make a significant impact on outcomes, for these ailments (4).

Veterans and Major depression

Currently, the Department of Veterans Affairs utilizes USPSTF guidelines and

recommends annual screening for all Veterans via the PHQ2 or PHQ9 (5). Among military Veterans, the point prevalence of major depressive disorder from primary care screenings after further evaluation is 5-13% vs. 3-5% in the general population (5).

Although there are multiple known risk factors associated with depression in the general population, data suggests that there may be some distinct attributes of Veterans with depression. Veterans with depression are twice as likely to commit suicide and deal with substance abuse than others with depression (56). In addition, age related risk factors for suicide among Veterans with depression are different than what is commonly seen; younger age is a risk factor for suicide among Veterans with depression where as in the general population the risk for suicide generally increases with age among those with depression (56). Also interestingly, a diagnosis of depression and PTSD among Veterans had a lower risk of suicide than a diagnosis of depression alone (56). This may be attributable to the greater stigmatization of depression compared to PTSD among Veterans or closer monitoring and services for Veterans who have a PTSD diagnosis (56).

Depression among OEF/OIF/OND Veterans may be distinct not only from the civilian population, but also from previous Veteran cohorts due to the uniqueness of their military experience, racial/ethnic diversity, younger age and greater number of women playing novel roles (15). In 2004, Hoge et al. found that 8 -15% of returning OIF Veterans and 7-14% of returning OEF Veterans screened positive for depression, while the prevalence before OEF/OIF/OND was 5-11% (6). It is imperative to appropriately characterize major depression among these diverse subgroups.

Health services research efforts have sought to assess varying primary care

models to better care for Veterans with depression. Translating Initiatives for Depression Into Effective Solutions (TIDES) is one such model that has proven efficacious; it comprises interdisciplinary collaboration between depression care-managers, mental health specialists, and primary care providers (56). This model has received endorsement through national directives and financial support (12). However, there may be reason to believe that this cohort of Veterans is distinct in their comorbid health care needs as discussed above. Also, because of their small population size, women Veterans –as is often the case – make up a small component of those assessed in these studies.

A few studies have found that among OEF/OIF/OND Veterans, women have a higher prevalence of depression diagnoses (19,57). Maguen et al. examined demographic and military service based correlates of major depression in women OEF/OIF Veterans through 2008 in a multivariable regression analysis (19). The study found that both men and women who were "White; divorced, separated, or widowed; Army members; active-duty personnel; or enlisted personnel" were more likely to have a depression diagnosis. Unlike men, women who were older than 40 were more likely to receive a diagnosis (19). Membership in the Navy/Air Force and officer status was significantly protective against depression in women and in men (19,58). Also, "never married status" was protective in men but not in women (19). Of note, their regression models did not appear to account for utilization, physical illness characteristics, nor comorbid psychiatric illnesses. Previous studies have also found that women with military sexual trauma report higher levels of major depression (59,60).

Gender and Depression

Among women in the general population the prevalence of major depression is twice that of men (22). The cause of women's increased risk for depression is not clearly understood. It is likely an intersection of genetic, hormonal, environmental and social, as well as psychological factors. There is a direct hormonal effect on the neurotransmitters that control mood and emotion (61). Before puberty, girls and boys have similar rates of depression; it is during adolescence that the gender disparity is initiated. Depression rates then decrease among women after menopause (62). Although, according to the National Comorbidity Survey, there is also a decline in depression diagnoses among men with increasing age, the gender gap in the elderly narrows (22,62). Interestingly, the National Survey of Psychiatric Morbidity in Britain found that in those above 55 years old, men had a higher prevalence of depressive episodes (62).

In addition to biological/hormonal differences there is a greater link between social stressors and depression among women. One study found that among adolescents with depression, 70% of women had an inciting stressful event while 14% of men did (63). However, it was unclear whether this was explicitly linked to a gender disparity in the number of traumas experienced (i.e. poverty, sexual abuse disparities) or a greater link between traumas and depression in women. The literature suggests that women experience more "life stressors" but may also have a prolonged response to the same stressors increasing their risk for depression (62,64)

With regard to coexisting illnesses, women with depression are more prone to having a coexisting anxiety disorder than men (20). Alcohol and substance abuse disorders tend to coexist with depression in both men and women (20,65). Serious

medical conditions (*See depression epidemiology and disease comorbidity*) seem to correlate with depression in both men and women within the general population (50). It is believed that women with depression are more likely to experience the somatic symptoms of depression (66-68). They are also more likely to exhibit atypical depression symptoms i.e. hypersomnia and increased appetite (69,70).

Among those with existing depression, women are more likely than men to receive a diagnosis (71). Even after controlling for Beck Depression Inventory (BDI) scores, one study found that women with high scores were more likely to receive a diagnosis than men with similar scores in the primary care setting (71). This was partially a function of higher levels of clinic utilization by women, a factor also correlated with depression diagnoses in men (71). After controlling for other identified confounders women were still 72% more likely to receive a diagnosis although this was not statistically significant (71).

Specifically, among OEF/OIF/OND Veterans utilizing VA health care, major depression diagnoses are more prevalent in women than they are among men and women are also more likely to utilize VA mental health services than men. (15,72). Previous research has found that women OEF/OIF Veterans exhibit a lower incidence of PTSD and a higher incidence of major depression than men within the first year home from a deployment (7,19,72). According to the VA's Women's Health Evaluation Initiative (WHEI), the most common ICD-9 mental health condition among all women Veteran patients is depression (Depression, Possible-Other) with official Major Depressive Disorder ranking fourth (16). After adjusting for age, the WHEI found that women were more likely to have Major Depression (OR=1.83), but they did not control for healthcare

utilization, comorbid medical conditions, and other demographic factors (16).

Historically, most studies of major depression among Veterans have been done in cohorts that were predominantly comprised of men. We seek to expand on the burgeoning literature of mental health in women Veterans by determining the relative impact of depression correlates in both women and men in the context of disease comorbidity in this psychosocially and medically complex group. A more comprehensive understanding of the characteristics associated with depression with attention to comorbid disease is important for developing strategies for tailoring mental health services to both women and men in the OEF/OIF/OND cohort (5).

STATEMENT OF PURPOSE

The purpose of this work is Part 1) to profile both women and men OEF/OIF/OND

Veterans with a major depression diagnosis in the context of selected demographic,

comorbid clinical factors and Part 2) to determine if there is a gender difference in the

prevalence of PHQ-9 symptoms among OEF/OIF/OND Veterans. Specifically, this thesis

aims to answer the following questions:

Part I.

    A) What are the demographic and clinical characteristics of women OEF/OIF/OND

        Veterans with a major depression diagnosis? What are the demographic and

        clinical characteristics of men OEF/OIF/OND Veterans with a major depression

        diagnosis? Among both gender groups, which characteristics studied increase the

        adjusted odds of a major depression diagnosis most?

            We believe that in both women and men marital status, education, and

            disease/disability have an association with a depression diagnosis. We also

            hypothesize that women Veterans with a depression diagnosis are more

            likely to be Black or Hispanic.

    B) Is the gender difference (women > men) in depression prevalence amongst

        OEF/OIF/OND Veterans maintained after controlling for selected socio-

        demographic and clinical factors?

            We believe that previously documented gender differences in the

            prevalence of depression among these Veterans may be partially attributed

            to the different demographic characteristics of the men and women

Veteran population. However controlling for the selected demographic and clinical characteristics women will have a clinically significant greater likelihood of a depression diagnosis.

Part II.

A) Is there a gender difference in the prevalence of the depressive symptoms men and women Veterans experience based on a PHQ-9 depression screening?

We believe that depressive symptoms are prevalent in both groups . We also believe that women are more likely to endorse the somatic symptoms of depression.

METHODS

Part I.

Data Sources

The study was conducted using the VA OEF/OIF/OND roster of Veterans provided by the Defense Manpower Data Center-Contingency (DMDC) on all military personnel discharged from the U.S. military from October 1, 2001 to September 30, 2010 who were deployed in support of OEF/OIF/OND. The DMDC includes information on Veterans' sex, race, date of birth, deployment dates, armed forces branch (Army, Navy, Air Force, Marines, or Coast Guard) and component (National Guard, Reserve, or active duty). Data on eligible Veterans were linked with VA administrative and clinical data contained within the VA National Patient Care Database, Decision Support Systems, and the Corporate Data Warehouse. These databases provide health care utilization and coded diagnostic information associated with all VA inpatient and outpatient encounters (73). These data repositories have been used in several studies and are amenable to empirical research (18,73).

Study Population

All U.S. military Veterans on the roster who deployed to OEF/OIF/OND and enrolled in VA health care before September 30, 2010 were eligible for our study. Our inclusion criteria were 1) Veterans who enrolled in VA health care and 2) Veterans who had at least one visit to the VA occurring after the end of their last deployment. Approximately half of all OEF/OIF/OND Veterans had enrolled at the time of the study

(74;75). We excluded Coast Guard members as this group is very small and is substantially different from the rest of the military in terms of function. We chose to include all Veterans who met this criteria regardless of overseas deployment or combat exposure because our goal is to characterize those in this cohort who utilize VA care rather than to form explicit associations between conflict exposure and depression. The final study cohort contained 493,747 subjects. This study was approved by the Human Investigation Committees at VA Connecticut Healthcare System and Yale University School of Medicine.

Variables

Our primary outcome of interest was a major depression diagnosis. This outcome, as well as all medical conditions used in the study were quantified by grouping diseases according to ICD-9-CM codes and specifications (73). Veterans were considered to have a diagnosis of major depression if they had two or more outpatient and one or more inpatient ICD-9-CM codes for the disorder. Outpatient codes are assigned by health care providers and are expected to be less complete than inpatient codes, which are assigned by professional coders. This methodology has been found to improve the accuracy of these codes for clinical diagnoses (76-78).

The sociodemographic and clinical characteristics of interest were

- Age
- Race/ethnicity
- Marital status (currently married, never married, or separated/ divorced/ annulled/widowed/other)

- Level of education (high school or less vs. greater than high school), and

- Service connected disability rating [categorized as 0% (no service related disability), 1-29% (disability but not eligible for retirement and dependent benefits), 30-99% (eligible for dependent and retirement benefits), and 100% (unable to be gainfully employed and benefit eligible)] (Blackstock 2012).

- A predefined group of highly correlated psychiatric illnesses
  - PTSD
  - Bipolar disorder
  - Schizophrenia

- Alcohol abuse disorder

- Substance abuse disorder

- Hypertension

- Unspecified back or joint disorder.

Veterans' sociodemographic were obtained from the DMDC. The highly correlated psychiatric illnesses were grouped together as one variable: "'other' psychiatric illnesses" and included PTSD, bipolar disorder, and schizophrenia. This variable, as described previously, was based on extensive comorbidity between these three disorders and omits interactions (79). The mental health conditions were chosen because of their prevalence in this cohort of Veterans. Although common, anxiety disorder could not be studied due to concern about ICD-9-CM coding consistency in this group. Hypertension was also of interest because of its high prevalence and link to cardiovascular diseases; depression has been implicated by temporal studies as a risk factor for hypertension in the general

population (80). Unspecified back or joint disorders encompass a significant amount of

pain and disability and were chosen because previous studies have suggested a high

prevalence among women Veterans in this cohort (77,81). TBI and military sexual

trauma were initially assessed as potential variables but were not included in the study

due to significant amounts of missing values. All ICD-9-CM diagnostic code groupings

were previously validated (82-84)

Statistical Analysis

In descriptive analyses, we used a t-test for age and a chi-squared test for

categorical variables to individually compare several characteristics of women and men

in the study. We then stratified by gender and compared the characteristics of those with

a major depression diagnosis and those without a major depression diagnosis within each

gender. Only statistically and clinically significant factors were included in the logistic

regression. Due to the large sample size, all p values below 0.0001 were deemed

statistically significant.

A logistic regression model was created to determine the independent association

between gender and a major depression diagnosis. Race/ethnicity was then added as an

independent variable to create a limited model for major depression. Subsequently age,

race/ethnicity, marital status, level of education, service connected disability rating,

'other' psychiatric illnesses (PTSD, bipolar disorder, or schizophrenia), alcohol abuse

disorder, substance abuse disorder, unspecified back or joint disorder, and hypertension

were included to complete the model. We tested for interactions and found that the fit of

the model for the data was validated by the Hosmer and Lemeshow Goodness-of-fit test;

p <0.0001 (85). We found a significant interaction between gender and race/ethnicity (model with interaction had larger Hosmer and Lemeshow Goodness-of-fit chi square value). Also, because we are interested in examining each population separately we created two separate models for men and women. The fit of the full model for each gender was validated by the Hosmer and Lemeshow Goodness-of-fit test; p <.0001 (85). The alpha level of statistical significance was fixed at 0.05 for two-sided hypothesis testing. Odds ratios with corresponding 95% confidence intervals were used to demonstrate the adjusted effect of each variable on predicting a major depression diagnosis. Statistical analyses were performed using SAS Enterprise Guide version 4.2 software (SAS Inc., Cary, NC).

Part II.

This phase of the study utilized Women Veterans Cohort Study (WVCS) baseline cross-sectional survey data from 289 men and 355 women OEF/OIF/OND Veterans (total n = 644) who enrolled for VHA services after October 1, 2001. The Women Veterans Cohort Study includes a prospective survey of men and women OEF/OIF/OND Veterans at two major VA facilities in the Midwest and Northeast United States. Letters were sent out to all eligible women Veterans and to a randomly selected group of men who lived within 100 miles of each facility (2000) (86-88). Additionally, an effort was made to recruit OEF/OIF/OND Veterans through the use of flyers posted in clinics at the 2 research sites. Participants met with the research coordinator either by phone or in person. The research coordinator read a description of the study, answered questions

about enrollment and adverse consequences of participation, and were screened for eligibility. Those who agreed to participate provided an informed consent.

Eligibility criteria included 1) the ability to fluently speak and read English and 2) participation in OEF or OIF. 644 out of 2000 Veterans met criteria and agreed to participate. They were given an appointment at which they were asked to complete the paper baseline survey. Participants were also asked to complete follow-up surveys after the baseline survey.

Institutional Review Board approval for the investigation was provided by the VA Connecticut Healthcare System and by the Yale University School of Medicine (86-88). For the purposes of the present analysis, only baseline survey data were utilized. A PHQ-9 screening within the survey measured the prevalence of depressive symptoms during the prior 2 weeks. Positive ('Several Days', 'More than half the days', or 'Nearly Everyday') responses to depressive symptoms on the PHQ-9 was assessed in each gender group and compared via chi square testing (See Appendix). All p values below .05 were deemed significant.

Student Role and Collaborators

Nkemka Esiobu conceived the study idea, conducted a literature review, performed the data analysis for the study using SAS 9.2, and wrote the paper. Harini Bathulupalli culled the variables requested from the national VA roster database and created the streamlined data set. Cynthia Brandt, Sally Haskell, Amy Justice as well as other faculty and staff collaborators provided guidance throughout the process.

RESULTS

Part I.

Characteristics of women and men OEF/OIF/OND Veterans

There were 493,747 Veterans studied; 59,419 (12.0%) were women and 434,328 (88.0%) were men. When compared with men, women OEF/OIF/OND Veterans were less likely to be White, more likely to have never been married, more likely to have been separated/divorced/widowed, more likely to have greater than a high school education and similar in age. In terms of medical illnesses, women were more likely to have a diagnosis of bipolar disorder and less likely to have alcohol abuse disorder, drug abuse disorder, PTSD, and hypertension. They were similarly as likely to have schizophrenia, unspecified back disorders, and unspecified joint disorders. They had similar service connected disability ratings when compared to men.

Table 1. Characteristics of women and men OEF/OIF/OND Veterans (n=493,747)					
	Women **n=59,419(12%)**		**Men** **n=434,328 (88%)**		**p** **value**
	n	**%**	**n**	**%**	
Age, Mean(SE) (n=493,662)	29(8.6)		31(9.4)		<.0001
Race/Ethnicity (n=460,257)					<.0001
White	28752	51.7	274877	67.9	
Black	15723	28.3	57502	14.2	
Hispanic	6218	11.2	46056	11.4	
Other	4916	8.8	26213	6.5	
Marital Status (n=493,477)					<.0001
Currently Married	20067	33.8	203979	47.0	
Never Married	33900	57.1	211594	48.7	
Separated/Divorced/Annulled/Other	5390	9.1	18547	4.3	
Education (n=493,730)					<.0001
High School and Less	43675	73.5	341629	78.7	
Greater Than High School	15742	26.5	92684	21.3	
Service Connected Disability Rating (n=481,961)					<.0001
0	35723	61.5	259354	61.2	
1-29	6999	12.0	49647	11.7	
30-99	14490	24.9	105824	25.0	
100	951	1.6	8973	2.1	
Psychiatric Illness (PTSD, Schizophrenia or Bipolar Disorder)	10890	18.3	98741	22.7	<.0001
PTSD	10018	16.9	94779	21.8	<.0001
Schizophrenia	107	0.2	1048	0.2	.0003
Bipolar Disorder	1727	2.9	9626	2.2	<.0001
Major Depression	5180	8.7	22329	5.1	<.0001
Alcohol Abuse Disorder	1821	3.1	29684	6.8	<.0001
Substance Abuse Disorder	887	1.5	14551	3.4	<.0001
Unspecified Back and/or Joint Disorders	22659	38.1	167831	38.6	.0172
Unspecified Back Disorder	14447	24.3	105827	24.4	.7822
Unspecified Joint Disorder	15318	25.8	112072	25.8	.9006
Hypertension	3243	5.5	40618	9.3	<.0001
Posttraumatic Stress Disorder (PTSD) *Missing values for each variable were excluded only for the variable's analysis. N=493,747 unless otherwise indicated.					

Gender, race/ethnicity, and major depression

Out of the 493,747 OEF/OIF/OND Veterans studied, 27,509 (5.6%) had a major

depression diagnosis. Overall, women were more likely to have a major depression

diagnosis (8.7% vs. 5.1%, p<.0001) (OR=1.76 (1.71, 1.82). As depicted in Figure 1, a

greater proportion of Black and Hispanic women Veterans had a major depression

diagnosis relative to White women Veterans. The prevalence of major depression

diagnoses by race/ethnicity and gender in descending order were: 1) Hispanic women

9.8%, 2) Black women 9.7%, 3) White women 8.4%, 4) 'Other' women 8%. 5) Hispanic

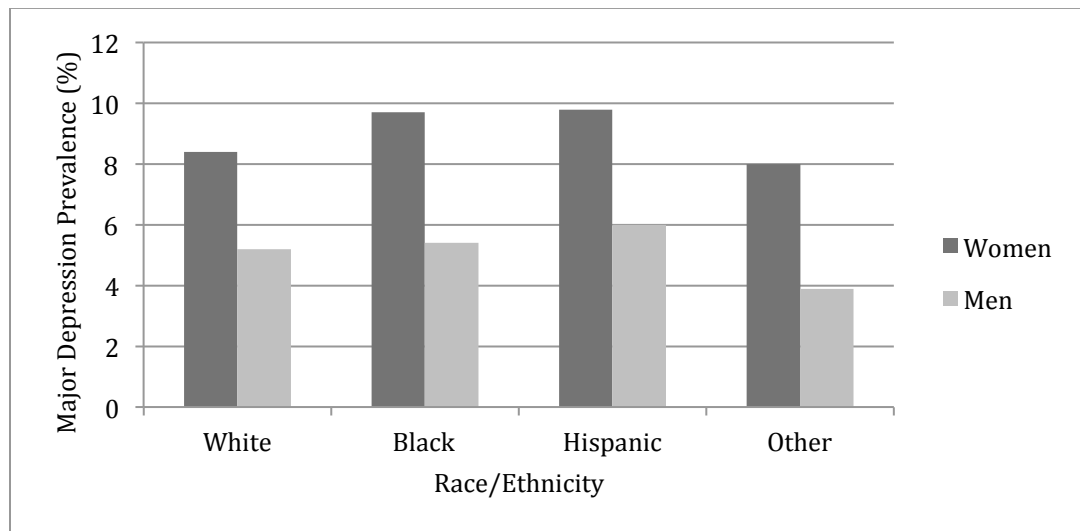men 6% 6) Black men 5.4% 7) White men 5.2% and 8) 'Other' men 3.9%.

Figure 1. Major depression diagnosis prevalence rates among OEF/OIF/OND Veterans
by race and gender

Characteristics of women and men OEF/OIF/OND Veterans with a major depression diagnosis

As seen in Table 2a, when women Veterans with a major depression diagnosis were compared to those without a major depression diagnosis we found that they were slightly more likely to be Black or Hispanic, more likely to be currently or previously married, have no greater than a high school education, and have significantly higher service connected disability ratings. Clinically, women with a depression diagnosis were more likely to have PTSD, schizophrenia, alcohol abuse disorder, substance abuse disorder, unspecified back disorders, unspecified joint disorders, and hypertension.

As seen in Table 2b, when men Veterans with a major depression diagnosis were compared to those without a major depression diagnosis we found that they were slightly more likely to be Hispanic, more likely to be currently or previously married, have no greater than a high school education, and have significantly higher service connected disability ratings. Clinically, men with a depression diagnosis were more likely to have PTSD, schizophrenia, alcohol abuse disorder, substance abuse disorder, unspecified back disorders, unspecified joint disorders, and hypertension.

Table 2a. Characteristics of women OEF/OIF/OND Veterans by major depression diagnosis (n=59,419)				
Characteristics	**Women without major depression diagnosis**		**Women with major depression diagnosis**	
	n=54,239	91.3%	n=5,180	8.7%
Age, Mean (SE*) (n=59,413)	28.8(8.6)		29.5(8.7)	
Race/ethnicity (n=55,609)				
White	26332	52.0	2420	49.0
Black	14205	28.0	1518	30.7
Hispanic	5609	11.1	609	12.3
Other	4523	8.9	393	8.0
Marital status (n=59,357)				
Currently married	18187	33.6	1880	36.3
Never married	31204	57.6	2696	52.1
Separated/divorced/annulled/other	4793	8.9	597	11.5
Education(n=59,417)				
High school and less	39733	73.3	3942	76.1
Greater than high school	14504	26.7	1238	23.9
Service connected disability rating (n=58,163)				
0	34267	64.7	1456	28.2
29-Jan	6436	12.1	563	10.9
30-99	11714	22.1	2776	53.8
100	589	1.1	362	7.0
Psychiatric illness (PTSD, schizophrenia or bipolar disorder)	7639	14.1	3251	62.8
PTSD	6950	12.8	3068	59.2
Schizophrenia	69	0.1	38	0.7
Alcohol abuse disorder	1098	2.0	723	14.0
Substance abuse disorder	501	0.9	386	7.5
Pain disorders (Unspecified back or joint pain)	19257	35.5	3402	65.7
Unspecified back disorder	12001	22.1	2446	47.2
Unspecified joint disorder	12847	23.7	2471	47.7
Hypertension	2626	4.8	617	11.9
p value<.0001 for all characteristics Standard Error (SE); Posttraumatic Stress Disorder (PTSD)				

Table 2b. Characteristics of men OEF/OIF/OND Veterans with and without a major depression diagnosis (n=434,328)				
	Men without major depression diagnosis		**Men with major depression diagnosis**	
	n=411,999	94.9%	n=22,329	5.1%
Age, Mean(SE) (n=434,249)	30.5(9.4)		30.6(9.4)	
Race/Ethnicity (n=404,648)				
White	260521	68.0	14356	67.5
Black	54389	14.2	3113	14.6
Hispanic	43285	11.3	2771	13.0
Other	25180	6.6	1033	4.9
Marital Status (n=434,120)				
Currently Married	193018	46.9	10961	49.1
Never Married	201398	48.9	10196	45.7
Separated/Divorced/Annulled/Other	17386	4.2	1161	5.2
Education (n=434,313)				
High School or Less	323060	78.4	18569	83.2
Greater Than High School	88924	21.6	3760	16.8
Service Connected Disability Rating (n=423,798)				
0	252912	63.0	6442	28.9
1-29	47613	11.9	2034	9.1
30-99	94153	23.5	11671	52.4
100	6857	1.7	2116	9.5
Psychiatric Illness (PTSD, Schizophrenia or Bipolar Disorder)	82023	19.9	16718	74.9
PTSD	78656	19.1	16123	72.2
Schizophrenia	799	0.2	249	1.1
Alcohol Abuse Disorder	23347	5.7	6337	28.4
Substance Abuse Disorder	11033	2.7	3518	15.8
Unspecified Back and/or Joint Disorders	152837	37.1	14994	67.2
Back Disorder	94918	23.0	10909	48.9
Joint Disorder	101595	24.7	10477	46.9
Hypertension	35922	8.7	4696	21.0
p value<.0001 for all characteristics Standard Error (SE); Posttraumatic Stress Disorder (PTSD)				

Logistic Regression Models

The unadjusted odds of a major depression diagnosis given a Veteran is a woman is 1.76 (1.71, 1.82) (Table 3 column 1). Based on the limited model of sex and race as predictors of major depression, women maintained higher odds of a major depression diagnosis than men (OR=1.75 (1.69, 1.81)) and both Hispanic Veterans (OR=1.16 (1.12, 1.21)) and Black Veterans (OR=1.07 (1.03, 1.10) had increased odds of a major depression diagnosis when compared to White Veterans. (Table 3 column 2).

After other variables were added to create the full model, female gender, Hispanic and Other race/ethnicity, older age, being separated/divorced/ widowed, greater than 0% service disability rating, psychiatric illness (PTSD, bipolar disorder and/or schizophrenia), alcohol abuse disorder, substance abuse disorder, unspecified back and joint disorders, and hypertension were significantly associated with a major depression diagnosis. Black race and having never been married were protective factors for a major depression diagnosis. Education level was not significantly associated with major depression. (Table 3 column 3)

After finding an interaction between gender and race (p=0.053) we stratified the population by gender to better explore the characteristics of women as well as men separately (Table 3, column 4 and 5). Characteristics that remained significantly associated with a major depression diagnosis in women Veterans, as determined by a fully adjusted multivariable logistic regression model from greatest to least in magnitude of association were 1) 'other' psychiatric illnesses 2) a 100% service connected disability rating 3) a 30-99% service connected disability rating 4) alcohol abuse disorder 5) substance abuse disorder 6) an unspecified back or joint disorder 7) a 1-29% service

connected disability rating 8) hypertension and 9) Hispanic ethnicity. A "never" marital status remained a protective factor in women. (Table 4)

For men Veterans, the factors positively associated with major depression from greatest to least in magnitude of association were 1) 'other' psychiatric illness 2) a 100% service connected disability rating 3) alcohol abuse disorder 4) substance abuse disorder 5) a 30-99% service connected disability rating 6) hypertension 7) back and/or joint disorders 8) 'Other' Race and 1-29% service connected disability rating and 9) older age. (Table 4). Never being married remained negatively associated with major depression among men as well, but being separated/divorced/widowed was not associated with major depression for either group.

Of note, after gender stratification, Black race was no longer a protective factor in men or women and a former marriage (divorced/separated/annulled/widowed) was no longer associated with a depression diagnosis. It was also noted that the odds of a major depression diagnosis increased with each categorical increase in service connected disability rating. (Figure 2).

Table 3. Results of logistic regression models predicting risk of major depression among all OEF/OIF Veterans and among Veterans stratified by gender.

	Adjusted OR (95% CI)				
	Limited Model		**Full Model**		
	All Veterans n=493,747	**All Veterans** n=460,257	**All Veterans** n=448,535	**Females** n=54,329	**Males** n=394,206
Gender	1.76 (1.71, 1.82)	1.75 (1.69, 1.81)	2.57 (2.47, 2.66)	NA	NA
Race/Ethnicity	…				
White		1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Black		1.07 (1.03, 1.10)	0.94 (0.90, 0.97)	1.03 (0.95, 1.11)	0.96 (0.91, 1.02)
Hispanic		1.16 (1.12, 1.21)	1.20 (1.15, 1.25)	1.26 (1.14, 1.40)	1.01 (0.94, 1.07)
Other		0.79 (0.74, 0.83)	1.07 (1.004, 1.13)	1.12 (0.99, 1.26)	1.14 (1.05, 1.25)
Age**	…	…	1.05 (1.03, 1.07)	0.98 (0.94, 1.03)	1.06 (1.04, 1.09)
Marital Status	…	…			
Currently Married			1.00 (referent)	1.00 (referent)	1.00 (referent)
Never Married			0.93 (0.90, 0.96)	0.92 (0.86, 0.99)	0.94 (0.90, 0.97)
Separated/Divorced/Annulled/Other			1.07 (1.01, 1.14)	1.11 (0.99, 1.24)	1.07 (0.997, 1.14)
Education	…	…			
Greater Than High School			1.00 (referent)	1.00 (referent)	1.00 (referent)
High School and Less			1.02 (0.98, 1.06)	1.08 (0.997, 1.18)	0.999 (0.96, 1.04)
Service Connected Disability Rating	…	…			
0			1.00 (referent)	1.00 (referent)	1.00 (referent)
1-29			1.21 (1.15, 1.27)	1.52 (1.36, 1.69)	1.14 (1.08, 1.21)
30-99			1.92 (1.86, 1.99)	2.68 (2.48, 2.90)	1.78 (1.72, 1.85)
100			3.01 (2.84, 3.19)	4.21 (3.57, 4.97)	2.81 (2.64, 3.00)
Psychiatric Illness (PTSD, Schizophrenia or Bipolar Disorder)	…	…	6.08 (5.88, 6.28)	5.41 (5.05, 5.81)	6.30 (6.07, 6.54)
Alcohol Abuse Disorder	…	…	2.14 (2.06, 2.22)	2.48 (2.19. 2.81)	2.11 (2.03, 2.19)
Substance Abuse Disorder	…	…	1.84 (1.76, 1.93)	1.90 (1.60, 2.26)	1.88 (1.76, 2.00)
Unspecified Back and/or Joint Disorders	…	…	1.46 (1.42, 1.50)	1.57 (1.46, 1.68)	1.44 (1.39, 1.49)
Hypertension	…	…	1.45 (1.39, 1.50)	1.35 (1.20, 1.51)	1.46 (1.41, 1.53)
* Population size differences are due to missing values for new variables added to model.					
**Age OR based on 10 year intervals					

Table 4. Significant predictors of a major depression diagnosis by gender					
	Women	OR		Men	OR
1	'Other' psychiatric illnesses	5.41	1	'Other' psychiatric illnesses	6.30
2	100% Service connected disability rating	4.97	2	100% Service connected disability rating	2.81
3	30-99% Service connected disability rating	2.90	3	Alcohol abuse disorder	2.11
4	Alcohol abuse disorder	2.48	4	Substance Abuse disorder	1.88
5	Substance Abuse disorder	1.90	5	30-99% Service connected disability rating	1.78
6	1-29% service connected disability rating	1.52	6	Hypertension	1.46
7	Unspecified Back/Joint Disorder	1.51	7	Unspecified Back/Joint Disorder	1.44
8	Hypertension	1.35	8	Other' race/ethnicity	1.14
9	Hispanic ethnicity	1.26		1-29% Service connected disability	1.14
			9	Older age	1.06
	Never Married	0.92		Never Married	0.94

Figure 2. Adjusted likelihood of major depression diagnosis associated with service connected disability rating by gender
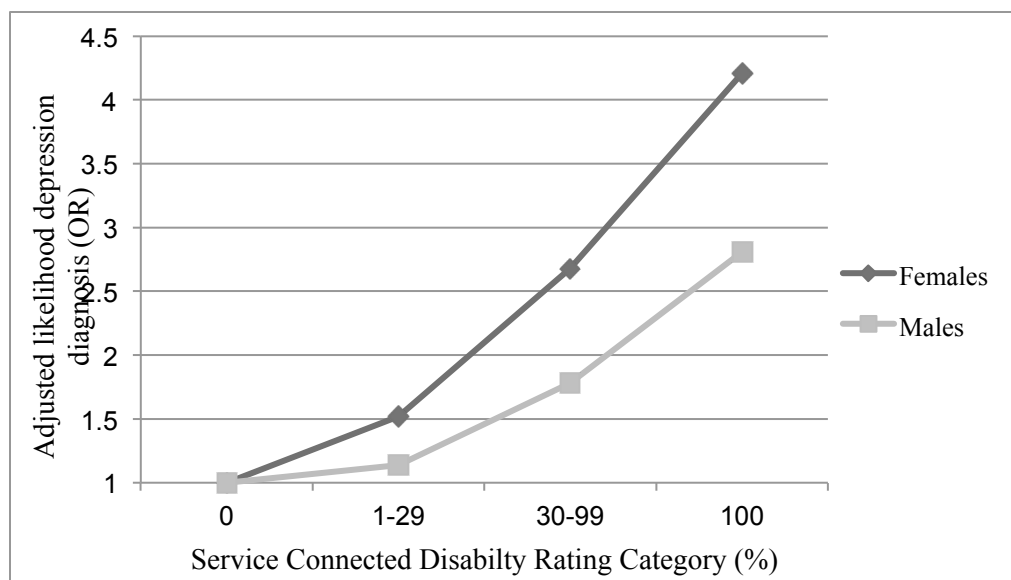
Part II.

The Women Veterans Cohort Study (WVCS) survey data revealed that depressive symptoms (as assessed in the PHQ-9) were prevalent in both men in women OEF/OIF/OND Veterans. The most prevalent symptom in both men and women was fatigue (women 75.5% vs. men 68.9%). Women were more likely to have changes in appetite (women 56.9% vs 48.8%, p=0.04) change while men were more likely to have suicidal ideation (women 11% vs. men 17% p= 0.03).

Table 5. PHQ-9 Symptoms by Gender based on WVCS survey			
	% Women (n=355)	**% Men (n=289)**	**P value**
1. Anhedonia	51.0%	54.3%	0.40
2. Depressed mood	56.1%	54.3%	0.66
3. Sleep change	71.5%	64.7%	0.06
4. Fatigue	75.5%	68.9%	0.06
5. Appetite change*	**56.9%**	**48.8%**	**0.04**
6. Low self-esteem	43.4%	43.6%	0.96
7. Concentration difficulty	45.4%	48.1%	0.49
8. Psychomotor change	25.6%	29.1%	0.33
9. Suicidality*	**11.0%**	**17.0%**	**0.03**
Women Veterans Cohort Study(WVCS); Patient Health Questionnaire 9 (PHQ-9); * = chi square p value < 0.05 An answer of 'Several days', 'More than half the days', or 'Nearly every day' on the PHQ-9 indicates a positive response			

DISCUSSION

We sought to characterize major depression in OEF/OIF/OND Veterans with particular attention to potential gender differences. We examined the associations between a major depression diagnosis and selected demographic and clinical characteristics in women and men OEF/OIF/OND Veterans expecting a significant difference in associations between demographics, clinical morbidity and a major depression diagnosis. Clinically, our significant findings were: i) Both men and women with comorbid illness (especially other psychiatric illness) and service connected disability had the strongest likelihood of a depression diagnosis ii) Service connected disability had a stronger association with a depression diagnosis in women. Demographically we found that: iii) Never being married was protective in both men and women iv) Hispanic ethnicity was associated with depression in women v) In men, older age and "other" race/ethnicity were associated with depression. We also assessed the prevalence of each of the DSM-V based depressive symptoms by gender using a PHQ-9 survey expecting that women would be more likely to exhibit the somatic symptoms of depression and found that i) most depressive symptoms were present in the majority of those studied and fatigue was mot prevalent ii) women were more likely to endorse changes in appetite and iii) men were more likely to endorse suicidal ideation. These findings add to the literature by shedding light on the characteristics of OEF/OIF/OND Veterans with depression, with particular attention to the understudied minority of women Veterans.

First, our finding that women Veterans were 1.76 times more likely to have a major depression diagnosis than men mirrors previous findings in OEF/OIF/OND

Veterans and in the general population. In the general population women are 70% more likely to experience major depression in their lifetime (19,22,72). These differences may be explained by various differences in biological, hormonal, and psychosocial factors as well as the mental health diagnosis internalizing-externalizing theory (61,62,89). After controlling for other factors the odds ratio rose to 2.57 (2.47, 2.66) for women Veterans suggesting that differences in education, age, marital status, education level and medical illnesses do not account for the higher depression prevalence in women.

Differences in characteristics of women and men OEF/OIF/OND Veterans

The overall profiles of OEF/OIF/OND women and men in this study were significantly different demographically and clinically. The fact that women more racially/ethnically diverse, slightly younger, more single, and more educated mirrored results of previous studies of this population (16,18,19). In terms of disease prevalence, we found a higher prevalence of bipolar disorder in women and lower prevalence of alcohol use disorder, substance use disorder, PTSD, and hypertension. Similar findings in the Women's Health Evaluation Initiative's (WHEI) profile of all women Veterans suggest that women in this cohort are similar to previous groups of women with regard to these medical conditions (16).

Demographic correlates of major depression in women and men OEF/OIF/OND Veterans

Older age as a predictor of depression in men Veterans was a new finding. Our result (OR=1.06 (1.04, 1.09) for each 10 year interval) is different from what is normally

seen in the civilian population, that increasing age is inversely associated with depression rates (36). One caveat for this finding is that the Veteran population is young so older Veterans are still relatively young. Comparing age as a categorical variable could better clarify this finding. However, it is possible that because older men Veterans have more combat exposure and multiple deployments than women Veterans and younger men Veterans, there is a compounded effect of re-traumatization (19). Multiple deployments have been shown to increase PTSD likelihood by three times and it may have a similar effect on depression risk (90). Although, older women Veterans may have had multiple exposures they have had less combat exposure (19).

Also, single marital status as a protective factor of depression in women in this cohort has not been demonstrated before. Maguen et al., found it to be protective of men Veterans but not for women Veterans (19). Although single marital status may be indicative or a lower social support, it also eliminates marriage related economic and relationship stressors. Marital stress is thought to be associated with a higher incidence of major depression by compromising emotion-responding processes (91).

Distinctively, we found a higher prevalence of major depression among Black and Hispanic women Veterans in descriptive analyses. Our understanding of the impact of race/ethnicity on depression is- complicated by access to healthcare and stigma disparities. After adjustment for gender, age, education, marital status, service connected disability, and disease comorbidities in the multivariable logistic regression, there was no significant association between Black race and major depression (Table 3, columns 2,3). Previous studies assessing the association between Black race and depression among women in the general population have also reported a decreased prevalence, but these

studies can be complicated by disparities in access to healthcare (44,92). In the general

population, Black individuals of lower SES had greater exposure to psychological

stressors than White individuals of similar SES levels but also exhibited more protective

characteristics such as strong community support (45,92). These observed interaction

between socioeconomic status and race in predicting psychological stressors may be

attributable to racial discrimination. It is also possible that cultural differences in

emotional responses to distress and clinician biases in assessing stressors may play a role.

A curious finding in our study was that Black race was initially protective

(OR=0.94 (0.90, 0.97) in the full model of all Veterans but was not after stratification by

gender. Although not statistically significant, Black race increased the likelihood of a

depression diagnosis in women (OR=1.03 (0.95, 1.11)), but was still protective in men

(OR=0.96 (0.92, 1.02). The possibility that Black race is a protective factor in men and

not in women is supported by the fact that race/ethnicity served as an interaction and

effect modifier in the general logistic regression model. In the National Black Women's

Health Project survey, 31.9% of respondents screened positive for depression based on

the CES-D assessment (93). Confounding factors such as socioeconomic status and

gender specific societal stressors may play a role in this group. Although our study

accounted for education level and access to care by excluding those who had not utilized

VA services, income level was not taken into account and likely also plays a significant

role (93).

Hispanic ethnicity remained significantly associated with a depression diagnosis

in women but not men. Our results align with studies in the general population that

suggest that Latina women are more likely to experience depression than both White and

Black women, citing risk factors such as acculturation, poverty, stress, poor health, unemployment, discrimination, and familial obligations (94,95).

The relationship between "Other race" and a major depression diagnosis in men was also an interesting finding. "Other race" as a classification comprised all men with disclosed race who did not identify as White, Black, or Hispanic; this included Asian/Pacific Islander, Native American, and multiracial individuals. Based on population data from the National Latino and Asian American Survey (NLAAS), depression rates are similar to the national average for Asian Americans, the most prevalent subgroup in this category (96). However, US born Asian Americans have been shown to report a high prevalence of depression and issues of stigma and self-silencing also impact mental health care seeking and diagnosis (96). Further examination of the ties between major depression and the individuals represented in these racial/ethnic subgroups of men Veterans is needed.

Clinical correlates of major depression in women and men OEF/OIF/OND Veterans

Depression and its link to other medical illnesses has been previously established (11,48). As expected, all medical conditions we studied were positively associated with a major depression diagnosis. Our findings revealed that the majority of all women (59.2%) and men (72.2%) Veterans with a major depression diagnosis also had a PTSD diagnosis and an even greater majority of women with a depression diagnosis also had unspecified back or joint disorders (significant for chronic pain and physical disability), reflecting the medical complexity of this population. The high prevalence of PTSD among those with

depression in our study of VA utilizers may partially be a reflection of the fact that people with both conditions are more likely to seek care.

A strong association between major depression and 'other' psychiatric illnesses (PTSD, "bipolar disorder", and/or schizophrenia) was sustained within our adjusted model among women and men (97). Because these disorders were combined due to multiple significant interactions, conclusions cannot be drawn about individual disease associations, particularly schizophrenia (very small prevalence). Another limitation of this variable is that a diagnosis of both major depression and bipolar disorder are clinically incompatible and likely represent an initial misdiagnosis of major depression and a diagnosis of bipolar disorder on a later date. 10.5 % of women with a depression diagnosis and 10.1% of men with a depression diagnosis had bipolar disorder, and should have been reclassified in the study. However, because the vast majority of those with "other psychiatric illness" actually had PTSD it is likely that results for that variable are attributable to that association. Co-morbid PTSD and major depression has been shown to result in an increased illness burden and poorer prognosis (48). Also, anxiety disorders could not be included within the study even though they're prevalent amongst women and men in this cohort. Despite this, the large effect size demonstrates a strong association between depression and other mental illnesses and is likely largely associated with PTSD.

Also, there is evidence that female Veterans have a higher prevalence of chronic pain than men (81). Previous studies also suggest that women may process pain differently (11,89,98). When chronic pain is linked with a trauma history, there is a significant risk for the development of major depression and PTSD (97,99,100). Our

findings support the notion that innovative interventions simultaneously addressing the triad of chronic pain, PTSD, and depression in women may be worth exploring (81,97,101-103). We also found that alcohol and substance abuse disorders as well as hypertension were associated with a greater odds of a major depression diagnosis, consistent with previous studies (11,19,48,104).

Service connected disability was also associated with depression. Although it can be argued that a diagnosis of major depression itself may directly increase service related disability ratings, our findings nevertheless confirm that the most disabled Veterans have the highest burden of depression. Also, the incremental trend displayed in Figure 2 revealed a steeper increase in the likelihood of major depression as service connected disability increased, suggesting that this link between overall disability and depression may be more significant among women Veterans. The successful treatment of major depression has been shown to improve overall health outcomes in patients with comorbid disease and the treatment of comorbid diseases has also been shown to improve major depression outcomes (11,48).

Gender differences in PHQ-9symptoms among OEF/OIF/OND Veterans

Our findings revealed that there was a high prevalence of depressive symptoms in the Veteran population. Fatigue—the most common PHQ-9 symptom endorsed in the WVCS survey by both men (68.9%) and women (75.5%)—appears to be more prevalent than in the general population. A national cross sectional survey of the U.S. workforce found the two week period prevalence of fatigue to be 37.9% (105) .

The discovery that women Veterans were more likely to endorse appetite change

is novel but consistent with the belief the women are more likely to exhibit the somatic symptoms of depression while men with depression are more likely to exhibit mood related symptoms (66-68). Kockler et al. found that elderly women with depression were more likely to exhibit appetite change while elderly men displayed more agitation (104). In addition, previous studies in this cohort have suggested that women Veterans are more likely than man and civilian women to be overweight or obese (72). More than half of women Veterans studied reported appetite changes and it is likely that a sizable portion of those reports are of hyperphagia (69,70); further investigating the ramifications and source of appetite changes in these Veterans may be useful in addressing obesity and its sequelae (69,70,106).

In our study, men were more likely to endorse suicidal ideation, which was especially notable because it has long been established in several cultures that women have a higher prevalence of suicidal ideation and suicide attempts, although men are more likely to complete suicide (107,108) Among Veterans, previous studies have suggested similar findings with regards to nonfatal suicide attempts and completed suicide completion rates; Depressed men Veterans were three times as likely to commit suicide than depressed women Veterans (56,109). Our finding suggests that there is greater prevalence of suicidal ideation in men Veterans than previously thought. It may be because men are less likely than women to report suicidal ideation during regular primary care screenings than in an anonymous survey (56).

These findings are also consistent with the gender based internalizing (women) externalizing (men) theory of depression and are particularly relevant to depression screening and symptom alleviation (89). An important caveat is that the symptoms

assessed in the PHQ-9 are rather nonspecific and our assessment was not limited to those with a known depression. Sleep disorders, medication use, as well as various medical conditions may contribute to these symptoms. Future work with the WVCS survey will couple results with the VA clinical data to assess the distribution of these symptoms specifically among those with a depression diagnosis.

Limitations

The results of our study should be interpreted in light of its methodology limitations. Assessing disease prevalence using ICD-9-CM codes may underestimate the true population with disease; those who are diagnosed may be different from those are not. In addition, a psychiatric diagnosis increases ones likelihood of receiving another by virtue of increased mental health care utilization. Also, because the study was cross sectional in nature, definite chronological associations between most variables of interest and major depression cannot be made and unidirectional association cannot be established (11). In addition, the WVCS Survey relied on responses to a mailed invitation, therefore there may be selection bias present (those with higher disease burdens or those that utilize VA healthcare more frequently may be more likely to respond). However, there is no reason to believe that this bias would modify any gender differences.

Conclusions

In summary, the study contributed to the knowledge of demographic and clinical characteristics associated with a major depression diagnosis in women and men OEF/OIF/OND Veterans. Perhaps particular attention to the psychosocial determinants of

depression by primary care providers and mental health services for Hispanic women, Black women, Older men, "Other" race/ethnicity men, and married Veterans during evaluation and treatment is needed. Continued emphasis on integrated primary and behavioral health care is necessary to address comorbid issues. Also, women Veterans would benefit from further research exploring the causal relationship in the strong correlation between service connected disability ratings and a depression diagnoses. In addition, clinicians should pay particular attention to the high burden of somatic depressive symptoms during screening and management of both women and men Veterans. Furthermore, additional focus on improved strategies to elicit existing suicidal ideation from Veteran men in the primary care setting is needed.

These data support the need for further research disentangling the intersection of gender and depression in this medically and psychosocially complex cohort of Veterans. Historically, the bulk of Veteran depression research has been done predominantly in men and our results provide evidence that stratifying by gender is imperative in order to better understand the factors at play (110). As the women Veteran population continues to grow, increasing our understanding of major depression, its risk factors, its symptoms, and its comorbidities is crucial to improving overall health outcomes for those with depression seeking VA health care.

Appendix. Women Veterans Cohort Study (WVCS) Baseline Survey PHQ-9 Depression Screening

Over the last 2 weeks how often have you been bothered by any of the following problems?

Little interest or pleasure in doing things.	[ ] Not at all [ ] Several days [ ] More than half the days [ ] Nearly everyday
Feeling down, depressed, or hopeless.	[ ] Not at all [ ] Several days [ ] More than half the days [ ] Nearly everyday
Trouble falling/staying asleep, sleeping too much	[ ] Not at all [ ] Several days [ ] More than half the days [ ] Nearly everyday
Feeling tired or having little energy	[ ] Not at all [ ] Several days [ ] More than half the days [ ] Nearly everyday
Poor appetite or overeating	[ ] Not at all [ ] Several days [ ] More than half the days [ ] Nearly everyday
Feeling bad about yourself or that you are a failure or have let yourself or your family down.	[ ] Not at all [ ] Several days [ ] More than half the days [ ] Nearly everyday
Trouble concentrating on things, such as reading the newspaper or watching television.	[ ] Not at all [ ] Several days [ ] More than half the days [ ] Nearly everyday
Moving or speaking so slowly that other people could have noticed. Or the opposite-being so fidgety or restless that you have been moving around a lot more than usual.	[ ] Not at all [ ] Several days [ ] More than half the days [ ] Nearly everyday
Thoughts that you would be better off dead or hurting yourself in some way.	[ ] Not at all [ ] Several days [ ] More than half the days [ ] Nearly everyday

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