RUNNING HEAD: gender differences in musculoskeletal disorders

Gender differences in demographic and clinical correlates among veterans with musculoskeletal disorders

Diana M. Higgins, Brenda T. Fenton, Mary A. Driscoll, Alicia A. Heapy, Robert D. Kerns, Matthew J. Bair, Constance Carroll, Penny L. Brennan, Diana J. Burgess, John D. Piette, Sally G. Haskell, Cynthia A. Brandt, Joseph L. Goulet

This is the author's manuscript of the article published in final edited form as:

Higgins, D. M., Fenton, B. T., Driscoll, M. A., Heapy, A. A., Kerns, R. D., Bair, M. J., ... & Haskell, S. G. (2017). Gender Differences in Demographic and Clinical Correlates among Veterans with Musculoskeletal Disorders. Women's health issues, 27(4), 463-470. https://doi.org/10.1016/j.whi.2017.01.008

Abstract

Background: Studies suggest that women may be at greater risk for developing chronic pain and pain-related disability. **Methods:** Because musculoskeletal disorders (MSD) are the most frequently endorsed painful conditions among veterans, we sought to characterize gender differences in sociodemographic and clinical correlates among veterans upon entry into VHA's Musculoskeletal Disorders Cohort (N=4,128,008). **Results:** Women were more likely to be younger, Black, unmarried, and veterans of recent conflicts. In analyses adjusted for gender differences in sociodemographics, women were more likely to have diagnoses of fibromyalgia, temporomandibular disorders, and neck pain. Almost one in five women (19.4%) had more than one MSD diagnosis, compared to 15.7% of men; this higher risk of MSD multimorbidity remained in adjusted analyses. Adjusting for sociodemographics, women with MSD were more likely to have migraine headache and depressive, anxiety, and bipolar disorders. Women had *lower* odds of cardiovascular diseases, substance use disorders, and several MSDs, including back pain conditions. Men were more likely to report "no pain" on the pain intensity numeric rating scale (NRS), whereas more women (41%) than men (34%) reported moderate to severe pain (NRS 4+). **Conclusion:** Because women veterans are more likely to have conditions such as fibromyalgia and mental health conditions, along with greater pain intensity in the setting of MSD, women-specific pain services may be needed.

Introduction

The number of Veterans accessing Veterans Health Administration (VHA) care increased from 6.8 million in 2002 to 8.9 million in 2013 (U.S. Department of Veterans Affairs, 2016). While the veteran population is projected to decrease substantially by 2043, the proportion of women veterans is projected to increase (National Center for Veterans Analysis and Statistics, 2014). Understanding the unique healthcare needs of women veterans is a priority for VHA.

A recent report on pain and pain management from the Institute of Medicine (IOM) identified both women and veterans as vulnerable groups (Institute of Medicine of the National Academies, 2011). A review of non-veteran samples suggests that women have a higher prevalence of musculoskeletal pain, neuropathic pain, and fibromyalgia than men (Fillingim, King, Ribeiro-Dasila, Rahim-Williams, & Riley, 2009). Similarly, rates of chronic pain are higher among women veterans relative to men (Haskell et al., 2012; Higgins et al., 2014), with prevalence rates as high as 78% (Haskell, Heapy, Reid, Papas, & Kerns, 2006). Among veterans reporting pain, women were more likely than men to have moderate/severe pain (Haskell et al., 2009). Among returning Operations Enduring Freedom/Iraqi Freedom/New Dawn (OEF/OIF/OND) veterans, musculoskeletal disorders (MSD), often associated with pain, are among the most frequently reported conditions, with prevalence especially high among women (Haskell et al., 2011). An examination of veterans with moderate or severe chronic pain receiving VHA care in the Pacific Northwest revealed several gender differences (Weimer et al., 2013). Specifically, women were more likely to have painful conditions including fibromyalgia, low back pain, migraine headache, neck or joint problems, and rheumatism/arthritis. Women veterans with chronic pain also had higher body mass index and more mental health diagnoses, but fewer substance use disorders, than men (Weimer et al., 2013).

There are several gaps in the literature characterizing gender differences in pain-relevant disorders. Only two previous studies have specifically examined gender differences in the prevalence of painful disorders (Weimer et al., 2013; Haskell, et al, 2012); the first included regional, not national

data, while the second focused on OEF/OIF/OND veterans. Few studies examine MSD specifically in the larger veteran population. Additionally, little is known about presence of pain at MSD diagnosis and comorbidities of these conditions among veterans. Most studies focus on pain severity, not MSD, and have been limited to samples of OEF/OIF/OND veterans (Haskell et al., 2009; 2012). This limitation is particularly significant because these veterans are, on average, younger and more racially and ethnically diverse than previous veteran cohorts. It is important to examine gender differences in pain intensity, MSD and comorbidities, given the high volume of veterans seeking health care each year for MSD and pain, and the increasing number of women seeking VHA care (Goulet et al., 2016).

The purpose of the current investigation is to characterize gender differences in relative proportion of specific pain-relevant diagnoses and sociodemographic characteristics, along with medical and mental health comorbidities at MSD diagnosis among veterans receiving VHA care.

Methods

Study population

Electronic searches for *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9CM) codes consistent with musculoskeletal disorders (MSD) were conducted to define the cohort (Goulet et al., 2016).).

Defining MSD: A total of 1,685 distinct ICD-9CM codes were identified and consolidated into 14 MSD groupings encompassing conditions of the back and neck, osteoarthritis, fractures, and inflammatory and degenerative disorders (Goulet et al., 2016). We searched VHA electronic clinical and administrative data for all outpatient and inpatient records with an MSD diagnosis noted between January 1, 2000 and December 31, 2013. For cohort inclusion, a veteran had to have two or more outpatient visits with an MSD diagnosis occurring within 18 months of one another, or one or more inpatient admissions with an MSD diagnosis (Justice et al., 2006). There were no other inclusion or

exclusion criteria. The index date for entry into the cohort was defined as the date of the first observed outpatient clinic visit or inpatient admission with an MSD diagnosis. The second ICD-9CM code served to validate the first MSD diagnosis. It was possible for a veteran to meet criteria for more than one MSD diagnosis on the index date. Because a confirmatory outpatient visit within 18 months of the MSD index date was required, data included only those veterans identified with an MSD between 2000 and 2011. See Goulet and colleagues (2016) for a detailed description of the MSD Cohort. The cohort was designed to be inclusive, therefore, we did not exempt patients whose MSD diagnoses changed between entry into the cohort and follow-up, as we have found that it generally does not change. For example, the diagnosis at time one was the same at time two in 95% of "osteoarthritis" diagnoses.

Variables

Sociodemographics: Sociodemographic characteristics of MSD Cohort members at the index date including age, gender, race/ethnicity, marital status, and OEF/OIF/OND status were examined.

Painful Conditions (MSD): We examined the most common diagnostic groups of MSD, including osteoarthritis, non-traumatic joint disorders (e.g., arthropathies, ankylosis), back pain, neck pain, osteoporosis, sprain and strain, fibromyalgia, fracture, traumatic joint disorder, rheumatoid arthritis, temporomandibular disorders (TMD), lupus, gout, spinal cord injury, "other" (all MSD which did not fit into the 14 specific diagnostic groupings), and MSD multimorbidity (more than one MSD diagnosed at cohort entry).

Medical and Mental Health Characteristics: High-prevalence, high-impact (Kazis et al., 1998; Yu et al., 2003) medical and mental health comorbid diagnoses were identified using the same criteria as MSD diagnoses (i.e., two or more outpatient codes within 18 months, or one or more inpatient code). However, only comorbid conditions noted in the year prior to and up to six months after the MSD

index date were retained for the analysis, as they were likely to be active at MSD diagnosis (concurrent comorbidity).

Cardiovascular comorbidities and cardiac risk factors (i.e., congestive heart failure, coronary artery disease [CAD], hypertension [HTN], hemorrhagic stroke, ischemic stroke, peripheral vascular disease), smoking status (i.e., categorized as never, past, current) and overweight/obesity as determined by body mass index (BMI), were examined as medical comorbidities because of their high prevalence among veterans (Kazis et al., 1998; Yu et al., 2003). BMI was calculated from the height and weight data on or closest to the MSD index date within the year prior to or up to six months after. BMI classifications (kg/m^2) used for analyses in this study were based on standard cutoffs as follows: underweight (BMI less than 18.5), normal weight (BMI 18.5-24.9), overweight (BMI 25 to 29.9), obesity (BMI 30+) (National Heart, Lung, and Blood Institute, 1998). Migraine was also included because prior studies have identified gender differences in this disorder (Fillingim et al., 2009; Weimer et al., 2013). Literature examining gender differences in medical comorbidities associated with painful conditions is limited but lends support for the comorbidities included in the current study. For example, Weimer and colleagues (Weimer et al., 2013) adjusted for Charlson comorbidity score, but did not specify medical conditions that were more prevalent among women veterans with painful conditions. Mental health conditions examined included depressive disorders (i.e., major depressive disorder, dysthymia, depression due to other causes or not otherwise specified), bipolar disorder, anxiety disorders (i.e., anxiety state not otherwise specified [NOS]/not elsewhere classified [NEC], panic disorder, generalized anxiety disorder, nervousness), PTSD, alcohol use disorders, and drug use disorders.

Pain Intensity Ratings: The Numeric Rating Scale (NRS) is used in routine clinical care to screen for the presence and intensity of pain at most clinical encounters when other vital signs are obtained (Veterans Health Administration, 2000). Patients are asked, “On a scale of 0 to 10, where 0 means no

pain and 10 means the worst possible pain, what is your current pain level?" NRS pain scores were identified on the MSD index day. When multiple NRS were recorded on the index date, we retained only the highest. An invalid NRS (i.e., a score that was not an integer value 0-10) was considered missing. NRS was invalid or missing in 19.7% of cases for women and 19.4% of cases for men. The NRS was categorized using standard cutoffs: 0=no pain, 1 to 3=mild pain, 4 to 6=moderate pain, and 7 or greater=severe pain (Tan, Jensen, Thornby, Rintala, & Anderson, 2008).

The study was approved by the Institutional Review Board at VA Connecticut Healthcare System--West Haven, CT.

Statistical analysis

Chi-square tests were used to examine unadjusted relationships between categorical covariates and gender and odds ratios presented. To adjust for confounding due to sociodemographic differences between women and men, we used logistic regression to calculate adjusted odds ratios (AOR) and 95% confidence intervals (CI) to assess the association of gender with MSD group as well as comorbidities among veterans with MSD. SAS (SAS 9.4, Cary, NC) was used for all analyses. In Tables 2-4, the variables controlled in the adjusted analyses were age, race/ethnicity, marital status, and OEF/OIF/OND status. Given the large sample, meaningful differences, consistent with criteria used by Goulet et al. (2016), required a 2% absolute difference or 2-fold difference in odds ratios.

Another factor considered in the present study is the relative impacts of unadjusted compared with adjusted analyses results. Unadjusted analyses describe the particular VHA population (i.e., all veterans in VHA care with MSD), such that observed differences may reflect gender differences in sociodemographics and comorbidities. The presentation of unadjusted results is important from a VHA policy and planning perspective. The adjusted analyses results are more generalizable with respect to understanding gender differences in MSDs among patients receiving care outside of the

VHA system (veterans and non-veterans). Adjusted analyses help to account for confounding variables that might obscure or distort the relationship between gender and disease prevalence. Because women veterans are more likely to be non-white and younger than men, with unadjusted analyses, we might risk attributing findings to gender when the results might instead be a function of younger age and non-white race.

Results

Sociodemographic characteristics: The sample consisted of 253,383 women (6.1%) and 3,874,625 men veterans (N=4,128,008). Women were younger, and more likely unmarried, Black, and an OEF/OIF/OND era veteran (Table 1; all significant at p<.0001).

******Insert Table 1 about here*******

Gender-differences in specific MSDs: Specific MSDs in women and men were examined at cohort entry. These disorder categories are not mutually exclusive. All differences in Table 2 reached significance at p<.0001, except rheumatoid arthritis (p=.056). Gender differences in 9 of 16 (56%) diagnostic groupings reached the threshold of a 2% absolute difference between women and men. Differences in non-traumatic joint disorders (women>men), back pain (women>men), and osteoarthritis (men>women), among others, were found to be clinically important. Almost one in five women (19.4%) had >1 MSD diagnosis upon cohort entry, while 15.7% of men did.

When age, race/ethnicity, marital status, and OEF/OIF/OND status were controlled for in adjusted analyses, all differences between women and men were significant except non-traumatic joint disorder. However, the direction of some associations changed. Specifically, women had significantly lower rates of osteoarthritis, back pain, sprain/strain, traumatic joint disorder, and gout than men.

******Insert Table 2 about here*******

Medical and mental health comorbidities among veterans with MSD: Results of unadjusted analyses are presented in Table 3. Women were less likely to have vascular disorders, overweight/obesity, and smoking, but more likely to have a migraine diagnosis. These associations remained unchanged in adjusted models. All associations were significant at $p < .0001$.

******Insert Table 3 about here*******

Results of unadjusted and adjusted analyses of gender differences in the prevalence of mental health comorbidities are presented in Table 4. All unadjusted and adjusted odds ratios were significant at $p<.0001$. Unadjusted ORs show women were significantly more likely to have bipolar disorder, depressive disorder, anxiety disorder, and PTSD. Men were more likely to have alcohol use and drug use disorders. Patterns remained after adjustment for sociodemographic variables, except PTSD. After adjustment, men were more likely to have PTSD concurrent with their MSD diagnosis. Clinically-meaningful gender differences (i.e., an absolute difference across genders of 2%) were observed in alcohol use disorder, bipolar disorder, and depressive and anxiety disorders.

******Insert Table 4 about here*******

Pain intensity: On MSD cohort entry, both men and women had a wide range of pain intensity ratings, with more men reporting no pain (34% for men vs. 28% for women). More women (41%) than men (34%) reported moderate or severe pain (pain intensity NRS 4+), often suggested as a clinically-actionable rating. Figure 1 demonstrates the frequencies of women and men reporting no pain, mild, moderate, and severe pain ($p<.0001$).

******Insert Figure 1 about here*******

Discussion

Our study highlights gender differences in veterans with MSD. Notably, women veterans with MSD are younger, more likely to be black, unmarried, and OEF/OIF/OND-era veterans. Consistent with prior research, women veterans with MSD were more likely than men to report moderate and severe pain, while men were more likely to report no pain (e.g., Haskell et al., 2009; 2012; Higgins et al., 2014). Adjusted analyses, discussed below, describe gender differences in MSD and its correlates among veterans in VHA care that are likely to be generalizable beyond those veterans receiving VHA care.

One study of the prevalence of MSD among post-deployment OEF/OIF/OND veterans (Haskell et al., 2012) demonstrated that, after controlling for sociodemographic characteristics, women were more likely to have back conditions and joint disorders than men. In contrast, adjusted analyses in the current study show that women veterans were *less likely* to have diagnoses of back conditions, sprain/strain, and traumatic joint disorder and there was no significant gender difference in non-traumatic joint disorder. This is potentially explained by the fact that women in this sample were younger and these diagnoses are often associated with older age. This discrepancy may also reflect the difference in study design, variation in time since last deployment, as well as MSD case definitions. Specifically, Haskell et al (2012) focused solely on veterans of the OEF/OIF/OND era in VHA care, regardless of presence of MSD. The current study contains a sample of all veterans receiving VHA care with one or more MSD. Veterans of different eras are likely to have encountered unique physical challenges, including different occupational roles for women in recent eras, and those of earlier conflicts (e.g., Vietnam) may be more likely to experience painful conditions affected by aging (e.g., osteoarthritis of lumbar spine). Compared with men, women with MSD in the current study were significantly more likely to have neck pain, fibromyalgia, and TMD diagnoses, consistent with prevalence rates of these conditions in both veteran (Weimer et al., 2013) and non-veteran

samples (Fillingim et al., 2009). Taken together, results of the current study reflect that women veterans with MSD appear similar in MSD prevalence of certain conditions (e.g., TMD, fibromyalgia) and pain intensity to their non-veteran counterparts. However, the finding that women veterans with MSD are less likely to have back pain conditions after controlling for sociodemographics is intriguing because it is inconsistent with a large literature. Also of note, women veterans were more likely to have MSD multimorbidity than men, suggesting women may have a higher burden of illness.

Consistent with previous studies, women with MSD were at lower risk of cardiovascular comorbidities and cardiac risk factors, including overweight/obesity and smoking, but were more likely to have depressive disorders, anxiety disorders, and bipolar disorder, even after adjusting for important sociodemographic factors. Women veterans were at significantly higher risk of migraine headaches compared to men. The PTSD finding in the unadjusted analyses was somewhat surprising, as other data suggest that men are more likely to report PTSD than women veterans (Freedy et al., 2010); however, this finding in the current study can be accounted for by sociodemographic differences (e.g., age, race/ethnicity) between men and women in the MSD Cohort.

These results suggest that women veterans with MSD are an important and unique and growing subgroup of veterans, whose particular needs should be considered with respect to clinical and policy implications. Women are more likely to be racial/ethnic minorities and may have different healthcare (U.S. Department of Veterans Affairs, 2016) and psychosocial experiences as a result. They are also younger and have fewer cardiovascular and cardiac risk factors but, in the current study, women were more likely to report moderate and severe pain. This level of pain intensity may have a larger impact on their physical, social, and emotional functioning. Improved access to interventions that foster adaptive pain self-management (as suggested by the IOM; Institute of Medicine of the National Academies, 2011) such as cognitive behavioral therapy for chronic pain,

seems intuitive for addressing these problems in women veterans. In addition, women veterans may have other, differential healthcare needs. For example, the rates of mental health conditions are high for both men and women in the current study, but are even higher among women. A recent study examining provision of women-specific programs for substance use disorders reported that VHA had fewer of these programs than other federal, state, local, tribal, and private healthcare facilities (Heslin, Gable, & Dobalian, 2015). Greater attention to comorbid depressive and substance use disorders may be indicated for all veterans with MSD, particularly women. Sensitivity to sexual orientation should also be considered within this context. Data suggest that the subpopulation of lesbian and bisexual women veterans is more likely to have experienced military and childhood sexual trauma and are more likely to engage in unsafe alcohol consumption, and to rate their mental health as worse than prior to deployment than their heterosexual counterparts (Mattocks, et al, 2013).

This is one of the few studies that examined gender differences in pain intensity at the time of MSD diagnosis. In contrast to much of the existing literature which examines pain intensity in samples of patients with existing chronic pain (Haskell et al., 2009; Weimer et al., 2013), the current study examined pain intensity on the day of MSD diagnosis (i.e., diagnosis occurring in the context of VHA care, specifically). For example, other studies (Haskell et al., 2009) focused on pain intensity at the initial pain screening, for any condition, in the first year of VHA treatment. Because the screening did not have to be associated with a pain diagnosis, it is unclear what prompted the patients' pain reports. One additional strength of the current study is that the pain intensity NRS is assessed at the time the MSD is diagnosed, allowing an inference to be made that the pain report is directly related to the MSD(s).

One limitation of this cohort is its sole reliance on existing electronic medical record (EMR) data for defining chronic pain conditions (MSD). It is possible that veterans in VHA care have MSDs but do not have diagnoses in the EMR and were not captured in the sample. In addition, a fairly large proportion of the sample had missing pain NRS values. This may reflect that these data were entered

incorrectly into the vital signs section of the EMR, or that patients were not asked about pain intensity during their clinical visit. Our reliance on pain intensity NRS at one time point (i.e., cohort entry) limits our ability to describe the intensity of a given patient's chronic pain longitudinally. Finally, the fact that there were so many pain intensity NRS scores of 0 may reflect the intermittent nature of pain among veterans with MSD.

Implications for Practice and Policy

The current study suggests that there is evidence of gender difference in some MSDs. The gender differences in mental health comorbidity among veterans with MSD suggest that veterans, particularly women, with chronic pain may benefit from multidisciplinary treatment models such as combined treatment for pain and depression (Kroenke et al., 2009; Stubbs et al., 2010). Women veterans may also benefit from non-pharmacologic and complementary and integrated health (CIH) approaches to manage MSD and comorbid conditions. For example, one study has found that women veterans receive more benefit (e.g., decrease in average pain and depression) from yoga for low back pain than men (Groessl, Weingardt, Johnson, Baxi, 2012). VHA and other organizations have made recent strides in recommending and expanding non-pharmacologic pain management options through their policy and practice efforts, including a recent *State Of The Art Conference on Non-pharmacological Approaches to Management of Chronic Musculoskeletal Pain* (VHA Office of Research and Development Health Services Research & Development SOTA, November 2016) that will provide some practice policy and research recommendations, including a focus on CIH delivery. The Comprehensive Addiction Recovery Act (CARA; United States 114th Congress, 2015-2016) highlights provisions for building capacity for CIH and integrated pain teams. Finally, the VHA's Office of Patient Centered Care and Cultural Transformation is undertaking a major "Whole Health" patient-centered initiative focused on CIH.

Treatment delivery modes may also have to account for barriers in access to care (e.g., childcare responsibilities, work schedules) for women veterans with MSD who are younger.

Telehealth approaches, such as interactive voice response (Heapy et al., 2016) and others (e.g., internet, telephone) have been shown to be effective for delivering behavioral pain self-management (Heapy, Higgins, Wandner, Cervone, & Kerns, 2015). Video-teleconferencing equipment has been successfully used to deliver treatment for pain and depression associated with trauma in women veterans (Tan et al., 2013). These delivery modalities may address barriers to pain care among women veterans.

Pain intensity, which was higher in women with MSD in the current study, is likely to present as an additional barrier to other previously mentioned challenges – both complicating the management of those comorbidities and making it more difficult to manage patients' pain in the context of those competing priorities (Butchart, Kerr, Heisler, Piette, & Krein, 2009). Indeed, women veterans have a harder time sustaining improvements in pain intensity following engagement in an intensive inpatient pain rehabilitation program relative to men (Murphy, Phillips, & Rafie, 2016). These challenges point to the importance of comprehensive pain assessment using a biopsychosocial framework, as suggested by the IOM (Institute of Medicine of the National Academies, 2011) and VHA pain management guidelines. Further, it will be important for VHA to develop a women's healthcare workforce that is specifically trained to conduct comprehensive pain assessment and treatment that addresses the needs of women veterans with chronic pain.

Research efforts to address the pain care needs of veterans, including women, have been expanded as well. A recent publication of partnered funding opportunities between VHA, the Department of Defense, and the National Institutes of Health (NIH), including the NIH Office of Women's Health Research, focused on non-pharmacological approaches to pain management. Further, the Department of Health and Human Service's National Pain Strategy (DHHS, 2016) highlights the need to address disparities in pain care so that disparities can be identified and characterized, allowing for examination of their root cause(s) and whether or not the root cause(s) are modifiable. Intervention mapping or targeting can be used to modify (tailor) and

improve services for women Veterans with MSD. For example, a collaborative care or peer-led intervention that assesses the unique needs and treatment preferences of women veterans and tailors intervention content and delivery to reduce identified disparities may lead to improved outcomes. Such research has broad-reaching practice and policy implications.

Conclusions

The proportion of women in the military, their roles, demographics, and exposure to combat have changed dramatically during OEF/OIF/OND. VHA must anticipate and prepare not only for increasing numbers of women Veterans enrolling in care, but also for the accompanying complexity and longevity of associated treatment needs. To begin the task of developing women veteran-specific pain treatment programs, it is vital to understand the patient-level characteristics among veterans with MSD, as well as to understand pain chronicity after MSD diagnosis. These analyses suggest that services targeting women veterans with MSD may be needed, particularly those tailored to the needs of women who are younger, black, and/or have limited spousal supports or mental health comorbidities. A focus on addressing specific painful conditions most commonly reported by women veterans with MSD such as fibromyalgia, TMD, and neck pain is also warranted.

References

Butchart, A., Kerr, E. A., Heisler, M., Piette, J. D., & Krein, S, L. (2009). Experience and management of chronic pain among patients with other complex chronic conditions. *Clin J Pain 24*(4), 293-298. doi: 10.1097/AJP.0b013e31818bf574

Cherkin, D. C., Deyo, R. A., Volinn, E., & Loeser, J. D. (1992). Use of the International Classification of Diseases (ICD-9-CM) to identify hospitalizations for mechanical low back problems in administrative databases. *Spine 17*(7),817-825.

Department of Health and Human Services (2016). National Pain Strategy: A comprehensive population health-level strategy for pain. 2016. Accessed December 28, 2016 from https://iprcc.nih.gov/docs/HHSNational_Pain_Strategy.pdf.

Fillingim, R. B., King, C. D., Ribeiro-Dasilva, M. C., Rahim-Williams, B., & Riley, J. L. (2009). Sex, gender, and pain: A review of recent clinical and experimental findings. *J Pain*, *10*(5), 447–485. doi:10.1016/j.jpain.2008.12.001.

Freedy, J. R., Magruder, K. M., Mainous, A. G., Frueh, B. C., Geesey, M. E., & Carnemolla, M. (2010). Gender differences in traumatic event exposure and mental health among veteran primary care patients. Jl Gen Intern Med, 175(10), 50–758.

Goulet, J. L., Kerns, R. D., Bair, M., Becker, W. C., Brennan, P., Burgess, D., …Brandt, C. A. (2016). The musculoskeletal diagnosis cohort: Examining pain and pain care among veterans. *Pain*, *157*(8), 1696-1703. doi: 10.1097/j.pain.0000000000000567 .

Groessl, E.J., Weingart, K.R., Johnson, N., Baxi, S.(2012). P02.113. The benefits of yoga for women veterans with chronic low back pain. *The Journal of Alternative and Complementary Medicine*, 18(9): 832-838.

Haskell, S. G., Brandt, C. A., Krebs, E. E., Skanderson, M., Kerns, R. D., & Goulet, J. L. (2009).. Pain among veterans of Operations Enduring Freedom and Iraqi Freedom: Do women and men differ? Pain Med, *10*(7):1167–1173. doi: 10.1111/j.1526-4637.2009.00714.x

Haskell, S.G., Heapy, A., Reid, M.C., Papas, R. , & Kerns, R.D. (2006). The prevalence and age-related characteristics of pain in a sample of women veterans receiving primary care. *J Womens Health*, *15(*7), 864-871. doi: 10.1089/jwh.2006.15.862

Haskell, S. G., Ning, Y., Krebs, E., Goulet, J., Mattocks, K., Kerns, R., & Brandt, C. (2012). Prevalence of painful musculoskeletal conditions in female and male veterans in 7 years after return from deployment in Operation Enduring Freedom/Operation Iraqi Freedom**.** *Clin J Pain*, *28*(2), 163-167. doi: 10.1097/AJP.0b013e318223d951

Haskell, S.G., Mattocks, K., Goulet J.L., Krebs, E.E., Skanderson, M., Leslie, D., Justice, A.C., Yano, E.M., & Brandt, C. (2011). The burden of illness in the first year home: Do male and female VA users differ in health conditions and healthcare utilization? *Women's Health Issues,* 21(1), 92–97.

Heapy, A.A., Higgins, D.M., LaChappelle, K.M, et al.(2016) Cooperative pain education and self-management (COPES): study design and protocol of a randomized non-inferiority trial of an interactive voice response-based self-management intervention for chronic low back pain. *BMC Musculoskelet Disorders,* 17; 85. doi: 10.1186/s12891-016-0924-z

Heapy A.A., Higgins, D.M., Cervone, D., Wandner, L., Kerns, R.D. (2016) A systematic review of technology-assisted self-management interventions for chronic pain; *Clinical Journal of Pain,*31(6), 470-92. doi: 10.1097/AJP.0000000000000185.

Heslin, K.C., Gable, A., & Dobalian, A. (2015). Special Services for Women in Substance Use Disorders Treatment: How Does the Department of Veterans Affairs Compare with Other Providers? *Womens Health Issues, 25-6, 666-672.*

Higgins, D. M., Kerns, R.D., Brandt, C. A., Haskell, S. G., Bathulapalli, H., Gilliam, W., & Goulet, J. L. (2014). Persistent pain and comorbidity among Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn veterans, *Pain Med, 15*(5), 782-790. doi: 10.1111/pme.12388

Institute of Medicine of the National Academies. (2011). Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Washington, DC: The National Academies Press.

Justice, A. C., Dombrowski, E., Conigliaro, J., Fultz, S. L., Gibson, D., Madenwald, T., …Bryant, K. (2006). Veterans Aging Cohort Study (VACS): Overview and description. *Med Care, 44*(8 Suppl), S13-S24. doi: 10.1097/01.mlr.0000223741.02074.66

Kazis, L. E., Miller, D. R., Clark, J., Skinner, K., Lee, A., Rogers, W., …Linzer, M. (1998). Health-related quality of life in patients served by the department of Veterans Affairs. *Arch Intern Med,158*(6), 626-632. doi:10.1001/archinte.158.6.626.

Kroenke, K., Bair, M. J., Damush, T. M., Wu, J., Hoke, S., Sutherland, J. M., & Tu, W. (2009). Optimized Antidepressant Therapy and Pain Self-Management in Primary Care Patients with Musculoskeletal Pain and Depression: A Randomized Controlled Trial. *JAMA, 301*(20), 2099-2110. doi: 10.1001/jama.2009.723

Mattocks, K. M., Sadler, A., Yano, E.M., Krebs, E.E., Zephyrin, L., Brandt, C., Kimerling, R., Sandfort, T., Dichter, M. E., Weiss, J.J., Allison, J. & Haskell, S.G. (2013). Sexual Victimization, Health Status, and VA Healthcare UtilizationAmong Lesbian and Bisexual OEF/OIF Veterans. *Journal of General Internal Medicine*, 28(Suppl 2); S604–8. DOI: 10.1007/s11606-013-2357-9

Murphy, J.L., Phillips, K.M., & Rafie, S. (2016). Sex differences between Veterans participating in interdisciplinary chronic pain rehabilitation. *Journal of Rehabilitation Research and Development***,** 53(1), 83-94.

National Center for Veterans Analysis and Statistics. (2014). *Projected Veteran Population 2013 to 2043*. Accessed on September 21, 2016 from http://www.va.gov/vetdata/docs/quickfacts/Population_slideshow.pdf

National Heart, Lung, and Blood Institute. (1998). Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: Evidence Report. Bethesda, MD: National Heart, Lung, and Blood Institute. Accessed on September 21, 2016 from http://www.ncbi.nlm.nih.gov/books/NBK2003/pdf/Bookshelf_NBK2003.pdf

Stubbs, D., Krebs, E., Bair, M., Damush, T., Wu, J., Sutherland, J., & Kroenke, K. (2010). Sex differences in pain and pain-related disability among primary care patients with chronic musculoskeletal pain. *Pain Med,11*(2), 232-239. doi: 10.1111/j.1526-4637.2009.00760.x

Tan, G., Jensen, M. P., Thornby, J. I., Rintala, D. H., & Anderson, K. O. (2008). Categorizing pain in patients seen in a veterans health administration hospital: Pain as the fifth vital sign. *Psychological Services, 5*(3), 239-250. doi: 10.1037/1541-1559.5.3.239

Tan, G. Teo, I.,Srivastava, D., Smith, D., Smith, S.L., Williams, W., & Jensen, M.P. (2013). Improving access to care for women veterans suffering from chronic pain and depression associated with trauma. *Pain Medicine, 14, 1010–1020*

U.S. Department of Veterans Afffairs. (2016). *National Center for Veterans Analysis and Statistics*. Accessed on September 21, 2016 from http://www.va.gov/vetdata/Utilization.asp

United States 114th Congress, 2015-2016. Comprehensive Addiction Recovery Act (CARA). Accessed on December 28, 2016; retrieved from https://www.congress.gov/bill/114th-congress/senate-bill/524/text.

Veterans Health Administration. (2000). Pain as the 5th vital sign toolkit. Accessed on September 21, 2016 from http://www.va.gov/PAINMANAGEMENT/docs/Pain_As_the_5th_Vital_Sign_Toolkit.pdf

Veterans Health Administration Office of Research & Development and Health Services Research & Development. (November 2016) State Of The Art (SOTA) Conference on Non-pharmacological Approaches to Management of Chronic Musculoskeletal Pain; Washington DC.

Weimer, M. B., Macey, T. A., Nicolaidis, C., Dobscha, S. K., Duckart, J. P., & Morasco, B. J. (2013). Sex differences in the medical care of VA patients with chronic non-cancer pain. *Pain Med, 14*(12), 1839-1847. doi: http://dx.doi.org/10.1111/pme.12177

Yu, W., Ravelo, A., Wagner, T. H., Phibbs, C. S., Bhandari, A., Chen, S., & Barnett, P. G. (2003). Prevalence and costs of chronic conditions in the VA health care system. *Med Care Res Rev*, *60*(3 Suppl), 146S-167S doi: 10.1177/1077558703257000.

Table 1: Sociodemographics of women and men who entered into the MSD Cohort 2001-2011

	Women (N=253,383) Percent	Men (N=3,874,625) Percent
Age		
<40	38.8	12.1
40-49	26.9	12.4
50-64	22.6	38.3
65+	11.7	37.2
Race/ethnicity		
Black	25.5	14.4
Hispanic	5.4	4.8
White	59.4	74.2
Other	2.9	2.4
Unknown	6.8	4.1
Marital status		
Married	33.9	56.5
Not Married	22.1	10.6
Sep/Divorced	35.7	24.5
Widowed	7.7	8.1
Unknown	0.6	0.3
Positive OEF/OIF/OND*	14.0	7.0

* Veterans of the Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn conflicts

Figure 1. Pain intensity at entry into the cohort—Women compared to Men

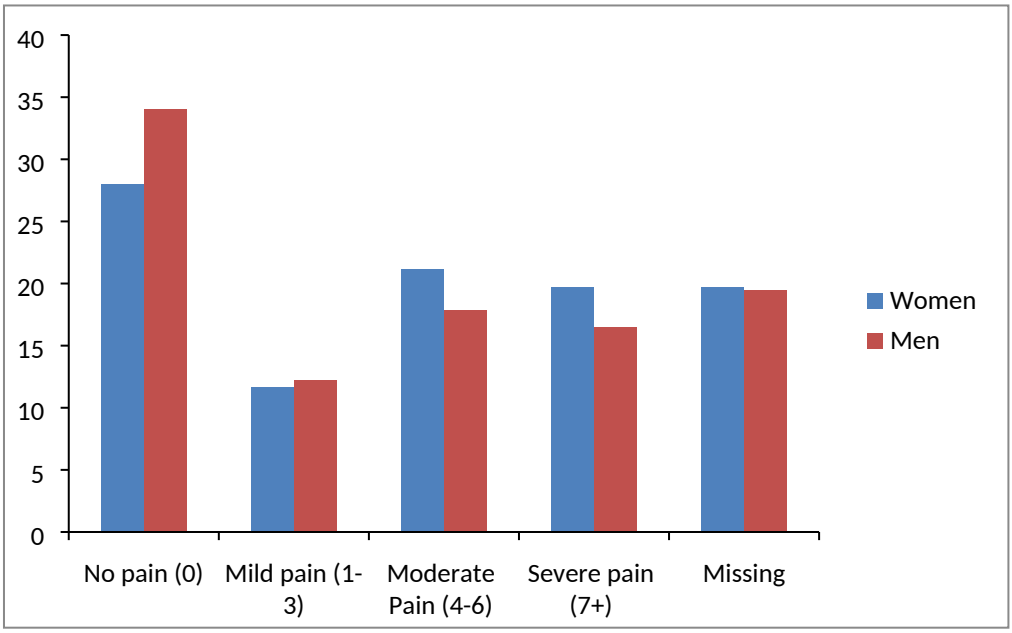

Table 2: Specific MSDs in women and men (unadjusted & adjusted ORs, women compared to men)*

	Unadjusted analyses			Adjusted analyses
	Women N=253,363 Percent	Men N=3,874,625 Percent	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Non-traumatic joint disorder§	32.5	27.9	1.24 (1.23, 1.25)	1.00 (0.99, 1.01)
Back pain §	28.3	25.8	1.14 (1.13,1.15)	0.87 (0.86, 0.88)
Osteoarthritis §	11.6	19.9	0.53 (0.52,0.53)	0.90 (0.89, 0.91)
Neck pain	7.0	5.2	1.39 (1.36, 1.41)	1.20 (1.18, 1.22)
Osteoporosis §	4.7	1.3	3.66 (3.59, 3.74)	11.02 (10.77, 11.28)
Sprain and strain	4.4	3.0	1.51 (1.48, 1.54)	0.93 (0.91, 0.95)
Fibromyalgia §	3.0	1.0	3.04 (2.96, 3.11)	2.81 (2.74, 2.89)
Fracture	2.7	3.2	0.84 (0.82, 0.86)	0.62 (0.61, 0.64)
Traumatic joint disorder	1.9	1.5	1.29 (1.26, 1.33)	0.77 (0.75, 0.79)
Rheumatoid arthritis	1.1	1.0	1.04 (1.00,1.08)	1.81 (1.74, 1.88)
Temporomandibular disorders §	1.1	0.3	4.48 (4.30, 4.68)	2.96 (2.83, 3.10)
Lupus §	0.7	0.2	4.77 (4.53, 5.02)	5.46 (5.16, 5.79)
Gout §	0.4	5.4	0.07 (0.07, 0.08)	0.13 (0.12, 0.14)
Spinal Cord injury	0.1	0.2	0.34 (0.29, 0.40)	0.26 (0.22, 0.31)
Other	23.4	22.1	1.08 (1.07,1.09)	1.18 (1.17, 1.20)
MSD multimorbidity §	19.4	15.7	1.29 (1.28, 1.31)	1.14 (1.13, 1.15)

*p<0.001
**P<0.056
§ indicates a clinically meaningful difference (i.e., absolute difference of 2%)

Table 3: Comorbid cardiovascular & other conditions (unadjusted & adjusted ORs, women compared to men)*

	Unadjusted analyses			Adjusted analyses
	Women	Men	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Congestive heart failure §	1.0	3.7	0.25 (0.24, 0.26)	0.51 (0.49, 0.53)
Coronary artery disease §	2.9	16.7	0.15 (0.15, 0.15)	0.34 (0.33, 0.35)
Hypertension§	25.3	50.3	0.33 (0.33, 0.33)	0.65 (0.64, 0.66)
Hemorrhagic stroke	0.1	0.2	0.55 (0.49, 0.61)	0.71 (0.63, 0.80)
Ischemic stroke	0.1	0.5	0.28 (0.25, 0.31)	0.47 (0.43, 0.53)
Peripheral vascular disease§	0.8	4.4	0.18 (0.17, 0.19)	0.38 (0.36, 0.39)
Migraine	8.3	1.1	7.86 (7.73, 7.99)	4.57 (4.49, 4.66)
Smoking [1§]				
Never	51.8	33.1	-	-
Past	32.8	36.7	0.57 (0.56, 0.58)	0.40 (0.40, 0.40)
Current	15.4	30.2	0.32 (0.32, 0.33)	0.49 (0.49, 0.50)
BMI[2]				
Underweight	1.5	1.1	1.03 (0.99, 1.06)	1.21 (1.17, 1.26)
Normal	29.4	21.3	1.00	1.0
Overweight §	32.4	39.3	0.60 (0.59, 0.60)	0.61 (0.61, 0.62)
Obese	36.6	38.4	0.70 (0.68, 0.70)	0.62 (0.61, 0.63

[1] This table includes 3,790,474 persons as 337,514 persons were missing smoking status.
[2] This table includes 3,959,919 persons as 168,069 persons were missing height or weight in the period of entry into the cohort.
* p<0.001
§ indicates a clinically meaningful difference (i.e., absolute difference of 2%)

Table 4: Comorbid mental health conditions in MSD (unadjusted & adjusted ORs, women compared to men)*

	Unadjusted analysis			Adjusted analysis
	Women Percent	Men Percent	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Alcohol use disorder§	3.9	7.7	0.48 (0.47, 0.49)	0.31 (0.30, 0.31)
Bipolar disorder§	5.2	2.4	2.29 (2.25, 2.33)	1.47 (1.44, 1.50)
Drug use disorder	2.5	3.7	0.68 (0.67, 0.70)	0.32 (0.32, 0.33)
Depressive disorder§	27.1	15.5	2.02 (2.00, 2.04)	1.62 (1.61, 1.63)
PTSD	10.0	8.2	1.23 (1.22, 1.25)	0.94 (0.92, 0.95)
Anxiety§	10.7	6.1	1.86 (1.83, 1.88)	1.45 (1.43, 1.47)

*$p<0.001$
§indicates a clinically meaningful difference (i.e., absolute difference of 2%)

Diana M. Higgins, PhD is a Clinical Research Psychologist at VA Boston Healthcare System and an Assistant Professor of Psychiatry at Boston University School of Medicine with more than 10 years of experience in clinical care, research, and policy focused on pain management. Her areas of expertise include development of cognitive-behavioral interventions for chronic pain, use of technology to improve access to pain care, and comorbid overweight/obesity and chronic pain.

Brenda T. Fenton, PhD MSc, is a Statistician and the Associate Director of the Biostatistics and Methods Core of the Pain Research, Informatics, Multimorbidities, & Education (PRIME) Center of Innovation at the VA Connecticut Healthcare System. She has more than 20 years of experience in research and evaluation as an epidemiologist/statistician in both the private and public sectors. Her areas of expertise include the evaluation and implementation of evidence-based practices, cohort and family study methodology, and the epidemiology of psychiatric disorders.

Mary A. Driscoll, PhD, holds an appointment as a Research Psychologist in the Pain Research, Informatics, Multi-morbidities and Education Center of Innovation at the VA Connecticut Healthcare System. She is also an Associate Research Scientist at the Yale School of Medicine and serves as Pain Consultant to VHA's Office of Women's Health Services. Her interests focus on gender disparities in pain and pain treatment, and development of evidence based non-pharmacologic interventions for women with pain.

Alicia A. Heapy, PhD is a health psychologist and a health services researcher at the Pain Research Informatics Multimorbidities and Education Center of Innovation at VA Connecticut Healthcare System and an Assistant Professor of Psychiatry at Yale University School of Medicine. Her research interests include the development and testing of technology-based cognitive behavioral interventions for chronic pain and pain assessment.

Robert D. Kerns, PhD is a Professor of Psychiatry, Neurology and Psychology at Yale University and a Research Psychologist at the VA Connecticut Healthcare System. He is a recognized expert in the field of pain management with over 35 years contributing to the scientific, practice, educational and policy literatures on this topic. Of particular relevance to the current manuscript is his longstanding interest in characterizing the experience of chronic pain and important comorbidities among military Veterans.

Matthew J. Bair, MD, MS is a general internist and Core Investigator at the VA HSR&D Center for Health Information and Communication in Indianapolis, Indiana. He is an Associate Professor of Medicine at Indiana University School of Medicine and Investigator at the Regenstrief Institute. Dr. Bair's main research interest is to develop and test interventions that combine pharmacologic and non-pharmacologic treatments that address some of the barriers to effective pain management that can be practicably applied in VA primary care settings.

Constance Carroll, MBA, MPH is a biostatistician at Yale University. She has a particular interest in quantitative social research.

Penny L. Brennan, PhD, is a Professor at the Institute for Health and Aging, University of California, San Francisco. Her research interests focus on aging and health: the course, predictors, and outcomes of late-life use of alcohol; social determinants of late-life pain; and long-term care environments that optimize resident-centered care, including the successful implementation and outcomes of consistent staff assignment scheduling practices.

Diana J. Burgess, PhD, is a Core Investigator at the Center for Chronic Disease Outcomes Research at the Minneapolis Veterans Affairs Healthcare System and an Associate Professor of Medicine at the University of Minnesota School of Medicine. Her areas of expertise include disparities in pain treatment and outcomes and nonpharmacological interventions for chronic pain.

John Piette, PhD is a Professor of Global Public Health and Internal Medicine, the Director of the University of Michigan Center for Managing Chronic Disease, and a VA Senior Research Career Scientist. His research focuses on developing and evaluating novel strategies for using patient-facing health technology to improve the accessibility and quality of care for patients with chronic illnesses.

Sally Haskell, MD is the Deputy Chief Consultant for Clinical Operations and the National Director of Comprehensive Women's Health for the Veterans Health Administration. She is a Professor of Internal Medicine at Yale School of Medicine.

Cynthia A. Brandt, MD is a Preventive Medicine physician, board certified biomedical informaticist and health services researcher. Her research interests include clinical informatics, database integration, electronic health records, personal health records, natural language processing and information extraction for clinical data, veterans health, women's health, and pain.

Joseph L. Goulet, MS, PhD is an epidemiologist and statistician at the VA Connecticut Healthcare System and an Assistant of Emergency Medicine and Psychiatry at the Yale School of Medicine. He has over 20 years' experience conducting health services research, including the development of several large VA administrative data-based cohort studies focusing on HIV, women veterans, and most currently musculoskeletal disorders.