UCSF UC San Francisco Previously Published Works

Title

ATP and Corpus Cavernosum

Permalink https://escholarship.org/uc/item/6n1158gs

Journal The Journal of Sexual Medicine, 11(1)

ISSN 1743-6095

Authors

Doyle, Claire Sergeant, Gerard P Hollywood, Mark A <u>et al.</u>

Publication Date 2014

DOI

10.1111/jsm.12364

Peer reviewed



NIH Public Access

Author Manuscript

J Sex Med. Author manuscript; available in PMC 2014 July 04

Published in final edited form as: *J Sex Med.* 2014 January ; 11(1): 75–83. doi:10.1111/jsm.12201.

Sexual Dysfunction in Male Iraq and Afghanistan War Veterans: Association with Posttraumatic Stress Disorder and Other Combat-Related Mental Health Disorders: A Population-Based Cohort Study

Benjamin N. Breyer, MD^{*}, Beth E. Cohen, MD^{$\dagger, \ddagger, \$$}, Daniel Bertenthal, MPH[§], Raymond C. Rosen, PhD^{*, ¶}, Thomas C. Neylan, MD^{$\ddagger, \$$}, and Karen H. Seal, MD^{$\dagger, \ddagger, \$$}

^{*}Department of Urology, University of California, San Francisco, San Francisco, CA, USA

[†]Department of Medicine, University of California, San Francisco, San Francisco, CA, USA

[‡]Department of Psychiatry, University of California, San Francisco, San Francisco, CA, USA

§San Francisco VA Medical Center, San Francisco, CA, USA

[¶]New England Research Institutes, Watertown, MA, USA

Abstract

Introduction—Mental health disorders are prevalent in the United States, Iraq, and Afghanistan war veterans. Mental illness, including posttraumatic stress disorder (PTSD) with or without

Category 1

- a. Conception and Design
 - Benjamin N. Breyer; Karen H. Seal
- b. Acquisition of Data
 - Daniel Bertenthal
- c. Analysis and Interpretation of Data

Benjamin N. Breyer; Karen H. Seal; Raymond C. Rosen; Beth E. Cohen; Thomas C. Neylan

Category 2

a. Drafting the Article

Benjamin N. Breyer; Karen H. Seal; Daniel Bertenthal

b. Revising It for Intellectual Content

Raymond C. Rosen; Beth E. Cohen; Thomas C. Neylan

Category 3

a. Final Approval of the Completed Article

Benjamin N. Breyer; Karen H. Seal; Raymond C. Rosen; Beth E. Cohen; Thomas C. Neylan

^{© 2013} International Society for Sexual Medicine

Corresponding Author: Benjamin N. Breyer, MD, MAS, Department of Urology, University of California, San Francisco, 400 Parnassus Avenue, A610, San Francisco, CA 94143, USA. Tel: 415-353-2207; Fax: 415-206-5153; bbreyer@urology.ucsf.edu. *Conflict of Interest:* All authors have completed and submitted the author statement form. No disclosures were reported. **Statement of Authorship**

psychiatric medications, can increase the risk for male sexual dysfunction, threatening quality of life.

Aims—We sought to determine the prevalence and correlates of sexual dysfunction among male Iraq and Afghanistan veterans.

Methods—We performed a retrospective cohort study of 405,275 male Iraq and Afghanistan veterans who were new users of U.S. Department of Veterans Affairs healthcare from October 7, 2001 to September 30, 2009 and had 2-year follow-up.

Main Outcome Measures—We determined the independent association of mental health diagnoses and sexual dysfunction after adjusting for sociodemographic and military service characteristics, comorbidities, and medications.

Results—Veterans with PTSD were more likely to have a sexual dysfunction diagnosis, be prescribed medications for sexual dysfunction, or both (10.6%), compared with veterans having a mental diagnosis other than PTSD (7.2%), or no mental health diagnosis (2.3%). In a fully adjusted model, PTSD increased the risk of sexual dysfunction by more than threefold (adjusted risk ratio = 3.61, 95% CI = 3.48-3.75). Veterans with mental health disorders, particularly PTSD, were at the highest risk of sexual dysfunction when prescribed psychiatric medications (adjusted risk ratio = 4.59, 95% CI = 4.41-4.77).

Conclusions—Among U.S. combat veterans, mental health disorders, particularly PTSD, increased the risk of sexual dysfunction independent of the use of psychiatric medications.

Keywords

Combat; Posttraumatic Stress Disorder; Sexual Dysfunction; Military Service

Introduction

Since the start of the Iraq and Afghanistan conflicts (Operation Iraqi Freedom [OIF] and Operation Enduring Freedom [OEF], principally Afghanistan), over 2 million Americans have served in the war. Over half of the 1.5 million who are eligible for Department of Veterans Affairs (VA) healthcare have enrolled upon returning from deployment [1]. Over half of these veterans have received mental health diagnoses, the most prevalent of which is posttraumatic stress disorder (PTSD) [1]. PTSD has been associated with multiple physical health complaints in OIF/OEF and prior-era veterans [2-3].

Sexual dysfunction is an underrecognized consequence of exposure to combat and traumatic stress. Small case series and cross-sectional studies have suggested that sexual dysfunction is associated with trauma-related mental illness, including PTSD [4-6]. Letourneau et al. surveyed 90 combat veterans with PTSD diagnoses and found that over 80% were experiencing clinically relevant sexual difficulties; erectile dysfunction (ED) and premature ejaculation were the most frequently reported problems [4]. In another study of veterans, 85% of those with PTSD reported ED compared with 22% of controls and those with PTSD scored significantly lower on scales of sexual satisfaction [5]. Finally, among 53 OIF/OEF veterans entering a PTSD residential recovery program, the majority reported sexual

dysfunction: 39 reported diminished libido, 26 reported ED, and 8 reported ejaculatory dysfunction [6].

Despite the high prevalence of mental health problems in returning veterans, and the central importance of sexual well-being to self-esteem and quality of life in this age group [7], there have been few large-scale studies of sexual health among male Iraq and Afghanistan veterans [8-10]. This may reflect that sexual dysfunction is a highly stigmatized condition and, as such, may be underreported or understudied.

Aims

The main aim of this study was to determine the prevalence and correlates of sexual dysfunction among a national sample of male Iraq and Afghanistan veterans. We focus exclusively on male sexual dysfunction because in a recent large study of women veterans using VA care, we found those with mental health disorders, particularly PTSD, had a substantially higher risk of receiving a sexual dysfunction diagnosis [8]. We hypothesized that sexual dysfunction is prevalent among young male veterans with mental health diagnoses, particularly PTSD, and that psychiatric medications used to treat these disorders increase the risk of sexual dysfunction.

Methods

Study Population

The study population was identified using the VA national OEF/OIF Roster, an accruing database of veterans who have returned from recent military service in Iraq and Afghanistan and have enrolled in the VA healthcare system. We examined administrative data from 647,203 Iraq and Afghanistan male veterans who entered VA healthcare from October 7, 2001 to September 30, 2009 (after their most recent deployment) and were followed for 2 years. The study end date was September 30, 2011 and veterans with <2 years follow-up time were excluded (N = 233,627). We also excluded veterans 65 years (N = 54), those with psychiatric prescriptions but no psychiatric diagnosis (N = 6,901), those with incomplete information on key covariates (N = 626), and those with prostate cancer (N = 720). The final study population consisted of 405,275 OEF/OIF veterans (Figure 1). The study was approved by the Committee on Human Research, University of California, San Francisco, and the Human Research Protection Program at the San Francisco VA Medical Center.

Data Source

The VA OEF/OIF Roster contains basic demographic and military service information [11]. The OEF/OIF Roster was linked to two other national administrative databases: (i) the VA National Patient Care Database to obtain information on VA clinic visits and associated clinical diagnoses; and (ii) the VA Decision Support System which contains detailed pharmacy records.

Main Outcome Measures

Dependent Variables—Sexual Dysfunction, Medications, and Urology Visits. Through medical literature review and consensus of the co-authors, a urologist (B.N.B.) and two internists (K.H.S. and B.E.C.), we identified International Classification of Diseases, Ninth Revision Clinical Modification (ICD-9-CM) codes that represented male sexual dysfunction: ED (607.84), hypogonadism (256.1), and "other sexual dysfunction," that included premature ejaculation (302.75); male orgasmic disorder (302.74); psychosexual dysfunction, unspecified (302.70); hypoactive sexual desire disorder (302.71); psychosexual dysfunction with inhibited sexual excitement (302.72); and other psychosexual dysfunction (302.79). We identified medications prescribed to treat ED and other sexual dysfunction at the VA: phosphodiesterase inhibitors (sildenafil citrate and vardenafil) and suppository or injection medication (alprostadil). Because sexual dysfunction diagnoses have a relatively low prevalence and may not be consistently coded in the medical record, we created a binary composite outcome variable for sexual dysfunction that captured 1 of the sexual dysfunction diagnostic codes or 1 prescription medications for sexual dysfunction, or both. Finally, we identified VA urology visits that were associated with either a sexual dysfunction diagnosis and/or a prescription for an ED medication (filled within at least 90 days of the urology visit).

Independent Variables—Mental health diagnoses were identified using ICD-9-CM diagnoses (290 to 319) corresponding to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition classifications [12]. Mental health diagnoses were categorized into three mutually exclusive groups: (i) no mental health diagnosis; (ii) mental health diagnoses excluding PTSD; and (iii) PTSD diagnoses with or without other mental health diagnoses. We did not create a separate category for PTSD alone given concerns that clinicians working in specialized PTSD clinics may not always code comorbid disorders, and that the vast majority of individuals with PTSD have comorbid mental health disorders [13]. Smoking, alcohol, and drug use disorders were excluded in the categorization of mental health disorders in order to examine each as separate independent covariates (see below).

We examined sociodemographic information (e.g., age, race/ethnicity, and marital status), military service information including component type (Active Duty vs. National Guard or Reserve), branch of service, rank (officer vs. enlisted), and number of deployments (1 vs. 2); other ICD-9-CM clinical diagnoses associated with sexual dysfunction, i.e., spinal cord injury (805,806), alcohol use disorders (305.00–305.03 and 303), substance use disorders (305.20–305.93 and 304), smoking (305.1), diabetes mellitus (250, 357.2), and hypertension (401–405); prescription medications known to contribute to sexual dysfunction, e.g., antidepressants, antipsychotics, and opioids; and number of visits to VA primary care and mental health clinics.

Statistical Analysis

Of the 405,275 male OEF/OIF veterans, we compared the prevalence of those with and without a composite sexual dysfunction diagnosis among particular subgroups of veterans (e.g., married vs. unmarried veterans). Next, we compared the prevalence of specific sexual dysfunction diagnoses, medications used to treat sexual dysfunction, and urology visits

across the three mental health diagnostic categories (defined above). We compared the proportion of sexual dysfunction diagnoses and prescription medications used to treat sexual dysfunction originating from primary care vs. urology and other specialty services.

Generalized estimating equations using a Poisson distribution and robust error variance were used to model the relative risk of sexual dysfunction [14]. In order to model whether outcomes occurred during the period when a patient was receiving any of the designated psychiatric medications (antidepressants or antipsychotics), medication use was modeled as a time-varying covariate [15]. Patients who received any of these medications for a portion of the follow-up period were represented twice in the model; one record for the time they were receiving medications and a second record for the time off these medications. We developed adjusted models accounting for sociodemographic, military service, comorbid disease, and opioid medication. As a sensitivity analysis, we adjusted for number of primary care and mental health clinic visits to account for possible ascertainment bias; the adjustment did not produce clinically important changes in the risk estimates. We chose a *P* value of <0.01 as our threshold for statistical significance given the large sample size. Analyses were conducted using SAS software 9.3 (SAS Institute Inc., Cary, NC, USA) and STATA 12.1 (StataCorp, College Station, TX, USA).

Results

Of 405,275 male veterans, the median age was 28 years (range 18–64 years); 54% were ethnic/minorities; 53% were unmarried; 42% had served in the National Guard/Reserve forces; and 36% had served 2 deployments (Table 1). A substantial proportion had been prescribed antidepressants (26%), antipsychotics (6%), and opioid medications (17%). In unadjusted analyses, factors most strongly associated with sexual dysfunction were increasing age, spinal cord injury, other medical comorbidities (e.g., diabetes), and the use of psychiatric and opioid medications. Table 2 demonstrates that overall, 5.3% (n = 21,494) of Iraq and Afghanistan veterans in the study population received diagnoses of sexual dysfunction and/or an erectile aid prescription. ED was the single most common sexual dysfunction diagnosis (1.7%); 17,686 (4.4%) men were prescribed at least one medication for sexual dysfunction. Compared with those with no mental health diagnoses or a mental health diagnosis other than PTSD, those with PTSD were more likely to have ED (0.8% vs. 2.4% vs. 3%, respectively); have been prescribed medication for sexual dysfunction (1.8% vs. 5.8% vs. 9.0%, respectively); or visited a urologist for sexual dysfunction (0.2% vs. 0.6% vs. 0.8%, respectively).

After adjusting for potential confounding variables, mental health diagnoses remained independently associated with sexual dysfunction, and the magnitude of this association was greater for PTSD than for other types of mental health diagnoses (Table 3). Further adjustment for psychiatric and opioid medications reduced the magnitude of these associations, but they remained significant. In an attempt to isolate the role of psychiatric medications and mental illness, we stratified veterans into five groups depending on their PTSD, mental health, and psychiatric medication status (Table 4). We found that veterans with mental health disorders, particularly PTSD, were at the highest risk of sexual

dysfunction when also prescribed psychiatric medications (ARR 4.59, 95% CI = 4.41-4.77) (Table 4).

Discussion

Sexual dysfunction is an important health condition found in a large number of returning combat veterans that can result in reduced quality of life, decreased sexual intimacy, and increased health-care utilization [16]. To our knowledge, this is the first report of the prevalence and correlates of sexual dysfunction in a large population of male Iraq and Afghanistan veterans enrolled in VA healthcare. Among younger male veterans with a median age of 28 years, those with mental health diagnoses, particularly PTSD, had an increased risk of receiving a sexual dysfunction diagnosis, being prescribed medication for sexual dysfunction, and utilizing specialty urological services. Among those with PTSD, sexual dysfunction diagnoses were relatively common (>10%), with a nearly fourfold risk in unadjusted analyses and a greater than threefold risk after adjustment for sociodemographic and military service characteristics, medical comorbidities, and medication use. Being prescribed psychiatric medications (used to treat both depression and PTSD) significantly increased the risk of sexual dysfunction, with the greatest risk in veterans with PTSD.

Our findings expand upon previous research that suggests an association between mental illness and sexual dysfunction [17-19]. Previous investigations have demonstrated that mental illness is associated with a myriad of medical conditions and greater healthcare usage [20-24]. Mental illness has been associated with diseases of aging such as coronary artery disease [25] and dementia [26]. There are several plausible and interrelated mechanisms that may contribute to sexual dysfunction in war veterans with mental health problems (particularly PTSD) [27,28]. First, military deployment negatively impacts neuropsychological health, in general [29], and more specifically, neuroendocrine, neurobiologic, and autonomic dysfunction produced by PTSD may promote sexual dysfunction. Second, conditions associated with mental illness such as cardiovascular disease may cause sexual dysfunction. Third, medications used to treat PTSD, such as selective serotonin reuptake inhibitors (SSRIs) and other psychotropic medications are known to cause erectile and ejaculatory dysfunction. Also, many veterans are deployed under the age of 25 during a formative time of their sexual development and their sexual wellness may be vulnerable to the stress of combat [30,31]. Finally, upon return from deployment, mental illness is associated with relational difficulties, marital disruption, reduced intimacy, spousal abuse, and lower marital satisfaction [30].

It is unclear whether this veteran cohort has a higher or lower prevalence of sexual dysfunction when compared with other male populations. Nationally and regionally representative samples and clinical series have used anonymous and confidential self-report questionnaires to determine the prevalence of sexual dysfunction. For men under age 35, estimates of ED based on direct questioning have ranged from 2% to 14% [18], and we found a prevalence of sexual dysfunction of 5.5% for this cohort overall. We relied on administrative data, which likely under-estimated prevalence as veterans returning from war are not systematically screened for sexual dysfunction and must specifically seek out treatment and receive a diagnosis. Nevertheless, we found that veterans who received a

diagnosis of PTSD had a prevalence of sexual dysfunction of over 10% which increased to nearly 13% among those prescribed psychiatric medication.

SSRIs are the most frequently prescribed medication nationally and a U.S. Food and Drug Administrations' approved treatment for PTSD and depression [32]. SSRIs are associated with ejaculatory dysfunction such as delayed ejaculation, inability to ejaculate, and absent or delayed orgasm [33]. Prior to initiating psychiatric medications, an evaluation of baseline sexual function may help quantify side effects, should they occur. If sexual dysfunction develops, efforts to adjust the medication regimen by either lowering dosages or switching to a new medication class to minimize sexual side effects may improve adherence to psychiatric medications and preserve quality of life [33]. This is particularly important considering the well-documented difficulties of retaining these young veterans in treatment for trauma-related disorders [34,35]. In addition, veterans with mental illness and sexual dysfunction may benefit from evaluation by a sex therapist [30].

Our results should be considered in light of several limitations. First, our measures were based on retrospective administrative and pharmacy data which may have failed to capture some clinical or subclinical problems compared with validated self-report instruments. Some veterans embarrassed about sexual dysfunction may not have disclosed their symptoms to their providers or may have sought care for sexual dysfunction from non-VA providers, and these visits and diagnoses would not have been recorded in VA databases. Second, our findings in this treatment-seeking cohort of Iraq and Afghanistan veterans may not generalize to other veterans, either those from prior eras, or those who receive care outside of the VA system, although the VA provides care to the majority of recently returned combat veterans [1]. Third, ascertainment bias may have led to inflated estimates of sexual dysfunction prevalence in veterans with mental health problems because of increased medical services utilization in veterans with mental illness [36]. However, in a sensitivity analysis, adjustment for health services utilization did not appreciably change the relative risk of sexual dysfunction. Fourth, we cannot infer causality in this study, though the finding of a robust and independent association between PTSD and sexual dysfunction in a large population of combat veterans is novel and represents a potentially important public health concern. In addition, it is possible that some patients obtained ED medications for recreational use, but had normal sexual function. We did not have access to data pertaining to vacuum-assisted ED devices or penile prosthetic utilization patterns. Finally, the effect of psychiatric medications may be confounded by indication in that greater symptom severity, and not the addition of medication per se, was associated with increased risk for SD.

Conclusions

Returned veterans with mental health diagnoses, particularly PTSD, had an increased risk of receiving a sexual dysfunction diagnosis, being prescribed medication for sexual dysfunction, and utilizing specialty urological services. Considering the limitation described previously, being prescribed psychiatric medications appeared to significantly increase the risk of sexual dysfunction with the greatest risk in veterans with PTSD. Future directions in clinical research on mental illness and sexual dysfunction among veterans should focus on

References

- 1. Department of Veterans Affairs Epidemiology Program PDHSHG, Office of Public Health., editor. Analysis of VA Health Care Utilization among Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) Veterans. 2012.
- Hoge CW, Terhakopian A, Castro CA, Messer SC, Engel CC. Association of posttraumatic stress disorder with somatic symptoms, health care visits, and absenteeism among Iraq war veterans. Am J Psychiatry. 2007; 164:150–3. [PubMed: 17202557]
- Andersen J, Wade M, Possemato K, Ouimette P. Association between posttraumatic stress disorder and primary care provider-diagnosed disease among Iraq and Afghanistan veterans. Psychosom Med. 2010; 72:498–504. [PubMed: 20368471]
- Letourneau EJ, Schewe PA, Frueh BC. Preliminary evaluation of sexual problems in combat veterans with PTSD. J Trauma Stress. 1997; 10:125–32. [PubMed: 9018683]
- Cosgrove DJ, Gordon Z, Bernie JE, Hami S, Montoya D, Stein MB, Monga M. Sexual dysfunction in combat veterans with post-traumatic stress disorder. Urology. 2002; 60:881–4. [PubMed: 12429320]
- Hirsch KA. Sexual dysfunction in male Operation Enduring Freedom/Operation Iraqi Freedom patients with severe post-traumatic stress disorder. Mil Med. 2009; 174:520–2. [PubMed: 20731284]
- Kubin M, Wagner G, Fugl-Meyer AR. Epidemiology of erectile dysfunction. Int J Impot Res. 2003; 15:63–71. [PubMed: 12605242]
- Cohen BE, Maguen S, Bertenthal D, Shi Y, Jacoby V, Seal KH. Reproductive and other health outcomes in Iraq and Afghanistan women veterans using VA health care: Association with mental health diagnoses. Womens Health Issues. 2012; 22:e461–71. [PubMed: 22944901]
- Helmer DA, Beaulieu GR, Houlette C, Latini D, Goltz HH, Etienne S, Kauth M. Assessment and documentation of sexual health issues of recent combat veterans seeking VHA care. J Sex Med. 2013; 10:1065–73. [PubMed: 23421874]
- Hosain GM, Latini DM, Kauth M, Goltz HH, Helmer DA. Sexual dysfunction among male veterans returning from Iraq and Afghanistan: Prevalence and correlates. J Sex Med. 2013; 10:516–23. [PubMed: 23088675]
- Maguen S, Ren L, Bosch JO, Marmar CR, Seal KH. Gender differences in mental health diagnoses among Iraq and Afghanistan veterans enrolled in veterans affairs health care. Am J Public Health. 2010; 100:2450–6. [PubMed: 20966380]
- American Psychiatric Association, American Psychiatric Association, Task Force on DSM-IV. Diagnostic and statistical manual of mental disorders: DSM-IV. 4th edition. American Psychiatric Association; Washington, DC: 1994.
- Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005; 62:593–602. [PubMed: 15939837]
- 14. Cummings P. Methods for estimating adjusted risk ratios. Stata J. 2009; 9:175-96.
- Zou G. A modified poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004; 159:702–6. [PubMed: 15033648]
- Litwin MS, Nied RJ, Dhanani N. Health-related quality of life in men with erectile dysfunction. J Gen Intern Med. 1998; 13:159–66. [PubMed: 9541372]
- 17. Kalmbach DA, Ciesla JA, Janata JW, Kingsberg SA. Specificity of anhedonic depression and anxious arousal with sexual problems among sexually healthy young adults. J Sex Med.
- Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: Results of the Massachusetts Male Aging Study. J Urol. 1994; 151:54–61. [PubMed: 8254833]

- 19. Kockott G, Pfeiffer W. Sexual disorders in nonacute psychiatric outpatients. Compr Psychiatry. 1996; 37:56–61. [PubMed: 8770528]
- Byers AL, Covinsky KE, Barnes DE, Yaffe K. Dysthymia and depression increase risk of dementia and mortality among older veterans. Am J Geriatr Psychiatry. 2012; 20:664–72. [PubMed: 21597358]
- Player MS, Peterson LE. Anxiety disorders, hypertension, and cardiovascular risk: A review. Int J Psychiatry Med. 2011; 41:365–77. [PubMed: 22238841]
- Bleich A, Solomon Z. Evaluation of psychiatric disability in PTSD of military origin. Isr J Psychiatry Relat Sci. 2004; 41:268–76. [PubMed: 15941022]
- Schnurr PP, Spiro A 3rd, Paris AH. Physician-diagnosed medical disorders in relation to PTSD symptoms in older male military veterans. Health Psychol. 2000; 19:91–7. [PubMed: 10711592]
- 24. Drescher KD, Rosen CS, Burling TA, Foy DW. Causes of death among male veterans who received residential treatment for PTSD. J Trauma Stress. 2003; 16:535–43. [PubMed: 14690350]
- Ahmadi N, Hajsadeghi F, Mirshkarlo HB, Budoff M, Yehuda R, Ebrahimi R. Post-traumatic stress disorder, coronary atherosclerosis, and mortality. Am J Cardiol. 2011; 108:29–33. [PubMed: 21530936]
- Yaffe K, Vittinghoff E, Lindquist K, Barnes D, Covinsky KE, Neylan T, Kluse M, Marmar C. Posttraumatic stress disorder and risk of dementia among US veterans. Arch Gen Psychiatry. 2010; 67:608–13. [PubMed: 20530010]
- 27. Arbanas G. Does post-traumatic stress disorder carry a higher risk of sexual dysfunctions? J Sex Med. 2010; 7:1816–21. [PubMed: 20214725]
- 28. Spivak B, Maayan R, Mester R, Weizman A. Plasma testosterone levels in patients with combatrelated posttraumatic stress disorder. Neuropsychobiology. 2003; 47:57–60. [PubMed: 12707485]
- Vasterling JJ, Proctor SP, Amoroso P, Kane R, Heeren T, White RF. Neuropsychological outcomes of army personnel following deployment to the Iraq war. JAMA. 2006; 296:519–29. [PubMed: 16882958]
- Cameron RP, Mona LR, Syme ML, Cordes CC, Fraley SS, Chen SS, Klein LS, Welsh E, Smith K, Lemos L. Sexuality among wounded veterans of Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND): Implications for rehabilitation psychologists. Rehabil Psychol. 2011; 56:289–301. [PubMed: 22121937]
- Hutchinson JW, Greene JP, Hansen SL. Evaluating active duty risk-taking: Military home, education, activity, drugs, sex, suicide, and safety method. Mil Med. 2008; 173:1164–7. [PubMed: 19149332]
- Hidalgo RB, Davidson JR. Selective serotonin reuptake inhibitors in post-traumatic stress disorder. J Psychopharmacol. 2000; 14:70–6. [PubMed: 10757257]
- Rosen RC, Lane RM, Menza M. Effects of SSRIs on sexual function: A critical review. J Clin Psychopharmacol. 1999; 19:67–85. [PubMed: 9934946]
- 34. Seal KH, Maguen S, Cohen B, Gima KS, Metzler TJ, Ren L, Bertenthal D, Marmar CR. VA mental health services utilization in Iraq and Afghanistan veterans in the first year of receiving new mental health diagnoses. J Trauma Stress. 2010; 23:5–16. [PubMed: 20146392]
- Harpaz-Rotem I, Rosenheck RA. Serving those who served: Retention of newly returning veterans from Iraq and Afghanistan in mental health treatment. Psychiatr Serv. 2011; 62:22–7. [PubMed: 21209295]
- Cohen BE, Gima K, Bertenthal D, Kim S, Marmar CR, Seal KH. Mental health diagnoses and utilization of VA non-mental health medical services among returning Iraq and Afghanistan veterans. J Gen Intern Med. 2010; 25:18–24. [PubMed: 19787409]



Figure 1. Cohort derivation

Correlates of sexual dysfunction^{*} among 405,275 Iraq and Afghanistan male veterans in VA healthcare from October 7, 2001 to September 30, 2009

	Total	No sexual dysfunction*	Sexual dysfunction*		
	(N = 405,275)	(N = 383,781)	(N = 21,494)		
	Ν	N (%)	N (%)	RR (95% CI)	Pr > Z
Age					
18–24	112,071	109,944 (98.1)	2,127 (1.9)		
25-34	151,840	146,401 (96.4)	5,439 (3.6)	1.89 (1.80, 1.98)	< 0.001
35–44	92,685	85,122 (91.8)	7,563 (8.2)	4.30 (4.10, 4.51)	< 0.001
45–54	40,617	35,520 (87.5)	5,097 (12.5)	6.61 (6.29, 6.95)	< 0.001
55–64	8,062	6,794 (84.3)	1,268 (15.7)	8.29 (7.76, 8.85)	< 0.001
Race and/or or ethnicity					
Non-White	216,655	204,117 (94.2)	12,538 (5.8)		
White	188,620	179,664 (95.3)	8,956 (4.7)	0.82 (0.80, 0.84)	< 0.001
Marital status					
Married	189,988	175,803 (92.5)	14,185 (7.5)		
Never married	198,604	192,890 (97.1)	5,714 (2.9)	0.39 (0.37, 0.40)	< 0.001
Divorced, widowed, or other	16,683	15,088 (90.4)	1,595 (9.6)	1.28 (1.22, 1.35)	< 0.001
Military branch					
Army	245,242	229,910 (93.7)	15,332 (6.3)		
Air force	45,382	43,435 (95.7)	1,947 (4.3)	0.69 (0.66, 0.72)	< 0.001
Marines	63,141	61,434 (97.3)	1,707 (2.7)	0.43 (0.41, 0.45)	< 0.001
Navy	51,510	49,002 (95.1)	2,508 (4.9)	0.78 (0.75, 0.81)	< 0.001
Active duty or reserve/National g	guard				
Active duty	235,498	225,583 (95.8)	9,915 (4.2)		
Reserve/guard	169,777	158,198 (93.2)	11,579 (6.8)	1.62 (1.58, 1.66)	< 0.001
Military rank					
Enlisted	372,054	352,223 (94.7)	19,831 (5.3)		
Officer	33,221	31,558 (95.0)	1,663 (5.0)	0.94 (0.89, 0.99)	0.012
Multiple deployments	144,728	136,641 (94.4)	8,087 (5.6)	1.09 (1.06, 1.12)	< 0.001
Spinal cord injury diagnosis	903	763 (84.5)	140 (15.5)	2.94 (2.52, 3.42)	< 0.001
Diabetes mellitus diagnosis	6,918	5,293 (76.5)	1,625 (23.5)	4.71 (4.50, 4.92)	< 0.001
Hypertension diagnosis	49,611	41,669 (84.0)	7,942 (16.0)	4.20 (4.09, 4.31)	< 0.001
Alcohol use disorder	40,525	36,830 (90.9)	3,695 (9.1)	1.87 (1.81, 1.93)	< 0.001
Drug use disorder	17,675	16,041 (90.8)	1,634 (9.2)	1.80 (1.72, 1.89)	< 0.001
Smoking	72,752	66,899 (92.0)	5,853 (8.0)	1.71 (1.66, 1.76)	< 0.001
Antidepressant medication	103,768	91,151 (87.8)	12,617 (12.2)	4.13 (4.02, 4.24)	< 0.001
Antipsychotic medication	25,035	21,140 (84.4)	3,895 (15.6)	3.36 (3.25, 3.47)	< 0.001
Opioid medication	69,207	61,588 (89.0)	7,619 (11.0)	2.67 (2.60, 2.74)	< 0.001

^{*}SD composite binary outcome consists of: (i) any sexual dysfunction diagnosis (hypogonadism, erectile dysfunction, premature ejaculation, male orgasmic disorder, psychosexual dysfunction [unspecified], hypoactive sexual desire disorder, psychosexual dysfunction with inhibited sexual

excitement, and other psychosexual dysfunction); and/or (ii) prescription for erectile dysfunction and other sexual dysfunction: phosphodiesterase inhibitors (sildenafil citrate and vardenafil) and suppository or injection medication (alprostadil)

Association of sexual dysfunction outcomes with mental health (MH) diagnostic category among 405,275 Iraq and Afghanistan male veterans in VA healthcare from October 7, 2001 to September 30, 2009

	Total (N = 405,275) N (%)	No MH Dx (N = 235,096) N (%)	MH Dx excluding PTSD (N = 59,956) N (%)	PTSD with and without other MH Dx (N = 110,223) N (%)
Sexual dysfunction Dx or Rx^*	21,494 (5.3)	5,496 (2.3)	4,306 (7.2)	11,692 (10.6)
Sexual dysfunction Dx	14,521 (3.6)	4,205 (1.8)	3,058 (5.1)	7,258 (6.6)
Hypogonadism	1,385 (0.3)	331 (0.1)	287 (0.5)	767 (0.7)
Erectile dysfunction	6,766 (1.7)	1,973 (0.8)	1,437 (2.4)	3,356 (3.0)
Other sexual dysfunction	9,402 (2.3)	2,637 (1.1)	1,981 (3.3)	4,784 (4.3)
Sexual dysfunction Rx (All)	17,686 (4.4)	4,265 (1.8)	3,476 (5.8)	9,945 (9.0)
Vardenafil	16,327 (4.0)	3,815 (1.6)	3,164 (5.3)	9,348 (8.5)
Sildenafil	2,688 (0.7)	766 (0.3)	576 (1.0)	1,346 (1.2)
Alprostadil	227 (0.1)	35 (0.0)	51 (0.1)	141 (0.1)
Urology visit for sexual dysfunction	1,631 (0.4)	392 (0.2)	349 (0.6)	890 (0.8)

Dx = diagnoses; Rx = Sildenafil, Vardenafil, Alprostadil

*SD composite binary outcome consists of: (i) any sexual dysfunction diagnosis (hypogonadism, erectile dysfunction, premature ejaculation, male orgasmic disorder, psychosexual dysfunction [unspecified], hypoactive sexual desire disorder, psychosexual dysfunction with inhibited sexual excitement, and other psychosexual dysfunction); and/or (ii) prescription for erectile dysfunction and other sexual dysfunction: phosphodiesterase inhibitors (sildenafil citrate and vardenafil) and suppository or injection medication (alprostadil)

Association of sexual dysfunction composite outcome with mental health (MH) diagnostic category among 405,275 Iraq and Afghanistan male veterans in VA healthcare from October 7, 2001 to September 30, 2009, treating antidepressant and/or antipsychotic prescriptions as a time-varying covariate and after stepwise adjustment for potential confounding

	No MH Dx (N = 235,096)	MH Dx excluding PTSD (N = 59,956)		PTSD with and without other MH Dx (N = 110,223)		
Sexual dysfunction composite outcome	RR/ARR (95% CI)	RR/ARR (95% CI)	<i>P</i> > z	RR/ARR (95% CI)	<i>P</i> > z	
Unadjusted relative risk $*$	1.00 (ref.)	2.73 (2.62, 2.84)	< 0.001	3.79 (3.65, 3.93)	< 0.001	
+ Sociodemographic and military service [†]	1.00 (ref.)	3.11 (2.98, 3.24)	< 0.001	4.65 (4.48, 4.83)	<0.001	
+ Comorbidities ^{\ddagger}	1.00 (ref.)	2.73 (2.62, 2.84)	< 0.001	3.95 (3.80, 4.10)	< 0.001	
+ Opioid medications§	1.00 (ref.)	2.60 (2.49, 2.71)	< 0.001	3.61 (3.48, 3.75)	< 0.001	

AUD = alcohol use disorder; DM = diabetes mellitus; DUD = drug use disorder; HTN = hypertension; PTSD = posttraumatic stress disorder; SCI = spinal cord injury

* Unadjusted relative risk (RR) with 95% confidence interval (CI)

 † Adjusted relative risk (aRr). Multivariable analysis adjusted for sociodemographic and military service (MS) characteristics

[‡]ARR. Multivariable analysis adjusted for sociodemographic and MS characteristics, comorbidities (HTN, dM, SCI, AUD, DUD, and smoking)

[§]ARR. Multivariable analysis adjusted for sociodemographic and MS characteristics, comorbidities (HTN, DM, SCI, AUD, DUD, and smoking), and opioid medications

Association of sexual dysfunction with PTSD with and without other mental health (MH) diagnoses (Dx), stratifying by psychiatric medication use, treating antidepressant, and/or antipsychotic prescriptions as a time-varying covariate^{*}

		Veterans with sexual	Adjusted [†]		Adjusted [‡]	
	N	n (%)	ARR (95% CI)	$\Pr > Z $	ARR (95% CI)	$\mathbf{P} > \mathbf{z} $
PTSD-MH-Rx-	235,096	5,496 (2.3)	1.00 [reference]		1.00 [reference]	
PTSD- MH+ Rx-	31,840	1,619 (5.1)	3.32 (3.18, 3.47)	< 0.001	2.77 (2.64, 2.89)	< 0.001
PTSD+ MH+ Rx-	32,075	1,609 (5.0)	3.89 (3.68, 4.12)	< 0.001	2.92 (2.76, 3.10)	< 0.001
PTSD- MH+ Rx+	28,116	2,687 (9.6)	4.48 (4.31, 4.66)	< 0.001	3.49 (3.35, 3.63)	< 0.001
PTSD+ MH+ Rx+	78,148	10,083 (12.9%)	6.62 (6.38, 6.86)	< 0.001	4.59 (4.41, 4.77)	< 0.001

AUD = alcohol use disorder; DM = diabetes mellitus; DUD = drug use disorder; HTN = hypertension; PTSD = posttraumatic stress disorder; Rx = Sildenafil, Vardenafil, Alprostadil; SCI = spinal cord injury

^{*}We excluded the combination in which PTSD and MH Dx are negative and psychiatric medications were positive because these veterans have been excluded. Also excluded are the categories of PTSD+ and MH– (irrespective of psychiatric medications) because PTSD is always considered with or without other mental health diagnoses.

 † Adjusted Relative Risk (ARR) with 95% confidence interval (CI). Multivariable analysis adjusted for sociodemographic and military service (MS) characteristics

⁴ARR with 95% CI. Multivariable analysis adjusted for sociodemographic and MS characteristics, comorbidities (hTn, DM, SCI, AUD, DUD, and smoking), and opioid medications.