Published in final edited form as:

J Dual Diagn. 2017 ; 13(3): 201–212. doi:10.1080/15504263.2017.1325033.

Trends in Opioid Use Disorder Diagnoses and Medication Treatment among Veterans with Posttraumatic Stress Disorder

Brian Shiner, MD, MPH^{1,2,3,4}, Christine Leonard Westgate, MS², Nancy C. Bernardy, PhD³, Paula P. Schnurr, PhD³, and Bradley V. Watts, MD, MPH^{2,4}

¹VA Medical Center, 215 North Main St., White River Junction, VT 05009

²Geisel School of Medicine at Dartmouth, 1 Rope Ferry Rd., Hanover, NH 03755

³National Center for PTSD, 215 North Main St., White River Junction, VT 05009

⁴National Center for Patient Safety, 24 Frank Lloyd Wright Dr., Ann Arbor, MI 48105

Abstract

Objective: Despite long-standing interest in posttraumatic stress disorder (PTSD) and opioid use disorder (OUD) comorbidity, there is a paucity of data on the prevalence of OUD in patients with PTSD. Therefore, there is limited understanding of the use of medications for OUD in this population. We determined the prevalence of diagnosed OUD and use of medications for OUD in a large cohort of patients with PTSD.

Methods: We obtained administrative and pharmacy data for Veterans who initiated PTSD treatment in the Department of Veterans Affairs (VA) between 2004 and 2013 (n=731,520). We identified those with a comorbid OUD diagnosis (2.7%; n=19,998) and determined whether they received a medication for OUD in the year following their initial clinical PTSD diagnosis (29.6%; n=5,913). Using logistic regression, we determined the predictors of receipt of OUD medications.

Results: Comorbid OUD diagnoses increased from 2.5% in 2004 to 3.4% in 2013. Patients with comorbid OUD used more health services and had more comorbidities than other patients with PTSD. Among patients with PTSD and comorbid OUD, use of medications for OUD increased from 22.6% to 35.1% during the same time period. Growth in the use of buprenorphine (2.0% to 22.7%) was accompanied by relative decline in use of methadone (19.3% to 12.7%). Patients who received buprenorphine were younger and more likely to be rural, white, and married. Patients who received methadone were older, urban, unmarried, from racial and ethnic minorities, and were more likely to see substance abuse specialists. While use of naltrexone increased (2.8% to 8.6%), most (87%) patients who received naltrexone also had an alcohol use disorder. Controlling for

Corresponding Author: Brian Shiner; VA Medical Center; 215 North Main Street, 11Q; White River Junction, VT 05009; (telephone) 802-295-9363; (fax) 802-291-6286; brian.shiner@va.gov.

Coauthor: christine.westgate@va.gov

Coauthor: nancy.bernardy@va.gov

Coauthor: paula.schnurr@va.gov

Coauthor: bradley.watts@va.gov

Disclosures: The sponsor did not have any role in the study design, methods, analysis, and interpretation of results, or in preparation of the manuscript and the decision to submit it for publication. The views expressed in this article are those of the authors and do not necessarily represent the position or policy of the US Department of Veterans Affairs. The authors report no conflicts of interest. All authors have completed author disclosure forms.

patient factors, there was a substantial increase in the use of buprenorphine, a substantial decrease in the use of methadone, and no change in use of naltrexone across years.

Conclusions: OUD is an uncommon but increasing comorbidity among patients with PTSD. Patients entering VA treatment for PTSD have their OUD treated with opioid agonist treatments in large and increasing numbers. There is a need for research both on the epidemiology of OUD among patients with PTSD and on screening for OUD.

Keywords

Stress Disorder; Posttraumatic; Opioid-Related Disorders; Psychotropic Drugs; Electronic Health Records; Health Services Research; Pharmacoepidemiology

1. Introduction

Posttraumatic stress disorder (PTSD) is a mental health condition that sometimes follows exposure to a traumatic event (APA, 2013). Symptoms include reexperiencing the trauma, avoidance of reminders of the trauma, hyperarousal, and negative cognitions. PTSD affects 6.8% of the United States (US) population during their lifetime (Kessler et al., 2005). Rates are higher in trauma-exposed populations such as survivors of natural disasters (Galea, Nandi, & Vlahov, 2005), people with severe mental illness (Mueser et al., 1998), and Veterans (Magruder et al., 2005). The population of patients with PTSD also has high rates of addictions, including 37.9% with nicotine dependence, 41.8% with alcohol use disorders, and 22.3% with drug use disorders (Pietrzak, Goldstein, Southwick, & Grant, 2011). Because PTSD researchers have typically combined opioid use disorders (OUDs) with other drug use disorders or all substance use disorders (SUDs) when performing epidemiologic surveys and retrospective cohort studies (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; Prior, Mills, Ross, & Teesson, 2016; Seal et al., 2011), there is limited knowledge regarding the specific prevalence and treatment of co-occurring OUD and PTSD.

There has been longstanding interest in OUD among patients with PTSD, as the neurobiology of these two disorders may be interconnected. Research has implicated monoaminergic dysregulation in the underlying neurobiology of PTSD (Rasmusson & Shalev, 2014). In a resilient state, stimulation of the amygdala in response to a stress activates dopamine, noradrenaline, and serotonin cell body regions in the brainstem (Goldstein, Rasmusson, Bunney, & Roth, 1996). Increased monoamine levels activate excitatory glutamatergic output from the prefrontal cortex, which stimulates interneurons in the amygdala to release inhibitory γ -aminobutyric acid (GABA), completing a feedback loop that regulates the stress response (Arnsten, 2009). However, in amygdala-dominant states such as PTSD, upregulation of prefrontal cortex monoamine receptors blunts the feedback loop regulating the amygdala (Pitman et al., 2012). Dopamine receptor subtypes may have synergistic actions at the amygdala, whereby the aforementioned upregulation of dopamine type 1 receptors decreases inhibition while upregulation of dopamine type 2 receptors increases responsivity (Friedman, 2015), contributing to disruptions in the endogenous opioid system (Vanderkolk, 1994). Opioid dysregulation may contribute to high rates of chronic pain among patients with PTSD (Beckham et al., 1997; Outcalt et al., 2014), prompting high levels of opioid pain medication use (Outcalt et al., 2014; Phifer et al.,

2011), which puts this population at risk for the development of OUDs (Chou et al., 2009; Edlund, Steffick, Hudson, Harris, & Sullivan, 2007).

There are three FDA-approved medications to treat OUD: naltrexone, methadone and buprenorphine. Naltrexone is an opioid antagonist that is thought to extinguish conditioned responses to opioids by blocking their effects, whereas methadone and buprenorphine are opioid agonist treatments (OATs) that act as a substitute for the opioid of abuse in order to support patients while they engage in counseling and other therapy to promote lifestyle change (Cornish, McNicholas, & O'Brien, 2004). Each of the medications is available in multiple formulations (e.g. liquids, pills, patches, long-acting injections, and implants). Naltrexone is also indicated for alcohol use disorder (AUD), and methadone is also indicated for pain.

The combined clinical practice guideline for the treatment of PTSD from the VA and Department of Defense (DoD) recommends that “addiction-focused pharmacotherapy should be discussed, considered, available and offered, if indicated,” for all patients with comorbid OUD (Friedman, Lowry, & Ruzek, 2010). However, there is limited research on the effectiveness of these medications in patients with PTSD. A small open label study of naltrexone for PTSD reported statistically significant decreases in intrusion and hyperarousal symptoms (Lubin et al., 2002). However, the changes were not clinically meaningful and patients with SUDs were excluded. Two randomized trials of naltrexone demonstrate superior alcohol use AUD and PTSD outcomes (Petrakis et al., 2006; Foa et al., 2013). However, neither study reported OUD outcomes. Naturalistic studies indicate that there is no disparity in benefit from methadone treatment for patients with PTSD (Trafton et al., 2006; Himelhoch et al., 2012). A limited body of evidence suggests that buprenorphine may also be effective for PTSD symptoms among patients with comorbid pain disorders (Seal et al., 2016).

In general, it appears that a relatively high percentage of VA users with OUD diagnoses receive OATs (Oliva, Harris, Trafton, & Gordon, 2012). Among 35,240 VA users diagnosed with opioid user disorders nationally in 2008, 22.2% received methadone and 5.1% received buprenorphine, although there was substantial variation among VA facilities, with the percentage of patients receiving an OAT ranging from none to 66% (Oliva et al., 2012). Interestingly, though buprenorphine became available on the VA formulary only in 2003 (Gordon et al., 2007) and rates of prescription increased drastically from 2004 to 2010, the rate of OAT treatment has remained steady at approximately a quarter of those with an OUD diagnosis (Oliva, Trafton, Harris, & Gordon, 2013). While naltrexone use among VA users increased between 2006 and 2009 (A. H. Harris et al., 2012), evaluation and implementation efforts have been targeted at treatment of alcohol use disorders rather than OUD (A. H. Harris et al., 2013).

Given historical concerns about OUD and PTSD as well as the lack of information about prevalence and the medical treatment of OUD patients with PTSD, our objective was to understand the use of medications for opioid dependence in a longitudinal cohort of VA users presenting with new episodes of PTSD and comorbid OUD. This included four specific aims: 1) To identify patients with comorbid PTSD and OUD and determine how

they differ from PTSD patients in general; 2) To determine the rate of OUD diagnosis in PTSD patients as well as the change in rate has changed over time; 3) To determine the rate of prescription of buprenorphine, methadone, and naltrexone in patients with PTSD as well as the change in rate over time; and 4) To determine how patient characteristics and health services use patterns influence whether patients with comorbid PTSD and OUD receive buprenorphine, methadone, or naltrexone.

2. Method

2.1 Data Source

We used the VA corporate data warehouse to identify patients with new PTSD treatment episodes from fiscal year 2004 through fiscal year 2013. We also obtained patient demographic information as well as encounter, diagnostic, and pharmacy data from the corporate data warehouse. The Dartmouth College Committee for the Protection of Human Subjects provided a waiver of informed consent, as this was a retrospective review, no patients were contacted, and all data were stored and analyzed on secure VA servers. The White River Junction VA Research and Development Committee and VA National Data Systems also approved this study.

2.2 Patients

We included VA users who received a primary diagnosis of PTSD at two or more outpatient encounters, at least one of which occurred in a mental health setting, over the course of 90 days between October 1, 2003 and September 30, 2013, and had not met this criterion during the prior two years. We examined one year of treatment receipt following the first diagnosis of the two qualifying diagnoses. When patients met the cohort inclusion criteria multiple times over the 10-year period, only their first episode was included. Patients who had any opioid abuse or dependence diagnosis in the year following their index PTSD diagnoses were classified as having OUD.

2.3 Medication Used

We examined all medications dispensed by VA pharmacies during the year following the index PTSD diagnosis. We identified prescriptions for naltrexone, buprenorphine, and buprenorphine-naltrexone combinations. Because the naltrexone in naltrexone-buprenorphine combinations is prescribed at low doses to prevent abuse, these prescriptions were not counted towards the naltrexone totals. Patients who attended methadone clinics were considered to have received methadone.

2.4 Covariates

We examined three groups of covariates. First, we examined patient factors including age, gender, marital status, race, military service era, rurality, VA disability rating, homelessness, and military exposures including combat and sexual trauma. Second, we examined treatment receipt factors including type of VA treatment setting (medical center versus community-based outreach clinic), number of outpatient primary care, mental health, and substance abuse visits, whether patients had at least one visit with a primary care, mental health, or substance abuse clinician with prescription privileges, residential substance abuse treatment,

inpatient admission for detoxification, and whether patients received an antidepressant that is effective for PTSD, including fluoxetine, sertraline, paroxetine, or venlafaxine (Jonas et al., 2013; Watts et al., 2013). Third, we examined medical comorbidity as summarized by the Charleston Comorbidity Index as well as relevant neurologic, psychiatric, and substance abuse comorbidities.

2.5 Analysis

First, we summarized cohort characteristics and compared patients with OUDs and those with no addiction diagnoses using t-test or χ^2 analysis, as appropriate. Second, we calculated annual rates of OUD diagnosis and utilization frequencies for each individual OUD medication for the overall 10-year period and for each individual fiscal year. Third, we developed multivariate logistic regression models to predict the odds of receiving each OUD medication, controlling for moderators listed above as well as year of the index episode in order to account for trends over time. We evaluated our regression models using the c-statistic. The c-statistic is an estimate of the discriminatory performance of a categorical statistical model and is equivalent to the area under the receiving operating characteristic curve when performing logistic regression (Fawcett, 2006; Swets, Dawes, & Monahan, 2000). A value of 0.5 represents no discrimination (akin to a coin flip); 0.7 is acceptable discrimination; 0.8 is excellent discrimination; 0.9 is outstanding discrimination; and 1.0 is perfect discrimination (Hosmer & Lemeshow, 2000).

Finally, we used publically available data from the National Survey on Drug Use and Health (NSDUH) for the years 2004 through 2013 to create an age and sex-matched non-VA population comparator for the rate of OUD, (SAMHSA, 2016). We classified NSDUH respondents by gender and five age categories (18-25, 26-34, 35-49, 50-64, and 65+). We assigned each group an OUD risk based on the prevalence of pain reliever or heroin abuse and dependence in the past year. We multiplied these risks by the number of patients in each relevant category among our VA PTSD cohort. The NSDUH does not have items regarding PTSD diagnoses. However, respondents can be classified as to whether they have any mental illness. Therefore, we created a contemporaneous age and sex matched general population rate for opioid disorder for those with any mental illness. A similar strategy has been previously used to contextualize the rate of diagnosed alcohol use disorders among VA users (A. H. Harris, Rubinsky, & Hoggatt, 2015).

3. Results

Among 731,520 patients identified as having PTSD between 2004 and 2013, 19,998 (2.7%) received an OUD diagnosis during their initial year of PTSD treatment. The proportion grew from 2.5% in 2004 to 3.4% in 2013, a 36.8% relative increase (Figure 1). By comparison, the rate of OUD among age-, sex-, and mental illness-matched NSDUH respondents between 2004 and 2013 was similar at 2.9%.

Patients with OUDs differed in many ways from the rest of the PTSD population (Table 1). While there was a statistically significant difference in every patient characteristic in this large dataset, many differences were large in magnitude. With regards to their demographic characteristics, patients with OUD were younger, less likely to be married, less likely to live

in rural settings, and less likely to have been exposed to combat. In addition, they were much more likely to be homeless and to have experienced sexual trauma while in the military. Patients with OUD used far more services than the rest of the PTSD population. They had more visits (especially mental health and substance abuse visits) and were more likely to see clinicians with prescription privileges (especially mental health and substance abuse clinicians). Patients with OUD were more likely to receive their care at a medical center (as opposed to a community-based outreach clinic). Not surprisingly, they were also more likely to be admitted for detoxification and residential substance abuse treatment. Finally, patients with OUD were more physically ill despite their younger age and had several fold higher rates of every neuropsychiatric and other substance use disorder diagnosis that we examined.

Among the 19,998 patients with new episodes of PTSD and a comorbid OUD diagnosis, 29.6% (n=5,913) received a medication for OUD. This included 25.8% (n=5,164) who received OATs, including buprenorphine (14.9%; n=2,972) and methadone (15.8%; n=3,167), as well as 5.0% (n=994) who received naltrexone. Over the 10-year time period, there were large relative increases in use of OATs (20.7% to 29.1%) and naltrexone (2.8% to 8.6%). Among OATs, an eleven-fold increase in the use of buprenorphine (2.2% to 22.7%) counteracted a more gradual decline in the use of methadone (19.3% to 12.7%). Importantly, the decrease in methadone use was a relative rather than total decline. From 2004 to 2013, the number of patients receiving methadone actually increased from 246 to 353, but at the same time the number of VA users with new episodes of PTSD who had comorbid OUD increased from 1,273 to 2,777 (Appendix 1). Almost all patients receiving naltrexone (87%) had an alcohol use disorder diagnosis. However, there was an increase in the use of naltrexone for patients without an alcohol use disorder diagnosis in the later years of the cohort, from 0.4% in 2009 to 1.2% in 2013.

Multivariate logistic regression models to predict the use of medications for opioid dependence in general or of specific agents had acceptable discriminative ability, with c-statistics of above 0.7 (Table 2). Those who received any medication for OUD (OATs or naltrexone) were younger, less likely to be rural, and more likely to have received substance use disorder services than those who did not receive a medication for OUD. They were generally less likely to have other mental health disorders. There was a mixed pattern of other substance use disorders, whereby they were less likely to have alcohol, marijuana, and amphetamine dependence but more likely to have nicotine, cocaine, and sedative dependence. Even after controlling for these factors, patients were more likely to receive a medication for OUD in successive years.

Different patterns emerged in predicting the choice of specific agents among the subgroup of 5,913 patients who initiated any medication for OUD. Patients who received buprenorphine were younger and more likely to be rural, white, and married. They were more likely to have visits with a general psychiatrist rather than a substance abuse specialist. They were less likely to have psychotic disorders, traumatic brain injuries, alcohol dependence, and cocaine dependence. Controlling for these factors, patients were far more likely to receive buprenorphine as opposed to other agents in successive years. Patients who received methadone were older, urban, unmarried, from racial and ethnic minorities, and were more likely to see substance abuse specialists. They were less likely to be diagnosed with mood

and anxiety disorders, as well as alcohol and hallucinogen dependence. Controlling for these factors, patients were much less likely to receive methadone as opposed to other agents as the years progressed. Finally, patients who received naltrexone tended to be married white women. They were more likely to receive inpatient detoxification, but less likely to see a substance abuse specialist. They were more likely to have mood disorders, traumatic brain injury, and marijuana dependence. The largest predictor of naltrexone receipt was comorbid alcohol use disorder. Controlling for these factors, there was no change in patients' likelihood of receiving naltrexone as opposed to other agents in successive fiscal years.

4. Discussion

A small but increasing proportion of VA patients newly identified with PTSD is also diagnosed with an OUD. The rate of OUD in our cohort of 2.7% was consistent with a rate of 2.9% in a contemporaneous age, gender, and mental illness-matched national sample of NSDUH participants. It is unclear whether the increase in rate of OUD in our cohort from 2.5% to 3.4% between 2004 and 2013 represents an actual increase in the prevalence of OUD among veterans with PTSD or simply an increase in recognition and hence increased diagnosis. Most published data on substance use disorder diagnoses in the VA user population does not separate OUD from other drug use disorders (Lan et al., 2016). Several studies have presented data on OUD diagnoses in the overall VA user population, although methods have varied. While Gordon et al. (2007) documented a 7% increase in the number of VA users with an OUD diagnosis between the 2003 and 2005 fiscal years, and Oliva et al. (2013) documented a 45% increase in OUD diagnoses between the 2004 and 2010 fiscal year, neither study presents a denominator data for all VA users. Most recently, Peglow et al. (2017) presented an OUD diagnostic rate of 17.7 per 1,000 VA users in the 2012 fiscal year. This compares to a rate of 32.6 per 1,000 in our cohort during the 2012 fiscal year (Appendix 1). Thus, while no published data are available to compare trends over time, the OUD diagnosis rate does appear to be higher in our cohort of patients with new PTSD episodes than in the overall VA user population.

There were large increases in the prescription of medications for OUD among patients with PTSD between 2004 and 2013. The substantial increase in buprenorphine use generally mirrors trends in treatment of OUD overall in the VA (Oliva et al., 2013). It appears VA patients with PTSD who are younger, rural, married, and white tended to receive buprenorphine while those who are older, urban, unmarried, and from minority populations tended to receive methadone. The total number of patients receiving methadone increased only slightly, while the total number receiving buprenorphine increased substantially. Given growth in the population of patients with comorbid PTSD and OUD, this meant that patients were less likely to receive methadone and more likely to receive buprenorphine over time. This lends support to the idea that new populations of patients are gaining access to OAT primary through buprenorphine.

The reason for differential use in OATs was unclear. It may reflect challenges in developing new methadone clinics and expanding existing methadone clinics. It may reflect relative advantages of buprenorphine such as the ability for patients to make less frequent visits to physicians who are not necessarily substance abuse specialists, which widens availability by

eliminating the need to visit specialized treatment clinics (Volkow, Frieden, Hyde, & Cha, 2014). Or it might suggest that buprenorphine is preferred by patients in our cohort due to possible impacts on PTSD symptoms (Seal et al., 2016). Our findings are similar to those of Oliva et al. (2013) in the overall VA user population, which indicate that “office-based” OAT treatment (buprenorphine) is growing more quickly than “clinic-based” OAT treatment (methadone). Recent reviews by evidence-based medicine authorities indicate that buprenorphine and methadone have similar effectiveness. For example, the Canadian Agency for Drugs and Technologies in Health determined that buprenorphine may have similar clinical effects as methadone and that it may be more cost-effective than methadone (CADTH, 2013). A recent Cochrane Collaboration review indicated that the buprenorphine and methadone are no different in effectiveness (Mattick, Breen, Kimber, & Davoli, 2014). Therefore, this may be a scenario of clinical equipoise, where intervention characteristics have favored growth in the use of buprenorphine over methadone.

The increase in naltrexone use mirrors that previously reported for alcohol use disorders (A. H. Harris et al., 2012), and our analyses indicate that alcohol use disorder comorbidity is driving this finding. The increase in recognition and treatment of AUD may be the result of the implementation of an electronic decision support tool for the identification and treatment of alcohol use disorders in 2008 (Lapham et al., 2012). The small non-significant increase in use of naltrexone in patients without an AUD in fiscal years 2011-2013 (Table 2) could be related to 2010 FDA approval of a long-acting injection of naltrexone. While the efficacy of oral naltrexone in the treatment of OUD has been called into question (Lobmaier, Gossop, Waal, & Bramness, 2010), the long acting injectable formulation appears to be effective across OUD populations (Krupitsky et al., 2011; Nunes et al., 2015).

Overall rates of substance use disorders were high in Veterans with comorbid PTSD and OUD. Nearly 60% had alcohol use disorder. Similarly elevated rates were seen for cocaine (34.8%), marijuana (27.5%), sedatives (13.4%), and amphetamines (7.6%). In each case the rates were higher in patients with PTSD and OUD than in patients with PTSD and no OUD. A similar trend was seen in psychiatric comorbidities, with high rates of major depressive disorder (73.5%), non-PTSD anxiety disorders (39.6%), and psychotic disorders (12.7%). Again patients with PTSD and OUD had a higher rates compared to patients with PTSD and no OUD. Taken together, this suggests that patients with PTSD and OUD also have a substantial higher risk of other SUDs and other mental health disorders.

While findings are consistent with research on OUD medication prescribing in the VA as a whole, there are several important differences between our study and key existing studies on OAT prescription (Gordon et al., 2007; Oliva et al., 2013; Peglow et al., 2017). Firstly, existing studies focus on facility-level (Gordon et al., 2007; Oliva et al., 2013) or state-level (Peglow et al., 2017) implementation, and do not consider patient factors. Secondly, these studies either do not consider the overall rate of OUD diagnosis (Gordon et al., 2007; Oliva et al., 2013), or do not measure changes in the rate over time (Peglow et al., 2017). Thirdly, none of the three studies consider naltrexone use. Existing research on naltrexone use does consider patient factors (A. H. Harris et al., 2012). However, our work is unique in that it shows that naltrexone prescription is driven by alcohol use disorder, even though it is also indicated for OUD. Finally, there appears to be a particularly high rate of OUD diagnoses in

the VA PTSD population. Therefore, it is especially important to understand the use of appropriate treatments in this subgroup.

While the VA is a unique healthcare system, recent research shows that VA OAT treatment is consistent with community practice at the local health system level (Peglow et al., 2017). Furthermore, as “expanding screening, diagnosis, and treatment of opioid use disorders, with an emphasis on increasing access to medication-assisted treatment” is the third of four priority areas in the Centers for Medicare & Medicaid Services’ Opioid Misuse Strategy (CMS, 2017), our work will be instructive for other health systems attempting to understand and improve OUD diagnosis and treatment in dual-diagnosis populations.

Our work comes with a number of limitations. Most notably we relied on the clinical diagnosis to establish rates of both PTSD and OUD. In the case of PTSD, the VA has a screening process in place (Shiner et al., 2014), and there are published data regarding the performance characteristics of a typical clinical diagnosis relative to a standardized assessment (Gravely et al., 2011; Holowka et al., 2014). However, there is no screening program for OUD and no literature outlining the sensitivity and specificity of clinical diagnosis of OUD. Thus, it is likely that some patients with OUD did not receive that clinical diagnosis, and we have no way to estimate that gap as there are no epidemiologic surveys on the prevalence of OUD in the VA user population. In order to provide reliable matched comparison data from the NSDUH, we had to pool respondents across years, so we were unable to determine a comparison trend.

A second limitation is that confounding could account differences in OUD diagnosis in several groups. With regards to rurality, prior research has shown that a move towards regional concentration of VA substance use disorder treatment facilities in urban areas was associated with a disparity in treatment access for rural VA users (Wallace, West, Booth, & Weeks, 2007), who are also more likely to obtain additional care outside of the VA (West, Weeks, & Charlton, 2017). This could lead to confounding in OUD diagnosis by rurality both because substance use disorder specialists may be better able to detect and diagnose OUD, and because those diagnoses may occur outside of the VA system. Community based outreach clinic users, many of whom live in rural areas, are similarly more likely to obtain part of their care outside of the VA system than VA medical center users (Liu et al., 2010). With regards to physical comorbidity, patients with diagnosed OUDs had far more visits. It is possible that patients who had increased contact with the medical system were subject to over-diagnosis of incidental disease (Carter et al., 2015).

A third limitation is that we selected patients for cohort membership based on receiving at least two diagnoses of PTSD, with at least one in a mental health clinic. This resulted in a cohort of patients who had high use of VA services. For example, the average patient in the cohort had approximately 18 visits to primary care, mental health, and substance abuse clinics. This frequency of contact may have provided an unusually high number of opportunities to detect and treat opioid use disorders. As a result there could be an ecologic fallacy in which higher healthcare utilizers could appear to have higher rates of OUD.

Our limitations point out the need for additional research in the related areas of epidemiology and clinical screening. Most notably there is a need for rigorous epidemiological work related to substance use disorders co-occurring with PTSD. The substantial number of both mental health and substance abuse comorbidities in patients with co-occurring PTSD and OUD suggests that highly specialized and intensive approaches may be needed for these complex patients.

While screening for opioid misuse represents an important area for research, there is insufficient evidence to recommend the implementation of a universal screening program at this time. There are three core issues in the evaluation of the potential benefits of screening programs: the probability of an adverse health outcome without screening, the degree to which screening identifies all people who would suffer the adverse health outcome, and the magnitude of the incremental benefit of earlier versus later treatment resulting from screening (R. Harris, Sawaya, Moyer, & Calonge, 2011). The adverse health outcomes of opioid misuse are well known and range from the very direct, such as opioid dependence, overdose, and death (Compton, Jones, & Baldwin, 2016)—to consequences of associated health behaviors, such as transmission of blood-borne pathogens in people who inject opioids (Lake & Kennedy, 2016)—to social and financial costs, such as increases in crime and medical expenditures (Ruetsch, 2010). However, less is known about the performance of screening instruments in the detection of opioid misuse, and whether screening leads to earlier treatment or increased use of treatment. For example, the United States Preventive Services Task Force (USPSTF) review of screening instruments for illicit drug use in primary care settings concluded that while the sensitivity and specificity of several instruments was acceptable, their predictive value in low prevalence populations is highly varied or unknown (Lanier & Ko, 2008). Therefore, the USPSTF assigned a insufficient evidence rating to screening for illicit drug use in adult primary care populations, due to “the absence of adequate evidence that standardized instruments for identifying asymptomatic illicit drug users are clinically useful in primary care settings, and that those identified through screening will benefit from treatments known to be effective” (Polen, Whitlock, Wisdom, Nygren, & Bougatsos, 2008). Similarly, the 2015 VA/DoD clinical practice guideline for the management of substance use disorders focuses screening recommendations on alcohol misuse rather than opioid misuse (Drexler, Kivlahan, & Perry, 2015). Given lack of data to support a screening program at this time, it may be more critical to increase the proportion of patients with an OUD who receives appropriate treatment.

Our work indicates that both identification of OUD and use of appropriate medications are increasing among patients with PTSD. Buprenorphine use is responsible for most treatment and growth in treatment. Longitudinal epidemiologic surveys are needed to understand the prevalence of OUD and other substance use disorders in the VA PTSD population.

Acknowledgements:

Not Applicable; this work has not been previously presented in any form.

Funding: This project was supported was supported by a Department of Veterans Affairs Health Services Research and Development Career Development Award to Dr. Shiner (CDA11-263).

Appendix

VA Author Manuscript

VA Author Manuscript

VA Author Manuscript

Appendix 1:

Data Table for Use of Medications Among Veterans with New Episodes of PTSD and Comorbid OUD, 2004–2013

Fiscal Year	Overall	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Change Abs. ^a	Change Rel. ^b
New PTSD Episode	731,520	51,750	60,078	59,048	69,604	77,631	82,813	84,850	83,921	79,279	82,546		
Comorbid OUD	2.7% (19,998)	2.5% (1,273)	2.3% (1,410)	2.3% (1,345)	2.3% (1,614)	2.5% (1,962)	2.7% (2,206)	2.8% (2,346)	3.0% (2,478)	3.3% (2,587)	3.4% (2,777)	0.9%	36.8%
Buprenorphine	14.9% (2,972)	2.0% (26)	3.8% (53)	6.6% (89)	7.9% (128)	11.9% (234)	14.5% (319)	20.1% (472)	19.5% (482)	20.8% (539)	22.7% (630)	20.7%	1,035.0%
Methadone MAT	15.8% (3,167)	19.3% (246)	22.1% (311)	18.5% (249)	18.8% (304)	18.7% (366)	14.1% (310)	14.7% (346)	13.8% (343)	13.1% (339)	12.7% (353)	-6.6%	-34.2%
Any OAT	25.8% (5,164)	20.7% (263)	24.5% (346)	22.1% (297)	23.4% (377)	25.0% (490)	24.5% (540)	28.3% (665)	26.8% (665)	27.6% (713)	29.1% (808)	8.4%	40.6%
Naltrexone	5.0% (994)	2.8% (36)	2.8% (39)	3.4% (46)	2.9% (47)	3.3% (65)	3.4% (76)	5.4% (127)	5.9% (147)	6.6% (171)	8.6% (240)	5.8%	205.6%
(With AUD)	4.3% (865)	2.6% (33)	2.6% (36)	3.0% (41)	2.6% (42)	3.0% (58)	3.1% (68)	4.9% (114)	5.1% (127)	5.3% (138)	7.5% (208)	4.9%	188.9%
(Without AUD)	0.6% (129)	0.2% (3)	0.2% (3)	0.4% (5)	0.3% (5)	0.4% (7)	0.4% (8)	0.6% (13)	0.8% (20)	1.3% (33)	1.2% (32)	0.9%	389.0%
OAT or Naltrexone	29.6% (5,913)	22.6% (288)	27.1% (382)	25.0% (336)	25.9% (418)	27.3% (535)	27.2% (601)	32.6% (764)	31.2% (774)	32.5% (841)	35.1% (974)	12.5%	55.3%

^a Absolute change in frequency of use from fiscal years 2004 through 2013; negative values represent decreased frequency over time.^b Relative change in frequency of use from fiscal years 2004 through 2013; negative values represent decreased frequency over time.

Note. PTSD=Posttraumatic Stress Disorder; OUD=Opioid Use Disorder; MAT=Medication Assisted Treatment; OAT=Opioid Agonist Treatment; AUD=Alcohol Use Disorder

References

- APA. (2013). Diagnostic and statistical manual of mental disorders : DSM-5 (5th ed.). Arlington, VA: American Psychiatric Association.
- Arnsten AFT (2009). Stress signalling pathways that impair prefrontal cortex structure and function. *Nature Reviews Neuroscience*, 10(6), 410–422. doi: 10.1038/nrn2648 [PubMed: 19455173]
- Beckham JC, Crawford AL, Feldman ME, Kirby AC, Hertzberg MA, Davidson JRT, & Moore SD (1997). Chronic posttraumatic stress disorder and chronic pain in Vietnam combat veterans. *Journal of Psychosomatic Research*, 43(4), 379–389. doi: 10.1016/S0022-3999(97)00129-3 [PubMed: 9330237]
- CADTH. (2013). Suboxone versus Methadone for the Treatment of Opioid Dependence: A Review of the Clinical and Cost-effectiveness. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/24716256>.
- Carter SM, Rogers W, Heath I, Degeling C, Doust J, & Barratt A (2015). The challenge of overdiagnosis begins with its definition. *BMJ*, 350, h869. doi: 10.1136/bmj.h869 [PubMed: 25740625]
- Chou R, Fanciullo GJ, Fine PG, Adler JA, Ballantyne JC, Davies P, ... O, Amer Pain Soc Amer Acad Pain Med. (2009). Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. *Journal of Pain*, 10(2), 113–130. doi: 10.1016/j.jpain.2008.10.008 [PubMed: 19187889]
- CMS. (2017). Opioid Misuse Strategy. Washington, DC: Centers for Medicare and Medicaid Services Retrieved from <https://http://www.cms.gov/Outreach-and-Education/Outreach/Partnerships/Downloads/CMS-Opioid-Misuse-Strategy-2016.pdf>.
- Compton WM, Jones CM, & Baldwin GT (2016). Relationship between Nonmedical Prescription-Opioid Use and Heroin Use. *N Engl J Med*, 374(2), 154–163. doi: 10.1056/NEJMra1508490 [PubMed: 26760086]
- Cornish JW, McNicholas LF, & O'Brien CP (2004). Treatment of Substance-Related Disorders In Schatzberg AF & Nemeroff CB (Eds.), *The American Psychiatric Publishing Textbook of Psychopharmacology* (pp. 1009–1029). Washington, DC: American Psychiatric Publishing.
- Drexler K, Kivlahan D, & Perry C (2015). VA/DoD clinical practice guideline for the management of substance use disorders. Retrieved April 11, 2016, from <http://www.healthquality.va.gov>
- Edlund MJ, Steffick D, Hudson T, Harris KM, & Sullivan M (2007). Risk factors for clinically recognized opioid abuse and dependence among veterans using opioids for chronic non-cancer pain. *Pain*, 129(3), 355–362. doi: 10.1016/j.pain.2007.02.014 [PubMed: 17449178]
- Fawcett T (2006). An Introduction to ROC Analysis. *Pattern Recognition Letters*, 27, 861–874.
- Friedman MJ (2015). The Human Stress Response In Friedman MJ & Bernardy NC (Eds.), *A Practical Guide to PTSD Treatment: Pharmacological and Psychotherapeutic Approaches* (pp. 9–19). Washington, DC: American Psychological Association.
- Friedman MJ, Lowry P, & Ruzek J (2010). VA/DoD clinical practice guidelines for the management of post-traumatic stress. Retrieved April 11, 2016, from <http://www.healthquality.va.gov>
- Galea S, Nandi A, & Vlahov D (2005). The epidemiology of post-traumatic stress disorder after disasters. *Epidemiol Rev*, 27, 78–91. doi: 10.1093/epirev/mxi003 [PubMed: 15958429]
- Goldstein LE, Rasmusson AM, Bunney BS, & Roth RH (1996). Role of the amygdala in the coordination of behavioral, neuroendocrine, and prefrontal cortical monoamine responses to psychological stress in the rat. *Journal of Neuroscience*, 16(15), 4787–4798. [PubMed: 8764665]
- Gordon AJ, Trafton JA, Saxon AJ, Gifford AL, Goodman F, Calabrese VS, ... Buprenorphine Work Group of the Substance Use Disorders Quality Enhancement Research, Initiative. (2007). Implementation of buprenorphine in the Veterans Health Administration: results of the first 3 years. *Drug Alcohol Depend*, 90(2-3), 292–296. doi: 10.1016/j.drugalcdep.2007.03.010 [PubMed: 17493771]
- Gravely AA, Cutting A, Nugent S, Grill J, Carlson K, & Spooner M (2011). Validity of PTSD diagnoses in VA administrative data: comparison of VA administrative PTSD diagnoses to self-reported PTSD Checklist scores. *J Rehabil Res Dev*, 48(1), 21–30. [PubMed: 21328160]
- Harris AH, Ellerbe L, Reeder RN, Bowe T, Gordon AJ, Hagedorn H, ... Trafton JA (2013). Pharmacotherapy for alcohol dependence: perceived treatment barriers and action strategies among

- Veterans Health Administration service providers. *Psychol Serv*, 10(4), 410–419. doi: 10.1037/a0030949 [PubMed: 23356858]
- Harris AH, Oliva E, Bowe T, Humphreys KN, Kivlahan DR, & Trafton JA (2012). Pharmacotherapy of alcohol use disorders by the Veterans Health Administration: patterns of receipt and persistence. *Psychiatr Serv*, 63(7), 679–685. doi: 10.1176/appi.ps.201000553 [PubMed: 22549276]
- Harris AH, Rubinsky AD, & Hoggatt KJ (2015). Possible Alternatives to Diagnosis-Based Denominators for Addiction Treatment Quality Measures. *Journal of Substance Abuse Treatment*, 58, 62–66. doi: 10.1016/j.jsat.2015.06.004 [PubMed: 26251046]
- Harris R, Sawaya GF, Moyer VA, & Calonge N (2011). Reconsidering the criteria for evaluating proposed screening programs: reflections from 4 current and former members of the U.S. Preventive services task force. *Epidemiol Rev*, 33, 20–35. doi: 10.1093/epirev/mxr005 [PubMed: 21666224]
- Holowka DW, Marx BP, Gates MA, Litman HJ, Ranganathan G, Rosen RC, & Keane TM (2014). PTSD diagnostic validity in Veterans Affairs electronic records of Iraq and Afghanistan veterans. *J Consult Clin Psychol*, 82(4), 569–579. doi: 10.1037/a0036347 [PubMed: 24731235]
- Hosmer DW, & Lemeshow S (2000). *Applied Logistic Regression* (2nd ed.). New York: John Wiley and Sons.
- Jonas DE, Cusack K, Forneris CA, Wilkins TM, Sonis J, Middleton JC, ... Gaynes BN (2013). *Psychological and Pharmacological Treatments for Adults With Posttraumatic Stress Disorder (PTSD)*. Rockville (MD).
- Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, & Walters EE (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*, 62(6), 593–602. doi: 10.1001/archpsyc.62.6.593 [PubMed: 15939837]
- Kessler RC, Sonnega A, Bromet E, Hughes M, & Nelson CB (1995). Posttraumatic stress disorder in the National Comorbidity Survey. *Arch Gen Psychiatry*, 52(12), 1048–1060. [PubMed: 7492257]
- Krupitsky E, Nunes EV, Ling W, Illeperuma A, Gastfriend DR, & Silverman BL (2011). Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial. *Lancet*, 377(9776), 1506–1513. doi: 10.1016/S0140-6736(11)60358-9 [PubMed: 21529928]
- Lake S, & Kennedy MC (2016). Health outcomes associated with illicit prescription opioid injection: A systematic review. *J Addict Dis*, 35(2), 73–91. doi: 10.1080/10550887.2015.1127712 [PubMed: 26670724]
- Lan CW, Fiellin DA, Barry DT, Bryant KJ, Gordon AJ, Edelman EJ, ... Marshall BD (2016). The epidemiology of substance use disorders in US Veterans: A systematic review and analysis of assessment methods. *Am J Addict*, 25(1), 7–24. doi: 10.1111/ajad.12319 [PubMed: 26693830]
- Lanier D, & Ko S (2008). *Screening in Primary Care Settings for Illicit Drug Use: Assessment of Screening Instruments: A Supplemental Evidence Update for the U.S. Preventive Services Task Force*. Rockville (MD).
- Lapham GT, Achtmeyer CE, Williams EC, Hawkins EJ, Kivlahan DR, & Bradley KA (2012). Increased documented brief alcohol interventions with a performance measure and electronic decision support. *Med Care*, 50(2), 179–187. doi: 10.1097/MLR.0b013e3181e35743 [PubMed: 20881876]
- Liu CF, Chapko M, Bryson CL, Burgess JF, Jr., Fortney JC, Perkins M, ... Maciejewski ML (2010). Use of outpatient care in Veterans Health Administration and Medicare among veterans receiving primary care in community-based and hospital outpatient clinics. *Health Serv Res*, 45(5 Pt 1), 1268–1286. doi: 10.1111/j.1475-6773.2010.01123.x [PubMed: 20831716]
- Lobmaier P, Gossop M, Waal H, & Bramness J (2010). The pharmacological treatment of opioid addiction--a clinical perspective. *Eur J Clin Pharmacol*, 66(6), 537–545. doi: 10.1007/s00228-010-0793-6 [PubMed: 20169438]
- Magruder KM, Frueh BC, Knapp RG, Davis L, Hamner MB, Martin RH, ... Arana GW (2005). Prevalence of posttraumatic stress disorder in Veterans Affairs primary care clinics. *Gen Hosp Psychiatry*, 27(3), 169–179. doi: S0163-8343(04)00136-7 [pii]10.1016/j.genhosppsych.2004.11.001 [PubMed: 15882763]

- Mattick RP, Breen C, Kimber J, & Davoli M (2014). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst Rev*(2), CD002207. doi: 10.1002/14651858.CD002207.pub4 [PubMed: 24500948]
- Mueser KT, Goodman LB, Trumbetta SL, Rosenberg SD, Osher f C, Vidaver R, ... Foy DW (1998). Trauma and posttraumatic stress disorder in severe mental illness. *J Consult Clin Psychol*, 66(3), 493–499. [PubMed: 9642887]
- Nunes EV, Krupitsky E, Ling W, Zummo J, Memisoglu A, Silverman BL, & Gastfriend DR (2015). Treating Opioid Dependence With Injectable Extended-Release Naltrexone (XR-NTX): Who Will Respond? *J Addict Med*, 9(3), 238–243. doi: 10.1097/ADM.000000000000125 [PubMed: 25901451]
- Oliva EM, Harris AH, Trafton JA, & Gordon AJ (2012). Receipt of opioid agonist treatment in the Veterans Health Administration: facility and patient factors. *Drug Alcohol Depend*, 122(3), 241–246. doi: 10.1016/j.drugalcdep.2011.10.004 [PubMed: 22115887]
- Oliva EM, Trafton JA, Harris AH, & Gordon AJ (2013). Trends in opioid agonist therapy in the Veterans Health Administration: is supply keeping up with demand? *Am J Drug Alcohol Abuse*, 39(2), 103–107. doi: 10.3109/00952990.2012.741167 [PubMed: 23421571]
- Outcalt SD, Ang DC, Wu JW, Sargent C, Yu ZS, & Bair MJ (2014). Pain experience of Iraq and Afghanistan Veterans with comorbid chronic pain and posttraumatic stress. *J Rehabil Res Dev*, 51(4), 559–570. doi: 10.1682/JRRD.2013.06.0134 [PubMed: 25144169]
- Peglow SL, Petrakis I, & Rosenheck RA (2017). Opioid Agonist Treatment in the Veterans Health Administration: Is Health Care Local? *Journal of Public Mental Health*, 16(1), 28–36.
- Phifer J, Skelton K, Weiss T, Schwartz AC, Wingo A, Gillespie CF, ... Ressler KJ (2011). Pain symptomatology and pain medication use in civilian PTSD. *Pain*, 152(10), 2233–2240. doi: 10.1016/j.pain.2011.04.019 [PubMed: 21665366]
- Pietrzak RH, Goldstein RB, Southwick SM, & Grant BF (2011). Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. *J Anxiety Disord*, 25(3), 456–465. doi: 10.1016/j.janxdis.2010.11.010 [PubMed: 21168991]
- Pitman RK, Rasmusson AM, Koenen KC, Shin LM, Orr SP, Gilbertson MW, ... Liberzon I (2012). Biological studies of post-traumatic stress disorder. *Nature Reviews Neuroscience*, 13(11), 769–787. doi: 10.1038/nrn3339 [PubMed: 23047775]
- Polen MR, Whitlock EP, Wisdom JP, Nygren P, & Bougatsos C (2008) Screening in Primary Care Settings for Illicit Drug Use: Staged Systematic Review for the United States Preventive Services Task Force. Rockville (MD).
- Prior K, Mills K, Ross J, & Teesson M (2016). Substance use disorders comorbid with mood and anxiety disorders in the Australian general population. *Drug Alcohol Rev* doi: 10.1111/dar.12419
- Rasmusson AM, & Shalev AY (2014). Integrating the Neuroendocrinology, Neurochemistry, and Neuroimmunology of PTSD to Date and the Challenges Ahead In Friedman MJ, Keane TM & Resick PA (Eds.), *Handbook of PTSD* (Second ed., pp. 275–299). New York, NY: The Guilford Press.
- Ruetsch C (2010). Empirical view of opioid dependence. *J Manag Care Pharm*, 16(1 Suppl B), S9–13. [PubMed: 20146549]
- SAMHSA. (2016). National Survey on Drug Use and Health. from <https://nsduhweb.rti.org>
- Seal KH, Cohen G, Waldrop A, Cohen BE, Maguen S, & Ren L (2011). Substance use disorders in Iraq and Afghanistan veterans in VA healthcare, 2001–2010: Implications for screening, diagnosis and treatment. *Drug Alcohol Depend*, 116(1-3), 93–101. doi: 10.1016/j.drugalcdep.2010.11.027 [PubMed: 21277712]
- Seal KH, Maguen S, Bertenthal D, Batki SL, Striebel J, Stein MB, Neylan TC (2016). Observational Evidence for Buprenorphine's Impact on Posttraumatic Stress Symptoms in Veterans With Chronic Pain and Opioid Use Disorder. *Journal of Clinical Psychiatry*, 77(9), 1182–1188. doi: 10.4088/JCP.15m09893 [PubMed: 27035058]
- Shiner B, Tang C, Trapp AC, Konrad R, Bar-On I, & Watts BV (2014). The provision of mental health treatment after screening: exploring the relationship between treatment setting and treatment

- intensity. *Gen Hosp Psychiatry*, 36(6), 581–588. doi: 10.1016/j.genhosppsy.2014.07.009 [PubMed: 25138536]
- Swets JA, Dawes RM, & Monahan J (2000). Better decisions through science. *Sci Am*, 283(4), 82–87.
- Vanderkolk BA (1994). The Body Keeps the Score - Memory and the Evolving Psychobiology of Posttraumatic Stress. *Harvard Review of Psychiatry*, 1(5), 253–265. doi: Doi 10.3109/10673229409017088 [PubMed: 9384857]
- Volkow ND, Frieden TR, Hyde PS, & Cha SS (2014). Medication-assisted therapies--tackling the opioid-overdose epidemic. *N Engl J Med*, 370(22), 2063–2066. doi: 10.1056/NEJMp1402780 [PubMed: 24758595]
- Wallace AE, West AN, Booth BM, & Weeks WB (2007). Unintended consequences of regionalizing specialized VA addiction services. *Psychiatr Serv*, 58(5), 668–674. doi: 10.1176/ps.2007.58.5.668 [PubMed: 17463348]
- Watts BV, Schnurr PP, Mayo L, Young-Xu Y, Weeks WB, & Friedman MJ (2013). Meta-analysis of the efficacy of treatments for posttraumatic stress disorder. *J Clin Psychiatry*, 74(6), e541–550. doi: 10.4088/JCP.12r08225 [PubMed: 23842024]
- West AN, Weeks WB, & Charlton ME (2017). Differences Among States in Rural Veterans' Use of VHA and Non-VHA Hospitals. *J Rural Health*, 33(1), 32–40. doi: 10.1111/jrh.12152 [PubMed: 26449177]

Figure 1:
Detection of OUD among Patients with New PTSD Episodes

Figure 2:
Medication use among Patients with New PTSD Episodes and OUD

Table 1:

VA Users with New Episodes of PTSD Care from 2004-2013 by Opioid Dependence

		Category	
	Overall (731,520)	Opioid Dependence Diagnosis (19,998)	No Opioid Dependence Diagnosis (711,522)
Demographic Characteristics			
Age, M (SD) **	49.9 (15.4)	45.2 (13.5)	50.0 (15.4)
Men, % (n) **	91.5 (669,663)	92.7 (18,544)	91.5 (651,119)
Married, % (n) **	53.2 (389,262)	27.6 (5,523)	53.9 (383,739)
White Non-Hispanic, % (n) **	62.6 (457,673)	64.7 (12,935)	62.5 (444,738)
OEF/OIF/OND Veteran, % (n) **	28.5 (208,796)	27.5 (5,490)	28.6 (203,279)
Rural, % (n) **	35.3 (258,177)	26.0 (5,195)	35.6 (252,982)
Combat Exposure, % (n) **	32.8 (239,686)	28.7 (5,730)	32.9 (233,956)
Sexual Trauma while in Military, % (n) **	9.0 (66,004)	13.2 (2,637)	8.9 (63,367)
VA Disability Level 70 or greater, % (n) **	59.0 (431,632)	49.9 (9,986)	59.3 (421,646)
Homeless, % (n) **	5.0 (36,875)	25.7 (5,131)	4.5 (31,744)
Service Use Characteristics			
Plurality of Care at a VA Medical Center, % (n) **	62.2 (455,184)	82.4 (16,484)	61.7 (438,700)
Plurality of Care at a CBOC, % (n) **	28.6 (209,086)	12.1 (2,410)	29.0 (206,676)
Primary Care Visits, M (SD) **	3.5 (3.5)	4.7 (4.9)	3.4 (3.4)
Mental Health Visits, M (SD) **	12.6 (15.1)	22.6 (24.7)	12.3 (14.7)
Substance Abuse Visits, M (SD) **	3.0 (13.1)	28.9 (45.9)	2.3 (9.8)
At least one visit with a primary care prescriber, % (n) *	49.2 (359,940)	48.3 (9,667)	49.2 (350,273)
At least one visit with a mental health prescriber, % (n) **	39.9 (291,941)	46.9 (9,387)	39.7 (282,554)
At least one visit with a substance abuse prescriber, % (n) ***	2.4 (17,852)	19.4 (3,873)	2.0 (13,979)
Residential Substance Abuse Treatment, % (n) **	0.7 (4,940)	6.6 (1,316)	0.5 (3,624)
Inpatient Admission for Detoxification, % (n) **	1.9 (13,538)	19.3 (3,860)	1.4 (9,678)
Receipt of Effective Antidepressant for PTSD, % (n) **	44.6 (326,470)	52.3 (10,451)	44.4 (316,019)
Comorbid Diagnoses			
Charlson Comorbidity Index 1 or greater, % (n) **	24.4 (178,575)	30.2 (6,039)	24.2 (172,536)
Pain Disorder, % (n) **	63.6 (464,900)	78.5 (15,694)	63.1 (449,206)
Headache Disorder, % (n) **	23.0 (168,461)	32.6 (6,516)	22.8 (161,945)
Psychotic Disorders, % (n) **	4.6 (33,919)	12.7 (2,538)	4.4 (31,381)
Bipolar Mood Disorders, % (n) **	6.2 (45,407)	18.1 (3,620)	5.9 (41,787)
Depressive Mood Disorders, % (n) **	58.8 (430,467)	73.5 (14,690)	58.4 (415,777)
Non-PTSD Anxiety Disorders, % (n) **	26.1 (191,098)	39.6 (7,924)	25.7 (183,174)

		Category	
		Opioid Dependence Diagnosis (19,998)	No Opioid Dependence Diagnosis (711,522)
Traumatic Brain Injury and Cognitive Disorders, % (n) **	10.6 (77,739)	16.4 (3,280)	10.5 (74,459)
Personality Disorders, % (n) **	4.0 (29,272)	16.9 (3,382)	3.6 (25,890)
Nicotine Use Disorder, % (n) **	39.6 (289,884)	75.2 (15,048)	38.6 (274,796)
Alcohol Use Disorder, % (n) **	21.5 (157,307)	59.6 (11,914)	20.4 (145,393)
Marijuana Use Disorder, % (n) **	5.4 (39,168)	27.5 (5,493)	4.7 (33,675)
Cocaine Use Disorder, % (n) **	4.1 (29,976)	34.8 (6,969)	3.2 (23,007)
Amphetamine Use Disorder, % (n) **	0.8 (5,973)	7.6 (1,524)	0.6 (4,449)
Tranquilizer & Sedative Use Disorder, % (n) **	0.7 (5,156)	13.4 (2,678)	0.3 (2,478)
Hallucinogen Use Disorder, % (n) **	0.1 (900)	1.4 (284)	0.1 (616)

Note. M=mean, SD=standard deviation;

*
p<0.05

**
p<0.001

Table 2:

Predictors of Medication Receipt among VA Users with New Episodes of PTSD Care and Comorbid OUD

	All (n=19,998)	Received Specific Medication (n=5,913)		
Model Performance (c-statistic)	Any Agent OR (95% CI) c=0.71	Buprenorphine OR (95% CI) c=0.78	Methadone OR (95% CI) c=0.76	Naltrexone OR (95% CI) c=0.77
Patient Characteristics				
Male Gender	1.14 (0.99-1.33)	0.89 (0.68-1.17)	1.26 (0.97-1.65)	0.66 (0.48-0.90)
Married	0.95 (0.88-1.03)	1.19 (1.03-1.37)	0.76 (0.66-0.87)	1.29 (1.08-1.54)
White Non-Hispanic	1.00 (0.93-1.08)	1.80 (1.57-2.07)	0.63 (0.55-0.73)	1.26 (1.05-1.52)
Age 30-45 versus 18-29	0.78 (0.69-0.87)	0.74 (0.61-0.90)	1.02 (0.85-1.23)	0.88 (0.70-1.11)
Age 45-60 versus 18-29	0.67 (0.59-0.77)	0.42 (0.33-0.53)	1.49 (1.18-1.88)	0.76 (0.57-1.01)
Age 61+ versus 18-29	0.53 (0.45-0.63)	0.39 (0.29-0.53)	1.73 (1.28-2.33)	0.70 (0.47-1.05)
OEF/OIF/OND Veteran	0.99 (0.87-1.11)	1.10 (0.90-1.36)	1.04 (0.85-1.28)	1.06 (0.82-1.36)
Rural	0.74 (0.69-0.81)	1.82 (1.56-2.11)	0.60 (0.52-0.70)	1.00 (0.83-1.20)
Combat Exposure	0.96 (0.89-1.04)	0.94 (0.82-1.08)	0.95 (0.83-1.09)	0.94 (0.79-1.13)
Sexual Trauma while in Military	0.99 (0.89-1.11)	0.89 (0.72-1.08)	1.02 (0.83-1.25)	1.10 (0.86-1.41)
VA Disability Level 70 or greater	0.96 (0.9-1.03)	0.98 (0.86-1.10)	0.96 (0.85-1.08)	1.12 (0.96-1.30)
Homeless	0.94 (0.87-1.02)	1.17 (1.02-1.36)	0.93 (0.80-1.07)	1.15 (0.96-1.36)
CCI 1 or greater	0.99 (0.91-1.07)	0.97 (0.84-1.12)	1.02 (0.88-1.18)	0.97 (0.81-1.18)
Service Use Characteristics				
Plurality of Care at VA Medical Center	1.04 (0.90-1.20)	1.11 (0.86-1.44)	0.79 (0.61-1.02)	1.22 (0.85-1.74)
Plurality of Care at a CBOC	0.57 (0.48-0.68)	0.94 (0.68-1.31)	0.66 (0.48-0.92)	1.29 (0.81-2.04)
At least one visit with a PC prescriber	0.78 (0.73-0.84)	0.98 (0.86-1.10)	0.95 (0.84-1.07)	1.11 (0.95-1.29)
At least one visit with a MH prescriber	0.81 (0.76-0.87)	1.28 (1.13-1.45)	0.73 (0.64-0.82)	1.15 (0.99-1.35)
At least one visit with a SA prescriber	3.81 (3.52-4.12)	1.10 (0.97-1.24)	1.57 (1.39-1.78)	0.81 (0.69-0.94)
Residential SA Treatment	1.22 (1.07-1.39)	1.01 (0.81-1.25)	0.89 (0.72-1.10)	1.21 (0.97-1.53)
Inpatient Admission for Detoxification	1.30 (1.19-1.41)	0.98 (0.85-1.14)	0.79 (0.68-0.91)	1.81 (1.53-2.13)
Effective Antidepressant for PTSD	1.00 (0.94-1.07)	1.04 (0.92-1.17)	0.89 (0.79-1.00)	1.19 (1.02-1.4)
Comorbid Diagnoses				
Pain Disorder	0.73 (0.68-0.79)	1.12 (0.98-1.30)	0.90 (0.79-1.04)	0.96 (0.80-1.15)
Headache Disorder	0.84 (0.78-0.91)	1.15 (1.00-1.32)	0.94 (0.82-1.07)	0.92 (0.78-1.09)
Psychotic Disorders	0.84 (0.76-0.94)	0.76 (0.63-0.93)	1.13 (0.93-1.37)	1.07 (0.84-1.34)
Bipolar Mood Disorders	0.81 (0.74-0.89)	0.97 (0.83-1.15)	0.81 (0.69-0.96)	1.32 (1.09-1.60)
Depressive Mood Disorders	0.84 (0.78-0.91)	0.95 (0.83-1.09)	0.86 (0.75-0.99)	1.23 (1.02-1.48)
Non-PTSD Anxiety Disorders	1.02 (0.95-1.1)	1.02 (0.90-1.16)	0.85 (0.75-0.96)	1.08 (0.92-1.27)
TBI and Cognitive Disorders	1.04 (0.95-1.14)	0.83 (0.70-0.97)	1.08 (0.92-1.27)	1.03 (0.85-1.25)
Personality Disorders	0.84 (0.76-0.92)	0.92 (0.77-1.09)	0.91 (0.76-1.08)	1.28 (1.05-1.56)
Nicotine Use Disorder	1.49 (1.37-1.62)	1.07 (0.92-1.24)	1.22 (1.05-1.41)	0.65 (0.54-0.80)
Alcohol Use Disorder	0.75 (0.7-0.81)	0.70 (0.61-0.80)	0.61 (0.54-0.69)	4.90 (3.98-6.02)
Marijuana Use Disorder	0.76 (0.7-0.82)	0.88 (0.77-1.02)	0.89 (0.78-1.02)	1.30 (1.11-1.53)

	All (n=19,998)	Received Specific Medication (n=5,913)		
Model Performance (c-statistic)	Any Agent OR (95% CI) c=0.71	Buprenorphine OR (95% CI) c=0.78	Methadone OR (95% CI) c=0.76	Naltrexone OR (95% CI) c=0.77
Cocaine Use Disorder	1.22 (1.13-1.32)	0.81 (0.71-0.92)	1.40 (1.23-1.60)	1.04 (0.88-1.22)
Amphetamine Use Disorder	0.77 (0.68-0.88)	0.93 (0.74-1.17)	0.86 (0.69-1.08)	1.17 (0.91-1.51)
Tranquilizer & Sedative Use Disorder	1.26 (1.14-1.39)	0.89 (0.75-1.05)	1.37 (1.16-1.61)	0.80 (0.66-0.98)
Hallucinogen Use Disorder	0.94 (0.72-1.24)	0.83 (0.52-1.32)	0.56 (0.34-0.92)	1.25 (0.75-2.07)
Fiscal Year				
2005 versus 2004	1.3 (1.08-1.57)	1.68 (1.01-2.79)	0.75 (0.49-1.16)	0.74 (0.45-1.23)
2006 versus 2004	1.17 (0.97-1.42)	3.50 (2.16-5.67)	0.55 (0.36-0.84)	0.92 (0.56-1.51)
2007 versus 2004	1.27 (1.06-1.52)	3.75 (2.35-5.99)	0.57 (0.38-0.85)	0.69 (0.42-1.13)
2008 versus 2004	1.43 (1.20-1.71)	5.89 (3.74-9.25)	0.50 (0.34-0.74)	0.77 (0.48-1.22)
2009 versus 2004	1.46 (1.22-1.73)	7.39 (4.71-11.58)	0.26 (0.17-0.37)	0.77 (0.49-1.22)
2010 versus 2004	1.86 (1.56-2.21)	9.86 (6.32-15.40)	0.22 (0.15-0.32)	0.94 (0.61-1.46)
2011 versus 2004	1.81 (1.52-2.15)	9.41 (6.03-14.70)	0.23 (0.15-0.33)	1.11 (0.72-1.72)
2012 versus 2004	1.91 (1.60-2.27)	9.93 (6.36-15.51)	0.20 (0.14-0.29)	1.16 (0.75-1.79)
2013 versus 2004	2.11 (1.78-2.51)	9.45 (6.06-14.74)	0.18 (0.12-0.26)	1.36 (0.89-2.09)

Note. ■ 95% CI Below 1.00 ■ 95% CI Above 1.00

VA =Department of Veterans Affairs; PTSD=Posttraumatic Stress Disorder; OUD=Opioid Use Disorder; OR=Odds Ratio; CI=Confidence Interval; OEF/OIF/OND=Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn; CCI=Charlson Comorbidity Index; CBOC=Community Based Outreach Clinic; PC=Primary Care; MH=Mental Health, SA=Substance Abuse; TBI=Traumatic Brain Injury