Pain Medicine 2018; 19: 774–787
doi: 10.1093/pm/pnx208

OXFORD

Original Research Article

Factors Associated with Opioid Initiation in OEF/OIF/OND Veterans with Traumatic Brain Injury

Teresa J. Hudson, PharmD, PhD,[*,†] Jacob T. Painter, PharmD, MBA, PhD,[*,‡] Laura E. Gressler, BS,[*,‡] Liya Lu, MS,[†] J. Silas Williams, BS,[*] Brenda M. Booth, PhD,[†] Bradley C. Martin, PhD,[‡] Mark D. Sullivan, MD, PhD,[§] and Mark J. Edlund, MD, PhD[¶,‖]

*HSR&D, Center for Mental Healthcare and Outcomes Research, Central Arkansas Veterans Healthcare System, Little Rock, Arkansas; [†]Department of Psychiatry, University of Arkansas for Medical Sciences, Little Rock, Arkansas; [‡]Division of Pharmaceutical Outcome and Policy, Department of Pharmacy Practice, University of Arkansas for Medical Sciences, Little Rock, Arkansas; [§]Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, Washington; [¶]Behavioral and Urban Health Epidemiology Program, RTI International, Research Triangle Park, Durham, North Carolina; [‖]Behavioral Health Services, St Luke's Health System, Twin Falls, Idaho, USA

Correspondence to: Teresa J. Hudson, PharmD, PhD, HSR&D, Center for Mental Healthcare and Outcomes Research, Central Arkansas Veterans Healthcare System, 2200 Fort Roots Drive, North Little Rock, AR 72114, USA. Tel: 501-257-1716; Fax: 501-257-1707; E-mail: hudsonteresaj@uams.edu.

Funding sources: This research was supported by the National Institute on Drug Abuse (grant No. R01 DA030300). Dr. Hudson also receives support from the VA HSR&D Center for Mental Healthcare and Outcomes Research.

Disclosure and conflicts of interest: None. The views expressed in this article are those of the authors and do not represent the views of the Department of Veterans Affairs or the United States Government.

Previous presentation: This study was presented as a poster at the Academy Health Annual Research Meeting; June 10, 2014; San Diego, CA.

Abstract

Objective. These analyses examined opioid initiation and chronic use among Iraq (OIF) and Afghanistan (OEF/OND) veterans with a new diagnosis of traumatic brain injury (TBI) in the Veterans Health Administration (VHA).

Methods. Data were obtained from national VHA data repositories. Analyses included OEF/OIF/OND veterans with a new TBI diagnosis in 2010–2012 who used the VHA at least twice, had not received a VHA opioid prescription in the 365 days before diagnosis, and had at least 365 days of data available after TBI diagnosis.

Results. Analyses included 35,621 veterans. Twenty-one percent initiated opioids; among new initiators, 23% used chronically. The mean dose was 24.0 mg morphine equivalent dose (MED) daily (SD = 24.26); mean days supplied was 60.52 (SD = 74.69). Initiation was significantly associated with age 36–45 years (odds ratio [OR] = 1.09, 95% CI = 1.01–1.17, $P = 0.04$), female gender (OR = 1.22, $P < 0.001$), having back pain (OR = 1.38, $P < 0.0001$), arthritis/joint pain (OR = 1.24, $P < 0.0001$), or neuropathic pain (OR = 1.415, $P < 0.02$). In veterans age 36–45 years, those living in small rural areas had higher odds of chronic opioid use (OR = 1.31, $P < 0.0001$, and OR = 1.33, $P = 0.006$, respectively) and back pain (OR = 1.36, $P = 0.003$). Headache/migraine pain was associated with decreased odds of chronic opioid use (OR = 0.639, $P = 0.003$).

Conclusions. Prevalence of opioid use is relatively low among OEF/OIF/OND veterans with newly diagnosed TBI who are using VHA. Among those who initiated opioids, about 25% use them chronically.

Prescribing was mostly limited to moderate doses, with most veterans using opioids for approximately two months of the 12-month study period.

Key Words. Opioid; Traumatic Brain Injury; Veteran; Pain

Introduction

Traumatic brain injury (TBI) has been called the "signature injury" of the conflicts in Iraq and Afghanistan [1,2]. An estimated 12–23% of veterans who served in Afghanistan (Operation Enduring Freedom [OEF]) and Iraq (Operation Iraqi Freedom [OIF] and Operation New Dawn [OND]) and who utilized Veterans Health Administration (VHA) care experienced a TBI while deployed [3]. Among the 613,391 returning veterans from Afghanistan and Iraq between 2009 and 2011, 40.2% have a primary pain diagnosis, 29.4% have a primary post-traumatic stress disorder (PTSD) diagnosis, and 9.6% have a primary TBI diagnosis. Among all veterans with TBI, a significant majority (62.5%) suffered from comorbidities related to pain and PTSD [4].

TBI is defined as a physical force to the brain sufficient to cause structural alteration or physiological disruption of brain functions that results in altered consciousness, amnesia, change in mental state, neurological deficits, or intracranial lesions [5]. TBI severity is generally categorized as mild, moderate, or severe, depending on the patient's level of arousal/consciousness at the time of injury, the duration of any loss of consciousness, and the duration of post-traumatic amnesia [6]. An estimated 50% of injuries are mild, with fewer veterans presenting to VHA care having moderate to severe TBI. Symptoms associated with TBI are typically physical symptoms, cognitive impairment, and emotional/behavioral problems [5,7]. Symptoms can resolve in as little as a few minutes or over a few days to weeks, particularly in mild TBI. However, in some cases, symptoms continue for months to years, not just in patients with moderate to severe TBI, but also in those categorized as having a mild injury [8].

Among civilians, patients with TBI are five times more likely to report persistent pain compared with those without TBI [4,8,9]. An epidemiologic analysis of TBI among OEF/OIF/OND veterans from 2010–2012 found that 71% of those with TBI had head, back, or neck pain, compared with only 33% of those without TBI [10]. A review of 23 studies of chronic headaches after TBI reported a prevalence of 57.8% (95% CI = 55.5–50.2) when combining civilian and military cohorts [11,12]. Although there is evidence that pain may be more prevalent immediately following TBI, pain can persist and even worsen in the years after even a mild TBI. Indeed, pain related to TBI has been documented in veterans up to five years after the initial injury [13]. While a headache is the most commonly documented pain condition, back and neck pain and neuropathic pain are also common [8].

TBI is also associated with a range of mental health comorbidities, particularly PTSD and depression. Estimates of the prevalence of PTSD among veterans with mild TBI range from 14% to 77% [2,14–19]. Estimates of the prevalence of major depressive disorder comorbidity with TBI range from 3% to 53% [11,14,20–22]. This is particularly striking when considering that the 12-month prevalence of depression in the general adult population is approximately 6.7% [11,23].

The high rates of comorbid pain and mental health (MH) diagnoses are particularly concerning when considering risks of opioid use in veterans with TBI. Opioid medications have become a common treatment for noncancer pain [24–26]. Increased opioid use has been accompanied by increased opioid misuse, emergency department visits, overdoses, and automobile accidents [27–31]. Factors that increase the likelihood of chronic opioid use include chronic noncancer pain, having diagnoses of MH and substance use disorders (SUD; i.e., PTSD, depression, nonopioid SUD, opioid SUD, tobacco use), and demographic characteristics (male gender, younger age, Caucasian race) [32–37]. Among OEF/OIF/OND veterans with TBI and chronic noncancer pain, those with a PTSD diagnosis have a higher relative risk of receiving opioid medications for 20 or more consecutive days in the year following the pain diagnosis (TBI + PTSD adjusted relative risk [RR] = 2.95, 95% confidence interval [CI] = 2.79–3.12) than those without PTSD (TBI without PTSD adjusted RR = 1.77, 95% CI = 1.60–1.95, $P < 0.01$) [27]. However, there is little information about the factors, other than PTSD, associated with opioid initiation among veterans with TBI not previously using opioids, regardless of pain condition, nor is there information about the factors associated with chronic use after opioid initiation. The overarching goal of this work is to understand how opioids are used in patients with TBI. To that end, the current study identified a cohort of OEF/OIF/OND veterans who are regular users of VHA care and who had a recent diagnosis of TBI, but who had not used opioids in the 365 days prior to the TBI diagnosis. We hypothesized that diagnoses of chronic pain and comorbid diagnosis of PTSD, depression, or nonopioid SUD would be associated with opioid initiation and chronic opioid use among OEF/OIF/OND veterans with TBI.

The high prevalence of comorbidities related to pain and MH makes this veteran population more likely to use opioids and therefore more susceptible to possible adverse effects. Identifying the factors related to the initiation and chronic use of opioids could educate and inform clinicians as to the characteristics that may put patients at high risk for poor outcomes and could provide them with the ability to reevaluate treatment decisions to minimize these risks. The evidence gained from this investigation can also provide data to VHA

policy makers and motivate changes in policies concerning this population.

Methods

Data Sources

Data for this study were obtained using three VHA data repositories: the Veterans Administration (VA) Corporate Data Warehouse (CDW), the OEF/OIF/OND Roster, and the VA Pharmacy Benefits Management Service (PBM). The project received approval from the institutional review boards of the Central Arkansas Veterans Healthcare System and the University of Arkansas for Medical Sciences. A data use agreement was executed with each repository.

Study Sample

We identified a study cohort of OEF/OIF/OND veterans who used VHA care at least twice in the 365 days prior to the index period but did not have an outpatient opioid prescription from a VHA provider in that time frame. This provided a cohort of patients who were known to be using VHA care and therefore had an opportunity to receive an opioid prescription from VHA but did not. As they were required to use the VHA at least twice, it implies some level of engagement in care and potentially increases the likelihood of getting prescription medications from the VHA rather than from an outside provider.

Included veterans had:

1. at least one TBI diagnosis in FY10 or later (the date of the first TBI diagnosis identified was assigned as the veteran's index date);
2. at least 365 days of observation available prior to the date of TBI diagnosis (this requirement decreases the risk that the veteran had been receiving treatment for TBI outside VHA);
3. at least two VHA outpatient visits in the 365 days after diagnosis.

Excluded veterans had:

1. an opioid prescription or visit to a methadone clinic before the identified index date;
2. residence in a VHA nursing home or domiciliary, or were enrolled in VHA hospice care in the 365 days prior to the index date;
3. an opioid prescription in injectable or suppository form or had incomplete opioid prescription records 365 days after the index date;
4. an average daily dose greater than 1,000 mg MED daily (these were treated as potentially invalid values and excluded from the analyses to protect against data entry errors);
5. a date of opioid initiation 90 or fewer days from the end of the observation period (this was to ensure the possibility of measuring chronic opioid use).

The final cohort of veterans had a new TBI diagnosis within VHA in FY10 and were regular users of VHA care but were not living in an environment that would influence how prescription medications are managed (e.g., domiciliary or nursing home) or had conditions where opioid prescribing could systematically differ from prescribing for noncancer pain (e.g., cancer diagnosis or hospice care).

Opioid Use

Data from the VHA PBM were used to create variables for opioid use. This was based on the days covered by prescriptions issued by the VHA in the 12 months after the index date. Any opioid use was defined as a VHA outpatient opioid prescription for any length of time in the 12 months after the index date. Chronic opioid use was defined as 91 or more days of outpatient opioid use issued by a VHA pharmacy in the 12 months after the index date. To calculate the number of opioid days covered, the prescriptions for the 12 months after the index date were sorted into chronological order based on the date dispensed. If any two prescriptions overlapped by more than 20% or more than 10 days, the overlapping portions of the prescription were assumed to be taken concurrently and the overlapping days were only included once in the opioid days' calculation. If the overlap was 20% or less and 10 or fewer days, the second prescription was shifted and the overlapping days from both the first and second prescription were included in the opioid days' calculation. To further describe opioid use in this cohort, the mean daily opioid dose in morphine equivalents was calculated for each opioid user, referred to as the morphine equivalent dose. The MED was calculated by multiplying the quantity of each prescription by the strength of the prescription (milligrams of opioid per unit dispensed). The quantity–strength of the product was then multiplied by conversion factors derived from published sources to estimate the milligrams of morphine equivalent to the opioids dispensed in the prescription [38–40].

TBI Definition

The CDW was used to identify veterans with at least one outpatient visit coded with an ICD-9 code for TBI. These codes were selected based on a literature review [41,42] and VHA publications [5].

Other Variables

Demographic and diagnostic data included the following: date of birth, race, marital status, gender, zip code, and diagnosis codes (ICD-9). The zip code was used to

classify veterans as living in an urban area, large rural city/town, small rural town, or isolated small rural town [43]. We identified common painful conditions experienced by veterans: neck, back, arthritis/joint, headache/migraine, neuropathic, and pain due to traumatic limb injuries, fractures, and amputations. These conditions were selected based on a literature search; they were found to be common among veterans, including those with TBI [9,44]. The definition of chronic pain requires at least two separate occasions of a pain diagnosis at least 30 but not more than 365 days apart. The ICD-9 codes used to identify veterans with these pain conditions are listed in Appendix Table A1. Veterans were categorized as having a painful condition if they had at least one outpatient visit coded with that condition within the 12-month period after the index date, and a second code for a painful condition at least 30 days but not more than 365 days later. While these are common chronic conditions, veterans in these analyses could have had chronic and nonchronic painful conditions we did not identify. However, given that these pain conditions are common among OEF/OIF/OND veterans and among those with TBI, they serve as appropriate tracer conditions in this cohort. Dummy variables were created to identify veterans with at least one recorded diagnosis of major depressive disorder, PTSD, alcohol use disorder, nonopioid SUD, opioid use disorder, or tobacco use. Definitions for these conditions are based on previous literature [34,45] and are consistent with definitions used by the VA Office of Mental Health Operations.

Military Characteristics

Military characteristics and education have been shown to be associated with persistent pain [9,46]. The OEF/OIF/OND Roster was used to identify both military characteristics including rank (enlisted, officer, warrant), component (reserve, guard, active duty), branch (Army, Navy, Air Force, Marines), and education level for subjects included in the analyses.

Analysis

Multivariable logistic regression was used to model the odds of initiating opioid use in the 12 months after the index date and to identify factors associated with chronic opioid use among opioid initiators. Veterans using VHA care are clustered within clinics that are clustered within medical centers. To avoid underestimating the standard error and erroneously identifying a variable as statistically significant, the VA Medical Center was specified as a random effect in each model.

Results

A total of 35,621 veterans met inclusion/exclusion criteria (see Table 1). The mean age of the cohort was 31.96 years (SD = 8.19). The cohort was generally Caucasian, male, had completed high school, and lived in urban areas. While serving in the military, the majority were enlisted and active duty military, rather than in the guard or reserve; the majority served in the Army. Less than 10% had an opioid or nonopioid SUD, 14% had an alcohol disorder, and 12% had documented tobacco use based on ICD-9 codes. Joint pain (7.08%) and back pain (6.14%) were the two most commonly diagnosed types of pain disorders. Opioids were initiated in 20.52% of the sample; 23.25% of those who initiated opioids used them chronically, defined as 90 or more days in the 365 days after the index date. Among opioid users, the mean dose was 24.0 mg MED daily (SD = 24.26). The mean days supplied was 60.52 (SD = 74.69), ranging from one to 365 days.

Results of a logistic regression model examining factors associated with opioid initiation are in Table 2. Cohort members age 36–45 had an 8.3% greater odds of receiving opioids compared with the age 26–35 reference group (OR = 1.08, 95% CI = 1.00–1.17, $P = 0.04$). Nonwhite persons and those with unknown race had lower odds of opioid initiation compared with white veterans. Women had higher odds of opioid initiation compared with men (OR = 1.22, 95% CI = 1.10–1.36, $P \leq 0.001$). Veterans who had a bachelor's degree or higher had significantly lower odds of initiating opioids compared with those who completed high school only (OR = 0.65, 95% CI = 0.55–0.77, $P < 0.0001$). There were no statistically significant findings related to opioid initiation based on rank while in the military. Those veterans who served in the National Guard had lower odds of initiating opioids compared with active duty personnel (OR = 0.86, 95% CI = 0.78–0.95, $P < 0.001$). Compared with those in the Navy, Marines had significantly lower odds of opioid initiation (OR = 0.84, 95% CI = 0.74–0.95, $P = 0.005$). Among clinical characteristics, the only statistically significant finding was that veterans with back pain (OR = 1.38, 95% CI = 1.24–1.53, $P < 0.001$), arthritis/joint pain (OR = 1.23, 95% CI = 1.11–1.36, $P < 0.001$), and neuropathic pain (OR = 1.42, 95% CI = 1.06–1.89, $P < 0.019$) had higher odds of initiating opioid medications.

Table 3 provides the results of the logistic regression model of chronic opioid use. Only 89% (N = 6,518) of opioid initiators were included in this model as 11% started opioids within 90 days of the end of the observation period and did not have sufficient time to meet the definition of chronic opioid use. Veterans who were married or had unknown marital status had much higher odds than unmarried veterans of using opioids chronically (OR = 1.27, 95% CI = 1.13–1.43, $P < 0.001$, and OR = 1.88, 95% CI = 1.63–2.16, $P < 0.001$, respectively). Veterans with a bachelor's degree or higher were significantly less likely to use opioids chronically compared with those who completed high school only (OR = 0.49, 95% CI = 0.34–0.72, $P = 0.0002$). Veterans living in rural areas had greater odds than those in urban areas of receiving opioids chronically, although this was only statistically significant for those living in small rural areas (OR = 1.33, 95% CI = 1.08–1.64, $P = 0.006$). Although women were more likely to initiate opioid

Table 1 Cohort characteristics (N = 35,621)

Variable	Level	Entire Cohort		No Opioid		Any Opioid Use		*P*—Comparing No Opioid Use and Any Opioid Use
		No.*	%†	No.*	%†	No.*	%†	*P*‡
Demographic characteristics								
Age, y	18–25	7,482	21	5,933	20.96	1,549	21.19	0.366
	26–35	18,961	53.23	15,130	53.44	3,831	52.4	
	36–45	6,150	17.27	4,835	17.08	1,315	17.99	
	46–55	2,596	7.29	2,065	7.29	531	7.26	
	>55	432	1.21	347	1.23	85	1.16	
Race	White	24,889	69.87	19,632	69.35	5,257	71.91	<0.0001
	Nonwhite	5,906	16.58	4,707	16.63	1,199	16.4	
	Unknown	4,826	13.55	3,971	14.03	855	11.69	
Marital status	Married	14,160	39.75	11,235	39.69	2,925	40.01	<0.0001
	Not married	16,675	46.81	13,421	47.41	3,254	44.51	
	Unknown	4,786	13.44	3,654	12.91	1,132	15.48	
Gender	Female	2,053	5.76	1,567	5.54	486	6.65	0.0003
	Male	33,568	94.24	26,743	94.46	6,825	93.35	
Education	BS or higher	1,991	5.59	1,695	5.99	296	4.05	<0.0001
	High school	31,222	87.65	24,702	87.26	6,520	89.18	
	Some college	2,408	6.76	1,913	6.76	495	6.77	
Rural/urban status	Urban	28,267	79.35	22,464	79.35	5,803	79.37	0.9886
	Large rural	4,099	11.51	3,253	11.49	846	11.57	
	Small rural	1,860	5.22	1,480	5.23	380	5.2	
	Isolated small rural	1,395	3.92	1,113	3.93	282	3.86	
Military characteristics								
Rank while in military	Enlisted	34,386	96.53	27,260	96.29	7,126	97.47	<0.0001
	Officer	1,095	3.07	937	3.31	158	2.16	
	Warrant Officer	140	0.39	113	0.4	27	0.37	
Military component	Guard	7,122	19.99	5,770	20.38	1,352	18.49	0.0005
	Active	24,570	68.98	19,396	68.51	5,174	70.77	
	Reserve	3,929	11.03	3,144	11.11	785	10.74	
Branch of military	Army	24,975	70.11	19,604	69.25	5,371	73.46	<0.0001
	Air Force	1,383	3.88	1,099	3.88	284	3.88	
	Marines	7,006	19.67	5,809	20.52	1,197	16.37	
	Navy	2,257	6.34	1,798	6.35	459	6.28	
Clinical characteristics								
PTSD diagnosis	No	17,401	48.85	13,875	38.95	3,526	9.9	0.2329
	Yes	18,220	51.15	11,435	40.52	3,785	10.63	
Depression	No	25,028	70.26	19,998	56.14	5,030	14.12	0.0022
Diagnosis	Yes	2,281	10,593	8,312	23.33	2,281	6.4	
Alcohol disorder	No	30,752	86.33	24,436	68.6	6,316	17,073	0.8600
	Yes	4,869	13.67	3,874	10.88	995	2.79	
Nonopioid SUD	No	33,549	94.18	26,724	75.02	6,825	19.16	0.0007
	Yes	2,072	5.82	1,586	4.45	486	1.36	
Opioid SUD	No	35,204	98.83	27,995	78.59	7,209	20.24	0.0453
	Yes	417	1.17	315	0.88	102	0.29	
Tobacco use	No	30,271	84.98	24,060	67.54	6,211	17.44	0.9431
	Yes	4,250	11.93	1,100	3.09	5,350	15.02	

(continued)

Table 1 Continued

Variable	Level	Entire Cohort		No Opioid		Any Opioid Use		*P*—Comparing No Opioid Use and Any Opioid Use
		No.*	%†	No.*	%†	No.*	%†	*P*‡
Painful conditions								
At least 1 chronic	No	30,481	85.57	24,370	68.41	6,111	17.16	<0.0001
Condition	Yes	5,140	14.43	3,940	11.06	1,200	3.37	
Neck pain	No	35,210	98.85	28,005	78.62	7,205	20.23	0.0078
	Yes	411	1.15	305	0.86	106	0.3	
Back pain	No	33,434	93.86	26,699	74.95	6,735	18.91	<0.0001
	Yes	2,187	6.14	1,611	4.52	576	1.62	
Arthritis/joint pain	No	33,099	92.92	26,410	74.14	6,689	18.78	<0.0001
	Yes	2,522	7.08	1,900	5.33	622	1.75	
Headache/migraine pain	No	34,024	95.52	27,039	75.91	6,985	19.61	0.9104
	Yes	1,271	3.57	326	0.92	1,597	4.48	
Neuropathic pain	No	35,386	99.34	28,143	79.01	7,243	20.33	0.0014
	Yes	235	0.66	167	0.47	68	0.19	
Amputation pain	No	35,542	99.78	28,245	79.29	7,297	20.49	0.5369
	Yes	79	0.22	65	0.18	14	0.04	
Opioid use								
Opioid	No	28,310	79.48	28,310	100	0	0	<0.0001
	Yes	7,311	20.52	0	0	7,311	100	
Chronic opioids	No	33,921	95.23	28,310	100	5,611	76.75	<0.0001
	Yes	1,700	4.77	0	0	1,700	23.25	
		Mean	SD	Mean	SD	Mean	SD	*P*
CCI score		0.0789	0.34	0.08	0.33	0.08	0.37	0.6100
Age at index		31.88	8.13	31.86	8.13	31.96	8.16	0.3500

CCI = Charlson Comorbidity Index; PTSD = post-traumatic stress disorder; SUD = substance use disorder.
*Some numbers do not add up to total number of patients because of missing data.
†Some percentages do not add up to 100 because of rounding.
‡*P* value is the difference between no opioid use and any opioid use.

medications, they were less likely to use them chronically. Members of the National Guard compared with the Reserve were more likely to use opioids chronically (OR = 1.04, 95% CI = 0.87–1.24, $P < 0.0001$). Veterans in the Army were less likely to use opioids chronically compared with those who served in the Navy (OR = 0.915, 95% CI = 0.697–1.20, $P < 0.001$). Veterans with a history of tobacco use were less likely to use opioids chronically (OR = 0.84, 95% CI = 0.72–0.97, $P = 0.02$). Veterans with back pain were more likely to use opioids chronically (OR = 1.37, 95% CI = 1.11–1.67, $P = 0.003$), while veterans with headache/migraine pain were less likely to use them chronically (OR = 0.634, 95% CI = 0.48–0.86, $P = 0.003$). There were no other statistically significant clinical characteristics associated with chronic opioid use. Interestingly, those with a diagnosis of chronic pain were not statistically more likely to use opioids chronically, nor were those with a diagnosis of depression, PTSD, alcohol disorders, or other substance use disorders.

Discussion

In these analyses, opioids were initiated in slightly more than 20% of the OEF/OIF/OND TBI cohort, but among opioid initiators, almost 25% used opioids chronically. This chronic use, however, is lower than in all veterans. In other analyses, we found that among all opioid users with chronic noncancer pain in the VHA nationwide, almost 57% of opioid users received them chronically [24]. This may suggest that opioid prescribing from VA providers is lower among OEF/OIF/OND veterans with TBI compared with other veteran cohorts. This finding may also be a function of the sample. We observed this cohort for 365 days after the index period. It is possible that opioid initiation may occur later than the first year after a diagnosis, suggesting that other pain management strategies may be used during that time. It is also possible that patients with new TBI diagnoses within the VA are less likely to initiate opioids within the VA compared with veterans who are treated in other health care systems before

Table 2 Logistic regression model of opioid initiation (N = 35,621)*

Variable	Level	Odds ratio	95% CI		*P*
Demographic characteristics					
Age, y	18–25	1.060	0.991	1.135	0.0915
	26–35	Ref			
	36–45	1.083	1.004	1.168	0.0395
	46–55	1.084	0.969	1.212	0.1580
	56–65	1.142	0.881	1.470	0.3038
Race	Nonwhite	0.889	0.826	0.957	0.0019
	Unknown	0.786	0.723	0.854	<0.0001
	White	Ref			
Marital status	Married	1.060	0.999	1.124	0.0552
	Unknown	1.246	1.149	1.352	<0.0001
	Not married	Ref			
Gender	Female	1.221	1.095	1.362	0.0003
	Male	Ref			
Education	BS or above	0.651	0.548	0.774	<0.0001
	Some college	0.942	0.845	1.049	0.2746
	High school	Ref			
Rural/urban status	Isolated rural	1.003	0.873	1.153	0.9642
	Large rural	0.984	0.903	1.072	0.7122
	Small rural	0.992	0.879	1.120	0.8961
	Urban	Ref			
Military characteristics					
Rank while in military	Officer	0.926	0.578	1.485	0.7497
	Warrant Officer	Ref			
	Enlisted	1.051	0.683	1.619	0.8199
Military component	Guard	0.859	0.775	0.952	0.0037
	Reserve	Ref			
	Active	1.023	0.935	1.118	0.6234
Branch of military	Air Force	1.064	0.897	1.263	0.4731
	Marines	0.835	0.737	0.946	0.0047
	Navy	Ref			
	Army	1.117	0.998	1.251	0.0548
Clinical characteristics					
Depression diagnosis	Yes vs no	1.036	0.974	1.100	0.2704
PTSD diagnosis	Yes vs no	1.010	0.954	1.069	0.7422
Alcohol disorder	Yes vs no	0.968	0.890	1.053	0.4461
Nonopioid SUD	Yes vs no	1.187	1.054	1.336	
Opioid SUD	Yes vs no	1.134	0.892	1.443	0.3047
Tobacco use	Yes vs no	0.976	0.905	1.053	0.5361
Painful condition					
Neck pain	Yes vs no	1.140	0.901	1.441	0.2741
Back pain	Yes vs no	1.376	1.236	1.531	<0.0001
Arthritis/joint pain	Yes vs no	1.231	1.112	1.363	<0.0001
Headache/migraine Pain	Yes vs no	0.887	0.778	1.011	0.0733
Neuropathic pain	Yes vs no	1.415	1.056	1.896	0.0199
Amputation pain	Yes vs no	0.709	0.393	1.276	0.2513

CI = confidence interval; PTSD = post-traumatic stress disorder; SUD = substance use disorder.
*All models controlled for physical health comorbidities with Charlson Comorbidity Score.

coming to the VA. The doses and number of days using opioids in the 365-day observation period were modest, with most people taking only 25 mg MED/day and using opioids for 60 or fewer days. Generally, low-dose morphine is approximately 10–40 mg MED/day, moderate is 40–120 mg MED/day, and high-dose is

Table 3 Model of chronic opioid use among opioid initiators (N = 6,518)*

Variable	Level	Odds ratio	95% CI		*P*
Demographic characteristics					
Age, y	18–25	0.990	0.867	1.131	0.885
	26–35	Ref			
	36–45	1.310	1.145	1.499	<0.0001
	46–55	1.026	0.826	1.274	0.8187
	56–65	1.095	0.665	1.803	0.7213
Race	Nonwhite	0.593	0.507	0.695	<0.0001
	Unknown	1.895	1.626	2.163	<0.0001
	White	Ref			
Married	Married	1.273	1.134	1.429	<0.0001
	Unknown	1.875	1.626	2.163	<0.0001
	Not married	Ref			
Gender	Female	0.840	0.662	1.066	0.151
	Male	Ref			
Education	BS or above	0.495	0.342	0.716	0.0002
	Some college	0.996	0.817	1.214	0.9689
	High school	Ref			
Rural/urban status	Isolated rural	1.113	0.860	1.440	0.4165
	Large rural	1.156	0.990	1.350	0.0675
	Small rural	1.334	1.084	1.641	0.0065
	Urban	Ref			
Military characteristics					
Rank while in military	Officer	1.064	0.413	2.743	0.8974
	Warrant Officer	Ref			
	Enlisted	0.996	0.817	1.214	0.6804
Military component	Guard	1.040	0.873	1.238	0.0097
	Reserve	Ref			
	Active	0.768	0.629	0.938	0.6624
Branch of military	Air Force	1.344	0.950	1.900	0.0948
	Marines	1.560	1.199	1.952	0.5204
	Navy	Ref			
	Army	0.915	0.697	1.200	0.0006
Clinical characteristics					
Depression diagnosis	Yes vs no	0.975	0.867	1.097	0.6776
PTSD diagnosis	Yes vs no	1.008	0.905	1.122	0.8853
Alcohol disorder	Yes vs no	0.843	0.708	1.003	0.0546
Nonopioid SUD	Yes vs no	0.845	0.649	1.099	0.2088
Opioid SUD	Yes vs no	1.462	0.909	2.353	0.1171
Tobacco use	Yes vs no	0.835	0.716	0.973	0.0213
Painful conditions					
Neck pain	Yes vs no	1.277	0.822	1.982	0.2766
Back pain	Yes vs no	1.366	1.110	1.670	0.0027
Arthritis/joint pain	Yes vs no	1.082	0.884	1.324	0.4470
Headache/migraine pain	Yes vs no	0.639	0.477	0.855	0.0026
Neuropathic pain	Yes vs no	1.353	0.783	2.337	0.2784
Amputation pain	Yes vs no	1.076	0.424	2.734	0.8770

CI = confidence interval; PTSD = post-traumatic stress disorder; SUD = substance use disorder.
*All models controlled for physical health comorbidities with the Charlson Comorbidity Score.

more than 120 mg MED/day [47]. Opioid initiators were more likely to have at least one pain diagnosis compared with those who did not initiate opioid medications. It is also important to note that diagnoses such as alcohol disorder and SUDs were not associated with opioid initiation.

Several of our findings are notably different than other studies examining opioid use in veterans. Other authors have found that male gender was associated with opioid use, including chronic opioid use [24,34,36]. However, in the current analyses, women were more likely to initiate opioids but not to use them chronically. This is a particularly interesting finding given that other studies have found that painful conditions such as musculoskeletal, headache, and back pain may be more common among women veterans, particularly those who served in Iraq and Afghanistan, than among their male counterparts [48]. Female veterans are more likely than male veterans to report severe pain and pain that interferes in their daily lives, to have an emergency department or primary care visit for a pain-related problem, to have a service-connected disability rating, and to have a rating of at least 50% [9,48–50]. In our cohort, 20% of women had a chronic pain diagnosis, compared with only 14% of men ($X2 = 46.82$, $P < 0.0001$).

In these analyses, education appeared to have a protective effect. Veterans in this cohort who had a bachelor's degree or higher were less likely to initiate opioids or use them chronically. Improving education among veterans may offer a target for a policy initiative that could benefit veterans and decrease risk of opioid initiation and chronic use.

In our analyses, neither PTSD nor depression was associated with opioid initiation or chronic opioid use. Previous work found that PTSD and depression were associated with increased odds of receiving opioids and of receiving them chronically, but most of those studies were in cohorts of veterans known to have chronic, painful conditions and used data from as far back as 2005. It is important to note that these analyses depended on diagnoses of mental health conditions that were documented in the VA medical record. It is possible that veterans in this cohort had comorbid mental health conditions that were undiagnosed or not documented in the VA electronic health record. Data for the current analyses are from 2010 and later. In 2009 and 2010, the VHA implemented new policies designed to decrease chronic opioid use and increase monitoring to identify opioid misuse [51–53]. The lack of association between opioid use and depression and PTSD may be a result of these policies. We reported earlier that depression, PTSD, and substance use disorders were not associated with opioid continuation beyond 90 days of use in the veteran population, as we have found in the civilian population [54].

The proportion of veterans with documented smoking in this study was approximately 12%. In other studies, smoking prevalence was approximately 23–30% [34,45]. This difference is likely related to the way we identified smoking in the cohort. We used one ICD-9 CM code for smoking (305.1, tobacco use disorder) and no V codes or supplementary codes for a history of smoking. Other authors used a wide range of codes that included the history of tobacco use; we limited the code used to identify current tobacco use only. Given the difference in identification of tobacco use and that it was not associated with opioid initiation but was associated with statistically lower odds of chronic use, it will be important to further examine this issue in future research.

Approximately 15% of the cohort had a pain diagnosis, which is lower than the epidemiologic estimates of pain conditions among veterans with TBI [10–12]. This low prevalence is likely due to the definition of a painful condition. The first date of TBI diagnosis in FY10 or later was considered the index date; veterans were followed for the 365-day period following the index date. The definition of chronic pain required at least two separate occasions of a pain diagnosis at least 30 but not more than 365 days apart. However, the goal was not to determine whether opioids were prescribed only in response to a pain diagnosis or to identify all diagnoses for which opioids are prescribed. The goal was to identify factors associated with opioid initiation among veterans with TBI as a cohort who had not used opioids in the previous 365-day period and had a relatively new TBI diagnosis, thereby making it possible to understand opioid initiation. The numerous pain conditions in this study served as tracer conditions to help understand the clinical conditions of these veterans, a strategy used in other studies [25]. Therefore, the findings likely cannot be generalized to all veterans or others with TBI or pain. However, it does help to understand how opioids are used in OEF/OIF/OND veterans with TBI who have a relatively new diagnosis.

Limitations

One of the challenges of studying TBI using data repositories is that there is no way to account for the severity of TBI or how recently it occurred. While the proposed inclusion/exclusion criteria used in these analyses will not necessarily completely identify veterans with a "new" TBI diagnosis, TBI not being coded by a VA provider in the previous 12 months may suggest that treatment related to TBI was not a key clinical focus in the 365 days prior to the index date. Other studies have noted that mild TBI is the most common type of TBI presenting to the VHA for care, so it is likely that most of the cases identified in these analyses are also mild TBI. It is also possible that some veterans who experienced TBI may not be diagnosed. Therefore, it is likely that the current findings are most generalizable to veterans who are newly diagnosed with TBI in the VHA.

Another key limitation of this study is the lack of information about opioid use and receipt of medical care outside the VHA. Identifying opioid prescriptions obtained from non-VHA providers is very difficult. To decrease the risk of underestimating opioid use because of non-VHA prescribing, we identified veterans who used VHA care at least twice in the 365 days prior to the index period but who did not have an outpatient opioid prescription from a VHA provider in that time frame. This implies some level of engagement in care

and potentially increases the likelihood of veterans mainly getting their prescription medications from the VHA rather than from an outside provider. Therefore, the findings from these analyses are likely generalizable to veterans within VHA who are using VHA care regularly. These veterans are also the ones most likely to be affected by system-wide policies and interventions related to opioid use.

Conclusion

These data suggest that the prevalence of opioid use is relatively low among OEF/OIF/OND veterans with newly diagnosed TBI who are using the VHA, but among those who initiated opioids, about 25% use them chronically. Prescribing was mostly limited to moderate doses, with most veterans using opioids for approximately two months of the 12-month study period. Future analyses should seek to better understand factors that influence outcomes of TBI and opioid use in this cohort, including longer observation periods to examine the trajectory of opioid use and gender-related differences in chronic use among opioid initiators.

Acknowledgments

The authors thank Ms. Cynthia Brace for editing and formatting the manuscript.

APPENDIX

Table A1 International Classification of Disease, Ninth Revision, Clinical Modification (ICD9-CM) codes used to identify pain diagnoses

Pain Diagnoses	ICD9-CM Codes
Neck pain	721.0, .1
	722.0, .31, .4, .71, .81, .91
	723.0, .1, .2, .3, .5, .6, .7, .8, .9
	739.1
	784.1
	847.0
Back pain	720.1, .2, .81, .89, 7.9
	721.2, .3, .41, .42, .5, .6, .7, .8, .9, .91
	722.10, .11, .2, .30, .32, .39, .51, .52, .6, .70, .72, .73, .80, .82, .83, .90, .92, .93
	724.00, .01, .02, .03, .09, .1, .2, .3, .4, .5, .6, .70, .71, .79, .8, .9
	737.10, .11, .12, .19, .20, .21, .22, .29, .30, .31, .32, .33, .34, .39, .40, .41, .42, .43, .8, .9
	738.4, .5
	739.2, .3, .4
	756.10, .11, .12, .13, .19
	839.20
	846.0
	847.1, .2, .3, .4, .9
Arthritis/joint pain	359.4, .5, .6, .71, .79, .81, .89, .9
	524.69, .61, .62, .63, .69
	696.0
	710.0, .1, .2, .3, .4, .5, .8, .9
	711.00, .02, .03, .04, .05, .06, .07, .08, .09, .10, .11, .12, .13, .14, .15, .16, .17, .18, .19, .20, .21, .24, .25, .26, .27, .29, .30, .31, .33, .34, .37, .39, .40, .41, .42, .43, .44, .45, .46, .47, .49, .50, .51, .53, .54, .56, .57, .58, .59, .60, .66, .67, .68, .69, .70, .71, .77, .80, .81, .82, .83, .84, .85, .86, .87, .88, .89, .90, .91, .92, .93, .94, .95, .96, .97, .98, .99
	712.10, .11, .12, .13, .14, .15, .16, .17, .18, .19, .20, .21, .22, .23, .24, .25, .26, .27, .28, .29, .30, .31, .32, .33, .34, .35, .36, .37, .38, .39, .80, .81, .82, .83, .84, .86, .87, .88, .89, .90, .91, .92, .93, .94, .95, .96, .97, .98, .99
	713.0, .1, .2, .3, .4, .5, .6, .7, .8
	714.0, .1, .2, .30, .31, .32, .33, .4, .81, .89, .9
	715.00, .04, .09, .10, 11, .12, .13, .14, .15, .16, .17, .18, .20, .21, .22, .23, .24, .25, .26, .27, .28, .30, .31, .32, 33, .34, .35, .36, .37, .38, .80, .89, .90, .91, .92, .93, .94, .95, .96, .97, .98

(continued)

Table A1 Continued

Pain Diagnoses	ICD9-CM Codes
	716.00, .01, .02, .03, .04, .05, .06, .07, .09, .10, .11, .12, .13, .14, .15, .16, .17, .18, .19, .20, .21, .22, .23, .24, .25, .26, .27, .28, .29, .30, .31, .32, .33, .34, .35, .36, .37, .38, .39, .40, .41, .42, .43, .44, .45, .46, .47, .48, .49, .50, .51, .52, .53, .54, .55, .56, .57, .58, .59, .60, .61, .62, .63, .64, .65, .66, .67, .68, .80, .81, .82, .83, .84, .85, .86, .87, .88, .89, .90, .91, .92, .93, .94, .95, .96, .97, .98, .99
	717.0, .1, .41, .42, .43, .49, .5, .7, .81, .82, .83, .84, .85, .89, .9
	718.00, .01, .02, .03, .04, .05, .07, .08, .09, .20, .21, .22, .23, .24, .25, .26, .27, .28, .29, .30, .31, .32, .33, .34, .35, .36, .37, .38, .39, .40, .41, .42, 43, .44, .45, .46, .47, .48, .49, .50, .51, .52, .53, .54, .55, .56, .57, .58, .59, .60, .65, .71, .73, .74, .75, .76, .77, .78, .79, .80, .81, .82, .83, .84, .85, .86, .87, .88., 89, .90, .91, .92, .93, .94, .95, .96, .97, .98, .99
	719.20, .21, .22, .23, .24, .25, .26, .27, .28, .29, .30, .31, .32, .33, .34, .35, .36, .37, .38, .39, .40, .41, .42, .43, .44, .45, .46, .47, .48, .49
	720.0
	725.0
	726.0, .10, .11, .12, .19, .30, .31, .32, .33, .39, .4, .5, .60, .61, .62, .63, .64, .65, .69, .71, .72, .73, .79, .8, .9, .91
	727.00, .01, .02, .09, .2, .3, .50, .59, .60, .61, .62, .63, .64, .65, .66, .67, .68, .69, .81, .82, .83, .89, .9
	728.0, .10, .11, .12, .13, .19, .3, .79, .81, .86, .89, .9
	729.0, .1, .4
	730.30, .31, .32, .34, .35, .36, .37, .38, .39
	731.0, .1, .2, .3, .8
	732.0, .1, .2, .3, .4, .5, .6, .7, .8, .9
	733.6, .7, .92
	736.00, .01, .02, .03, .04, .05, .06, .07, .09, .1, .20, .21, .22, .29, .30, .31, .32, .39, .41, .42, .5, .6, .70, .71, .72, .73, .74, .75, .76, .79, .89, .9
	737.0
	738.2, .3, .6
	739.5, .6, .7
	840.4, .7
	845.09
Headache/migraine pain	307.81
	339.00, .01, .02, .03, .04, .05, .10, .11, .12, .20, .21, .22, .3, .41, .42, .43, .44, .81, .82, .83, .84, .85, .89
	346.00, .01, .02, .03, .10, .11, .12, .13, .20, .21, .22, .23, .30, 31, .32, .33, .40, .41, .42, .43, .50, .51, .52, .53, .60, .61, .62, .63, .70, .71, .72, .73, .80, .81, .82, .83, .90, .91, .92, .93
	784.0
Neuropathic pain	336.8
	337.0
	338.0
	339.09
	340.0
	350.1
	352.1
	353.0, .1, .2, .3, .4, .6, .8, .9
	354.0, .1, .2, .3, .4, .5, .8, .9
	355.0, .1, .2, .3, .4, .5, .6, .71, .79, .8, .9
	356.0, .2, .4, .8, .9
	357.0, .1, .2, .3, .4, .5, .6, .7, .81, .82, .89, .9
	723.4
	729.2
	806.00, .01, .02, .03, .04, .05, .06, .08, .09, .10, .13, .14, .15, .18, .19, .20, .21, .23, .24, .25, .26, .27, .28, .29, .30, .34, .35, .36, .37, .39, .4, .5, .6, .61, .62, .69, .70, .72, .79, .8, .9

(continued)

Table A1 Continued

Pain Diagnoses	ICD9-CM Codes
	907.2, .3, .4, .5, .9
	952.00, .01, .02, .03, .04, .05, .06, .07, .08, .09, .10, .11, .12, .13, .14, .15, .16, .17, .18, .19, .2, .3, .4, .8, .9
	953.0, .1, .2, .3, .4, .5, .8, .9
	954.0, .1, .8, .9
	955.0, .1, .2, .3, .4, .5, .6, .7, .8, .9
	956.0, .1, .2, .3, .4, .5, .8, .9
	957.0, .1, .8, .9
Amputation pain	878.0, .1, .2, .3, .4, .5, .6, .7, .8, .9
	885.0, .1
	886.0, .1
	887.0, .1, .2, .3, .4, .5, .6, .7
	894.2
	895.0, .1
	896.0, .1, .2, .3
	897.0, .1, .2, .3, .4, .5, .6, .7, .9
	997.60, .61
	998.30
	E87.85
	V49.60, .61, .62, .63, .64, .65, .66, .67, .70, .71, .72, .73, .74, .75, .76, .77
	V54.10, .11, .12, .13, .14, .15, .16, .17, .19

References

1 Taylor B, Hagel EM, Cutting A, et al. Fiscal year 2011 VA utilization report for Iraq and Afghanistan war veterans diagnosed with TBI. Prepared for the VA Polytrauma and Blast-Related Injuries QUERI #PLY 05-2010-2. 2012. Available at: http://www.queri.research.va.gov/ptbri/docs/FY10-TBI-Diagnosis-HCU-Report.pdf (accessed September 2014).

2 Tanielian T, Jaycox LH, Adamson DM, et al. Invisible Wounds of War: Psychological and Cognitive Injuries, Their Consequences, and Services to Assist Recovery. Santa Monica, CA: RAND Corporation; 2008.

3 O'Neil ME, Carlson KF, Storzbach D, et al. Complications of mild traumatic brain injury in veterans and military personnel: A systematic review. VA-ESP Project #05-225. 2013. Available at: http://www.hsrd.research.va.gov/publications/esp/mild_tbi-REPORT.pdf (accessed September 2014).

4 Cifu DX, Taylor BC, Carne WF, et al. Traumatic brain injury, posttraumatic stress disorder, and pain diagnoses in OIF/OEF/OND veterans. J Rehabil Res Dev 2013;50:1169–76.

5 Minneapolis Veterans Affairs Medical Center, Minnesota Evidence Synthesis Program, Center for Chronic Disease Outcomes Research. The assessment and treatment of individuals with history of traumatic brain injury and post-traumatic stress disorder: A systematic review of the evidence. Available at: http://www.hsrd.research.va.gov/publications/esp/TBI-PTSD-2009-REPORT.pdf (accessed September 2014).

6 Fabrizio KS, Keltner NL. Traumatic brain injury in Operation Enduring Freedom/Operation Iraqi Freedom: A primer. Nurs Clin North Am 2010;45:569–80, vi.

7 Silver JM, McAllister TW, Arciniegas DB. Depression and cognitive complaints following mild traumatic brain injury. Am J Psychiatry 2009;166:653–61.

8 Sherman KB, Goldberg M, Bell KR. Traumatic brain injury and pain. Phys Med Rehabil Clin N Am 2006; 17:473–90, viii.

9 Higgins DM, Kerns RD, Brandt CA, et al. Persistent pain and comorbidity among Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn veterans. Pain Med 2014;15:782–90.

10 Taylor BC, Campbell E, Nugent S, et al. Fiscal year 2012 VA utilization report for Iraq and Afghanistan war veterans diagnosed with TBI. Prepared for the VA Polytrauma and Blast-Related Injuries. QUERI #PLY 05-2010-2. 2014. Available at: http://www.queri.research.va.gov/ptbri/docs/FY12-TBI-Diagnosis-HCU-Report.pdf (accessed September 2014).

11 Sullivan-Singh SJ, Sawyer K, Ehde DM, et al. Comorbidity of pain and depression among persons with traumatic brain injury. Arch Phys Med Rehabil 2014;95:1100–5.

12 Nampiaparampil DE. Prevalence of chronic pain after traumatic brain injury: A systematic review. JAMA 2008;300:711–9.

13 Brickell TA, Lange RT, French LM. Health-related quality of life within the first 5 years following military-related concurrent mild traumatic brain injury and polytrauma. Mil Med 2014;179:827–38.

14 Hoge CW, McGurk D, Thomas JL, et al. Mild traumatic brain injury in U.S. soldiers returning from Iraq. N Engl J Med 2008;358:453–63.

15 Carlson KF, Nelson D, Orazem RJ, et al. Psychiatric diagnoses among Iraq and Afghanistan war veterans screened for deployment-related traumatic brain injury. J Trauma Stress 2010;23:17–24.

16 Congress of the United States, Congressional Budget Office. The Veterans Health Administration's treatment of PTSD and traumatic brain injury among recent combat veterans. 2012. Available at: http://www.cbo.gov/sites/default/files/cbofiles/attachments/02-09-PTSD.pdf (accessed September 2014).

17 Taber KH, Hurley RA. OEF/OIF deployment-related traumatic brain injury. PTSD Res Quart 2010;21: 1–8. Available at: http://www.ptsd.va.gov/professional/newsletters/research-quarterly/v21n1.pdf (accessed September 2014).

18 Lippa SM, Fonda JR, Fortier CB, et al. Deployment-related psychiatric and behavioral conditions and their association with functional disability in OEF/OIF/OND veterans. J Trauma Stress 2015;28:25–33.

19 Carlson KF, Kehle SM, Meis LA, et al. Prevalence, assessment, and treatment of mild traumatic brain injury and posttraumatic stress disorder: A systematic review of the evidence. J Head Trauma Rehabil 2011;26:103–15.

20 Hart T, Brenner L, Clark AN, et al. Major and minor depression after traumatic brain injury. Arch Phys Med Rehabil 2011;92:1211–9.

21 Gould KR, Ponsford JL, Johnston L, Schonberger M. The nature, frequency and course of psychiatric disorders in the first year after traumatic brain injury: A prospective study. Psychol Med 2011;41:2099–109.

22 Bombardier CH, Fann JR, Temkin NR, et al. Rates of major depressive disorder and clinical outcomes following traumatic brain injury. JAMA 2010;303: 1938–45.

23 Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62:617–27.

24 Edlund MJ, Austen MA, Sullivan MD, et al. Patterns of opioid use for chronic noncancer pain in the Veterans Health Administration from 2009 to 2011. Pain 2014;155:2337–43.

25 Sullivan MD, Edlund MJ, Fan MY, et al. Trends in use of opioids for non-cancer pain conditions 2000-2005 in commercial and Medicaid insurance plans: The TROUP study. Pain 2008;138:440–9.

26 Braden JB, Fan MY, Edlund MJ, et al. Trends in use of opioids by noncancer pain type 2000-2005 among Arkansas Medicaid and HealthCore enrollees: Results from the TROUP study. J Pain 2008;9:1026–35.

27 Seal KH, Shi Y, Cohen G, et al. Association of mental health disorders with prescription opioids and high-risk opioid use in US veterans of Iraq and Afghanistan. J Am Med Assoc 2012;307:940–7.

28 Beaudoin FL, Straube S, Lopez J, Mello MJ, Baird J. Prescription opioid misuse among ED patients discharged with opioids. Am J Emerg Med 2014;32 :580–5.

29 Atluri S, Sudarshan G, Manchikanti L. Assessment of the trends in medical use and misuse of opioid analgesics from 2004 to 2011. Pain Physician 2014; 17:E119–28.

30 Cicero TJ, Lynskey M, Todorov A, Inciardi JA, Surratt HL. Co-morbid pain and psychopathology in males and females admitted to treatment for opioid analgesic abuse. Pain 2008;139:127–35.

31 Gwira Baumblatt JA, Wiedeman C, Dunn JR, et al. High-risk use by patients prescribed opioids for pain and its role in overdose deaths. JAMA Intern Med 2014;174:796–801.

32 Burgess DJ, Nelson DB, Gravely AA, et al. Racial differences in prescription of opioid analgesics for chronic non-cancer pain in a national sample of veterans. J Pain 2014;15(4):447–55.

33 Morasco BJ, Duckart JP, Dobscha SK. Adherence to clinical guidelines for opioid therapy for chronic pain in patients with substance use disorder. J Gen Intern Med 2011;26:965–71.

34 Dobscha SK, Morasco BJ, Duckart JP, Macey T, Deyo RA. Correlates of prescription opioid initiation and long-term opioid use in veterans with persistent pain. Clin J Pain 2013;29:102–8.

35 Weimer MB, Macey TA, Nicolaidis C, et al. Sex differences in the medical care of VA patients with chronic non-cancer pain. Pain Med 2013;14: 1839–47.

36 Macey TA, Morasco BJ, Duckart JP, Dobscha SK. Patterns and correlates of prescription opioid use in OEF/OIF veterans with chronic noncancer pain. Pain Med 2011;12:1502–9.

37 Wu PC, Lang C, Hasson NK, Linder SH, Clark DJ. Opioid use in young veterans. J Opioid Manag 2010;6:133–9.

38 Ashburn MA, Lipman AG, Carr D, Rubingh C. Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain, 5th edition. Glenview, IL: American Pain Society; 2003.

39 Vieweg WVR, Carlyle Lipps WF, Fernandez A. Opioids and methadone equivalents for clinicians. Prim Care Companion J Clin Psychiatry 2005;7:86–8.

40 US Department of Justice, Drug Enforcement Administration, Office of Diversion Control. Controlled substance schedules. Available at: http://www.deadiversion.usdoj.gov/schedules/index.html (accessed Sepetember 2014).

41 Taylor BC, Hagel EM, Carlson KF, et al. Prevalence and costs of co-occurring traumatic brain injury with and without psychiatric disturbance and pain among Afghanistan and Iraq war veteran V.A. users. Med Care 2012;50:342–6.

42 Gironda RJ, Clark ME, Ruff RL, et al. Traumatic brain injury, polytrauma, and pain: Challenges and treatment strategies for the polytrauma rehabilitation. Rehabil Psychol 2009;54:247–58.

43 Rural Health Research Center. RUCA data: Using RUCA data. 2012. Available at: http://depts.washington.edu/uwruca/ruca-uses.php (accessed September 2014).

44 Epidemiology Program, Post-Deployment Health Group, Office of Public Health, Veterans Health Administration, Department of Veterans Affairs. Analysis of VA health care utilization among Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) veterans: Cumulative from 1st Qtr FY 2002 through 4th Qtr FY 2013 (October 1, 2001–September 30, 2013). 2014. Available at: http://www.publichealth.va.gov/docs/epidemiology/healthcare-utilization-report-fy2013-qtr4.pdf (accessed September 2014).

45 Morasco BJ, Duckart JP, Carr TP, Deyo RA, Dobscha SK. Clinical characteristics of veterans prescribed high doses of opioid medications for chronic non-cancer pain. Pain 2010;151:625–32.

46 Hudson TJ, Edlund MJ, Steffick DE, Tripathi SP, Sullivan MD. Epidemiology of regular prescribed opioid use: Results from a national, population-based survey. J Pain Symptom Manage 2008;36:280–8.

47 Agency Medical Directors Group. Interagency guideline on opioid dosing for chronic non-cancer pain: An educational aid to improve care and safety with opioid therapy. 2010. Available at: http://www.agencymeddirectors.wa.gov/Files/OpioidGdline.pdf (accessed September 2014).

48 Frayne SM, Phibbs CS, Friedman SA, et al. Sourcebook: Women Veterans in the Veterans Health Administration, Volume 2. Sociodemographics and Use of VHA and Non-VA Care (Fee). Washington, DC: Women's Health Evaluation Initiative, Women's Health Services, Veterans Health Administration, Department of Veterans Affairs; 2012.

49 Kaur S, Stechuchak KM, Coffman CJ, Allen KD, Bastian LA. Gender differences in health care utilization among veterans with chronic pain. J Gen Intern Med 2007;22:228–33.

50 Haskell SG, Brandt CA, Krebs EE, et al. Pain among veterans of Operations Enduring Freedom and Iraqi Freedom: Do women and men differ? Pain Med 2009;10:1167–73.

51 US Department of Veterans Affairs, Office of Acquisition and Logistics (OAL). VA directives and handbooks. 2013. Available at: http://www.va.gov/oal/library/dms.asp (accessed September 2014).

52 Veterans Health Administration, Department of Defense. VA/DoD clinical practice guideline for the management of opioid therapy for chronic pain, version 2.0. 2010. Available at: http://www.healthquality.va.gov/guidelines/Pain/cot/COT_312_Full-er.pdf (accessed September 2014).

53 US Department of Veterans Affairs, Veterans Health Administration. VHA directive 2009-053: Pain management. 2009. Available at: http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2781 (accessed September 2014).

54 Vanderlip E, Sullivan M, Edlund M, et al. National study of discontinuation of long-term opioid therapy among veterans. Pain 2014;155:2673–9.