



Suicidal ideation and suicidal self-directed violence following clinician-initiated prescription opioid discontinuation among long-term opioid users



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ABSTRACT

Objective: Little is known about patient outcomes following discontinuation of opioid therapy, which may include suicidal ideation (SI) and suicidal self-directed violence (SSV). The purpose of this study was to examine correlates of SI and non-fatal SSV in a sample of patients discontinued from long-term opioid therapy (LTOT). **Method:** Five hundred-nine Veterans Health Administration (VHA) patients whose clinicians discontinued them from LTOT were selected from a national cohort of VHA patients who discontinued opioids in 2012. The sample comprised patients with a substance use disorder and matched controls. Patient electronic health records were manually reviewed to identify discontinuation reasons and the presence of SI or SSV in the 12 months following discontinuation.

Results: Forty-seven patients (9.2%) had SI only, while 12 patients (2.4%) had SSV. In covariate-adjusted logistic regression models, mental health diagnoses associated with having SI/SSV included post-traumatic stress disorder (aOR = 2.56, 95% CI = 1.23–5.32) and psychotic disorders (aOR = 3.19, 95% CI = 1.14–8.89). Other medical comorbidities, substance use disorder and pain diagnoses, opioid dose, and benzodiazepine prescriptions were unrelated to SI/SSV.

Conclusions: Among patients with a substance use disorder and matched controls, there are high rates of SI/SSV following opioid discontinuation, suggesting that these “high risk” patients may require close monitoring and risk prevention.

1. Introduction

Opioids are commonly prescribed to treat chronic pain [1–2]. Estimates of the prevalence of receipt of prescription opioid therapy among U.S. patients with chronic pain are as high as 20% [3]. However, recent clinical guidelines, including the 2016 CDC guidelines for prescribing opioids for chronic pain [4], discourage use of opioids as a primary analgesic therapy. Guidelines further recommend that clinicians weigh the benefits and risks of opioid therapy for each patient and discontinue opioid therapy when risks outweigh benefits. In addition, recent data from the Veterans Health Administration (VHA) indicate that the overall rate of high-dose opioid prescribing is

decreasing and that the rate of decrease may have accelerated with the implementation of national strategies designed to reduce risky opioid prescribing [5]. These trends suggest that a sizeable proportion of patients in the U.S. prescribed long-term opioid therapy may have their opioid doses lowered and, in some cases, discontinue opioid therapy in the coming years.

While some patients may discontinue opioid therapy of their own volition, data suggest that the majority of opioid discontinuations are initiated by opioid-prescribing clinicians, due to patient high-risk behaviors such as use of other illicit or prescribed controlled substances, opioid misuse, opioid diversion, poor-adherence to the treatment plan, or other patient safety concerns [6]. Despite the heightened

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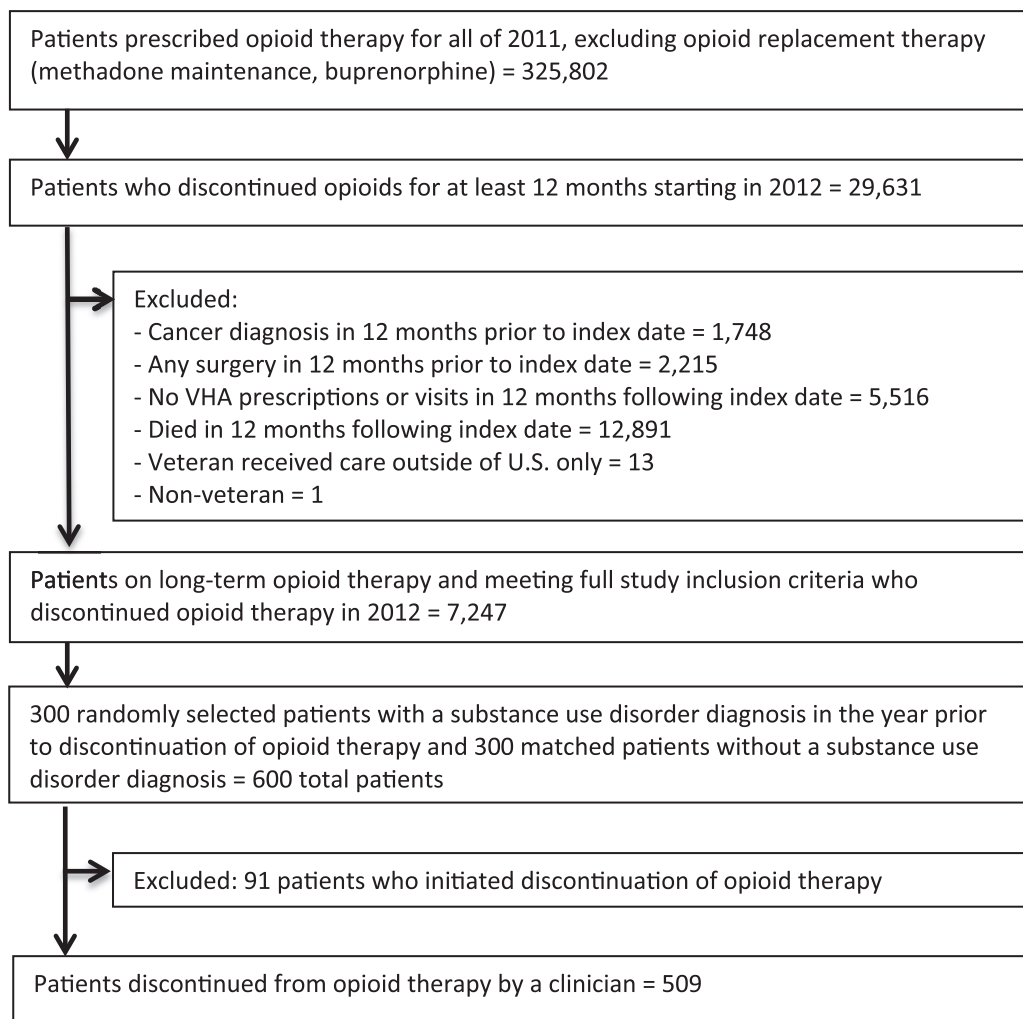


Fig. 1. Sample selection for patients who discontinue opioid therapy. Veterans Health Administration (VHA) patients prescribed opioid therapy for all of 2011 and who subsequently discontinued opioid therapy for at least 12 months beginning in 2012 comprised the study cohort. From this cohort, 300 patients with substance use disorder diagnoses were randomly selected and 300 patients without substance use disorder diagnoses were matched to the substance use disorder sample in order to conduct comprehensive chart review. A total of 509 patients were discontinued from opioid therapy by a clinician and comprise the analytic sample.

risk these patients may face for opioid-related adverse events, some clinicians have expressed concerns about discontinuing opioid therapy for patients they deem to be unstable or who may possess fewer pain coping resources and pain self-management skills [7]. Of particular concern to clinicians is the possibility that discontinuing opioid therapy may cause or exacerbate suicidal ideation in some patients [8]. Concerns about suicide risk are warranted given that those with chronic pain are at elevated risk for suicide and this risk is even greater in those receiving higher opioid doses [9–10]. However, the extent to which opioid discontinuation is associated with suicide risk has not been examined previously.

The primary objective of this study was to identify predictors of suicidal ideation (SI) and non-fatal suicidal self-directed violence (SSV) following clinician-initiated discontinuation of long-term opioid therapy. A secondary objective was to examine incidence and correlates of SI and SSV among patients who did not have SI or SSV prior to opioid discontinuation.

2. Methods

This study was approved by the U.S. Department of Veterans Affairs Portland Health Care System Institutional Review Board.

2.1. Sample selection

Data were extracted from the VHA Corporate Data Warehouse (CDW) to identify a national cohort of all VHA patients prescribed long-term opioid therapy, which we defined as continuous opioid therapy for all of 2011. The CDW is a national data repository that provides comprehensive information contained in VHA patients' electronic medical records. Similar to prior studies [11–12], our definition of continuous opioid therapy allowed prescription refill gaps of no > 30 days between completion of an opioid prescription and refill of the next opioid prescription to account for delayed prescription refills resulting from travel, prescription mail order delays, and other circumstances. The mean number of days prescribed opioids in 2011 for this cohort was 351 of 365 days (standard deviation = 17 days).

From this cohort, we identified patients who discontinued prescription opioid therapy—i.e., had no VHA opioid prescriptions—for at least 12 consecutive months starting some time in 2012. We chose a 12-month discontinuation interval to ensure discontinuation was an intended treatment decision and not due to factors that may delay prescription refills of active opioid prescriptions such as geographic relocation, switching care to another VHA facility, and extended inpatient hospitalizations. The date of the last opioid refill was used as an index date for each patient to ascertain patient sociodemographic and clinical characteristics prior to discontinuation. Because this study

focuses on patients with chronic non-cancer pain, we excluded patients with the following characteristics in the year prior to the index date: (1) the only opioid therapy prescribed was through a VHA opioid substitution program (i.e., buprenorphine or methadone maintenance therapy), (2) a diagnosis of cancer, (3) enrollment in hospice or long-term care, or (4) having received surgery for which opioids may have been prescribed. We also excluded patients with no VHA contact (i.e., no VHA clinical encounters or medications prescribed) or who died in the year following discontinuation, as well as non-veterans or veteran patients whose only medical care was obtained at a facility located in a U.S. territory.

From the cohort of 7247 patients who discontinued opioid therapy in 2012, we selected 600 patients in order to ascertain detailed information about reasons for discontinuation of opioid therapy and post-discontinuation incidence of SI and SSV based on comprehensive electronic health record review. Consistent with the U.S. Centers for Disease Control and Prevention's classification system for self-directed violence, we defined SSV as "behavior that is self-directed and deliberately results in injury or the potential for injury to oneself" and "there is evidence, whether implicit or explicit, of suicidal intent" (p. 21) [13]. Data for the current study were derived from a research project where the goal was to examine differences in reasons for discontinuation of opioid therapy between patients with and without substance use disorders. The sample thus comprised 300 patients with a substance use disorder diagnosis (randomly selected from 1868 patients with a substance use disorder diagnosis) and 300 propensity score-matched patients without a substance use disorder diagnosis (selected from the 5379 patients without a substance use disorder diagnosis) in the year prior to the index date. Details about the matching procedures have been described elsewhere [6]. Fig. 1 details sample selection and the number of patients meeting each exclusion criterion.

2.2. Data sources and study variables

2.2.1. Electronic health record review

A trained research associate experienced with reviewing and coding VHA medical charts for opioid-related studies performed all electronic health record reviews. Additional details about the training and quality assurance procedures have been described elsewhere [6]. Review of patients' electronic health records identified patient and clinician reasons for discontinuation of opioid therapy. Patients could be coded as having multiple patient- or clinician-initiated discontinuation reasons (e.g., a patient may have had an aberrant urine toxicology screen and been suspected of diverting opioid medication). However, all reasons for discontinuation for each patient were classified as either patient-initiated or clinician-initiated in this sample. Of the 600 patients who discontinued opioid therapy, 509 discontinuations (85%) were initiated by clinicians; these 509 patients comprise the study's analytic sample.

Clinician-initiated discontinuation reasons included (1) "Aberrant Behaviors", comprising aberrant urine drug tests, suspected use of alcohol or other substances, opioid misuse, opioid diversion, and non-adherence to plan of care (e.g., failing to present for a urine drug test when asked); (2) "Patient Safety Concerns", comprising prior opioid overdose, high risk for an opioid-related adverse event, and contraindication with other prescribed medication such as benzodiazepines; (3) "Lack of Efficacy", comprising opioids not indicated for type of chronic pain, opioids not decreasing pain, and opioids not improving functioning; (4) opioids now prescribed by a non-VHA prescriber; (5) no reason documented in the electronic medical record; and (6) other reason. These discontinuation reasons have been described in greater detail elsewhere [6].

For the current study, chart review also identified documentation in patients' electronic health records of SI and non-fatal SSV in the year following opioid discontinuation. SI and SSV were ascertained by reviewing all VHA inpatient and outpatient clinical notes (including

primary and specialty medical and mental health care) in the specified time frame. By definition, any patient with SSV was also considered to have SI. A secondary aim of this study was to identify whether the SI and SSV within this sample were new or pre-existing. As such, for patients with documentation of SI or SSV post-opioid discontinuation, we expanded our review of the electronic health record for these patients to determine if SI or SSV had also been documented in the record in the 12 months prior to discontinuation of opioid therapy. We did not review electronic health records for pre-discontinuation SI or SSV in patients who did not have electronic health record documentation of SI or SSV post-discontinuation.

2.2.2. Administrative data

Data were abstracted from the CDW for the 12 months prior to opioid discontinuation. We obtained demographic characteristics (age, gender, race/ethnicity) and rurality of patients' place of residence based on rural-urban commuting area codes [14]. Medical comorbidities were assessed with the Elixhauser Comorbidity Index [15], where higher scores indicate a greater number of comorbidities. VHA Service Connected Disability status, which is disability granted to veteran patients as a result of military service-related injuries or traumas, was also obtained. Diagnoses of mental health disorders, substance use disorders, chronic pain syndromes, and sleep disorders were obtained for the year prior to discontinuation. Opioid-related variables assessed over the year prior to discontinuation included average daily dose of opioids in morphine equivalents (a metric used to standardize opioid dose across different opioid medications), and number of opioid prescribers in the year prior to discontinuation. We also identified patients who were prescribed benzodiazepines in the year prior to discontinuation.

2.3. Statistical analyses

We utilized chi-square tests of association for categorical variables and independent sample *t*-tests for continuous variables to compare sociodemographic, medical comorbidity, and clinical care variables between patients with and without SI/SSV. We next conducted multivariate logistic regression to examine the covariate-adjusted associations of these variables with SI/SSV. Sample size limitations precluded identification of variables associated with SSV alone, due to the low number of documented cases of SSV in this sample. In Step 1 of the model, we included sociodemographic variables found to be associated with SI/SSV in prior studies: age, gender, and race/ethnicity [16–18]. In Step 2, we added to the model measures of medical comorbidity, disability status, and clinical diagnoses previously found to be associated with SI/SSV [16–18]. Step 2 variables included the Elixhauser Comorbidity Index, any VHA Service Connected Disability (yes vs. no), and diagnoses given in the 12 months prior to opioid discontinuation of depressive disorder, bipolar disorder, post-traumatic stress disorder (PTSD), other anxiety disorders, psychotic disorders (e.g., schizophrenia), any alcohol or other substance use disorder (excluding tobacco use disorder), tobacco use disorder, chronic pain diagnoses (i.e., musculoskeletal pain, neuropathic pain, and migraine headache), and sleep disorder. Finally, in Step 3, we added to the model clinical care variables that may increase patients' risk of SI/SSV. These included benzodiazepine prescriptions, opioid dose in the year prior to opioid discontinuation (measured in average daily morphine equivalents), and opioid discontinuation reasons that may place patients at increased risk for adverse events, namely, opioid-related aberrant behaviors and patient safety concerns. To examine correlates of *new onset* SI/SSV, we repeated the 3-step multivariate logistic regression described above, excluding patients with SI/SSV in the year after discontinuation of opioid therapy who also had documented SI/SSV in the medical record in the year prior to discontinuation ($n = 25$). All inferential analyses used two-sided tests of significance and $\alpha = 0.05$.

Table 1

Demographic and clinical characteristics based on presence of suicidal ideation or non-fatal suicidal self-directed violence in the 12 months following discontinuation of long-term opioid therapy.

Variable	Full sample N = 509 %(n) or M ± SD	SI/SSV n = 59 %(n) or M ± SD	No SI/SSV n = 450 %(n) or M ± SD	p-Value
Sociodemographic characteristics				
Age	55.0 ± 10.4	52.5 ± 9.6	55.3 ± 10.4	0.05
Male gender	94.3% (480)	94.9% (56)	94.2% (424)	0.83
Race/ethnicity				0.01
White, non-Hispanic	70.7% (360)	72.9% (43)	70.4% (317)	
Black, non-Hispanic	16.9% (86)	11.9% (7)	17.6% (79)	
Hispanic	2.2% (11)	8.5% (5)	1.3% (6)	
Other/unknown	10.2% (52)	6.8% (4)	10.7% (48)	
Rural-urban continuum				0.72
Isolated	4.9% (25)	8.5% (5)	4.4% (20)	
Small rural	12.2% (62)	11.9% (7)	12.2% (55)	
Large rural	8.4% (43)	8.5% (5)	8.4% (38)	
Urban	74.1% (377)	71.2% (42)	74.4% (335)	
Unknown	0.4% (2)	0.0% (0)	0.4% (2)	
Clinical diagnoses and medical comorbidities				
Elixhauser Comorbidity Index	1.6 ± 1.4	1.7 ± 1.3	1.6 ± 1.4	0.59
Any VHA Service Connected Disability	55.4% (282)	57.6% (34)	55.1% (248)	0.72
Mental health diagnoses				
Depressive disorder	24.4% (124)	30.5% (18)	23.6% (106)	0.24
Bipolar disorder	8.1% (41)	11.9% (7)	7.6% (34)	0.25
PTSD	30.6% (156)	44.1% (26)	28.9% (130)	0.02
Other anxiety disorder	25.3% (129)	30.5% (18)	24.7% (111)	0.33
Psychotic disorder	8.1% (41)	15.3% (9)	7.1% (32)	0.03
Substance use disorder diagnoses				
Alcohol use disorder	27.5% (140)	25.4% (15)	27.8% (125)	0.70
Amphetamine use disorder	2.2% (11)	5.1% (3)	1.8% (8)	0.10
Cannabis use disorder	5.9% (30)	5.1% (3)	6.0% (27)	0.78
Cocaine use disorder	7.9% (40)	11.9% (7)	7.3% (33)	0.22
Opioid use disorder	13.2% (67)	18.6% (11)	12.4% (56)	0.19
Sedative use disorder	2.6% (13)	6.8% (4)	2.0% (9)	0.03
Other substance use disorder	6.1% (31)	10.2% (6)	5.6% (25)	0.16
Tobacco use disorder diagnosis	44.4% (226)	45.8% (27)	44.2% (199)	0.82
Pain diagnoses				
Musculoskeletal	85.1% (433)	84.7% (50)	85.1% (383)	0.94
Neuropathy	5.5% (28)	5.1% (3)	5.6% (25)	0.88
Migraine headache	10.4% (53)	16.9% (10)	9.6% (43)	0.08
Sleep disorder diagnosis	7.5% (38)	6.8% (4)	7.6% (34)	0.83
Clinical care				
Prescribed benzodiazepine	13.0% (66)	11.9% (7)	13.1% (59)	0.79
Average MEDD	75.7 ± 89.6	88.6 ± 93.7	74.0 ± 89.0	0.24
Number of opioid prescribers	2.6 ± 1.6	2.9 ± 1.7	2.5 ± 1.6	0.11
Reason for discontinuation of opioid therapy				
Aberrant behaviors	75.0% (382)	81.4% (48)	74.2% (334)	0.23
Patient safety concerns	7.3% (37)	13.6% (8)	6.4% (29)	0.05

Demographic characteristics, clinical diagnoses, medical comorbidities, and prescription information were obtained for the year prior to discontinuation of opioid therapy.

MEDD = Morphine Equivalent Daily Dose, PTSD = Post-Traumatic Stress Disorder, SI = Suicidal Ideation, SSV = Non-fatal Suicidal Self-directed Violence, VHA = Veterans Health Administration.

Items in bold are significant at $p \leq 0.05$.

3. Results

This study sample comprised 509 patients prescribed long-term opioid therapy for chronic pain, predominantly musculoskeletal pain (85%), whose clinicians discontinued patients' prescriptions for opioid therapy. Similar to the population of veterans prescribed opioid therapy through VHA [12,19], the study sample had a mean age of 55 years, was predominantly male (94%), non-Hispanic white (71%), and resided in urban locations (74%). Sixty-one percent of patients in this sample received a diagnosis for at least one mental health disorder in the year prior to discontinuation of opioid therapy, including PTSD (31%), anxiety disorders other than PTSD (25%), depressive disorders (24%), bipolar affective disorders (8%), and psychotic disorders (8%). Per study design, approximately half of patients were diagnosed with at least one substance use disorder in the year prior to discontinuation; the most common diagnoses were alcohol use disorder (28%), opioid use disorder (13%), and cocaine use disorder (8%). The majority of patients

(75%) were discontinued from opioid therapy due to aberrant behaviors. Table 1 provides characteristics of the full sample and the subsamples of patients with and without SI/SSV.

Approximately 12% of patients in this sample (n = 59) had SSV and/or SI documented in the VHA medical record in the 12 months following discontinuation of opioid therapy. Forty-seven had SI only, while 12 had SSV. Of the 12 patients with documented SSV, 6 patients attempted to overdose on prescription medication (4 of the 6 on benzodiazepines), 1 attempted to overdose using amphetamines and cocaine, 3 patients cut their wrists, 1 patient attempted to hang himself, and another attempted to take his life using a firearm but someone intervened before he could complete the act. Of the 59 patients with documented SI/SSV in the 12 months following discontinuation of opioid therapy, 34 had no documentation in the medical record of SI/SSV in the year prior to discontinuation, and thus met our definition of new onset SI/SSV.

Table 2
Multivariate correlates of any suicidal ideation or non-fatal suicidal self-directed violence in the year following discontinuation of long-term opioid therapy.

	Model 1	Model 2	Model 3
Demographic characteristics			
Age	0.97 (0.95–1.00)*	0.98 (0.95–1.01)	0.97 (0.95–1.00)
Male gender	1.36 (0.39–4.81)	1.39 (0.39–5.01)	1.39 (0.37–5.21)
Race			
White, non-Hispanic	Reference	Reference	Reference
Black, non-Hispanic	0.67 (0.29–1.56)	0.72 (0.30–1.72)	0.76 (0.31–1.83)
Hispanic	6.48 (1.88–22.35)*	7.94 (2.15–29.28)*	7.25 (1.96–27.18)*
Other/unknown	0.62 (0.21–1.82)	0.66 (0.22–2.00)	0.65 (0.21–2.01)
Clinical diagnoses and medical comorbidities			
Elixhauser Medical Comorbidity Index	–	0.87 (0.65–1.16)	0.87 (0.65–1.16)
Any VHA Service Connected Disability	–	0.73 (0.38–1.40)	0.71 (0.37–1.37)
Mental health diagnoses			
Depressive disorder	–	1.31 (0.68–2.50)	1.29 (0.67–2.49)
Bipolar disorder	–	1.52 (0.60–3.85)	1.40 (0.53–3.67)
PTSD	–	2.33 (1.14–4.78)*	2.56 (1.23–5.32)*
Other anxiety disorders	–	0.98 (0.50–1.89)	0.92 (0.46–1.82)
Psychotic-spectrum disorders	–	3.34 (1.23–9.11)*	3.19 (1.14–8.89)*
Substance use disorder diagnosis	–	1.09 (0.60–1.98)	0.98 (0.53–1.80)
Tobacco use disorder diagnosis	–	1.06 (0.58–1.92)	1.02 (0.56–1.88)
Chronic pain diagnoses			
Muskuloskeletal pain	–	0.88 (0.39–2.00)	0.82 (0.36–1.90)
Neuropathic pain	–	0.99 (0.27–3.69)	0.93 (0.24–3.61)
Migraine headache	–	1.14 (0.48–2.68)	1.17 (0.49–2.81)
Sleep disorder diagnosis	–	0.67 (0.20–2.18)	0.72 (0.22–2.38)
Clinical care			
Prescribed benzodiazepine in the year prior to discontinuation	–	–	0.68 (0.26–1.81)
Average MEDD in the year prior to discontinuation	–	–	1.00 (1.00–1.01)
Reason for discontinuation of opioid therapy			
Aberrant behaviors	–	–	1.61 (0.76–3.42)
Patient safety concerns	–	–	2.06 (0.82–5.18)

Results presented as adjusted odds ratios (95% confidence intervals). The analytic sample comprised 59 patients with SI/SSV and 450 patients without SI/SSV in the year following discontinuation of opioid therapy.

Demographic characteristics, clinical diagnoses, medical comorbidities, and prescription information were obtained for the year prior to discontinuation of opioid therapy. Substance use disorder diagnosis category includes alcohol use disorder diagnoses and excludes tobacco use disorder diagnoses.

MEDD = Morphine Equivalent Daily Dose; PTSD = Post-traumatic Stress Disorder; SI = Suicidal Ideation, SSV = Non-fatal Suicidal Self-directed Violence, VHA = Veterans Health Administration.

* $p < 0.05$.

3.1. Correlates of SI/SSV following clinician-initiated discontinuation of opioid therapy

Younger age (OR = 0.97 [95% CI = 0.95–1.00]) and self-identifying as Hispanic ethnicity (OR = 6.48 [1.88–22.35]) were associated with an increased likelihood of SI/SSV in the year following discontinuation of opioid therapy (see Table 2, Model 1). However, only Hispanic ethnicity remained a significant demographic correlate of SI/SSV in the fully adjusted model (Model 3). Having a PTSD diagnosis (OR = 2.33 [1.14–4.78]) or psychotic-spectrum disorder diagnosis (OR = 3.34 [1.23–9.11]) in the year prior to opioid discontinuation was also significantly associated with SI/SSV at model entry (see Table 2, Model 2) and these associations remained significant in the fully adjusted model. Although opioid discontinuation due to patient safety concerns was associated with an increased likelihood of having SI/SSV in bivariate analyses (see Table 1), it was unrelated to SI/SSV in the covariate-adjusted model (OR = 2.06 [0.82–5.18]). Table 2 provides effect size estimates as measured by the odds ratio for each variable at model entry and in the final, fully adjusted model.

3.2. Correlates of new onset SI/SSV

Multivariate analyses were conducted for the reduced sample of $n = 484$ patients (34 with new onset SI/SSV and 450 without SI/SSV in the year following discontinuation of opioid therapy). Results were generally unchanged from those for the full sample described above. In the fully adjusted model, only Hispanic ethnicity, PTSD diagnosis, and psychotic disorder diagnosis were significantly related to SI/SSV (see

Table 3 for effect size estimates for each variable at model entry and in the final, fully adjusted model). The one exception was that age was unrelated to SI/SSV in the reduced sample at model entry (see Table 3, Model 1).

4. Discussion

In this national sample of VHA patients with substance use disorder diagnoses and similar matched patients who were discontinued from long-term opioid therapy by their opioid-prescribing clinicians, nearly 12% had documentation in the medical record of SI/SSV in the year following discontinuation—9.2% with SI only and 2.4% with SSV. This is higher than the 12-month incidence of self-reported suicidal ideation (3.8%) and attempts (0.4%) found in a community sample of veterans in two U.S. states surveyed through the Behavioral Risk Factor Surveillance System Veteran's Health Module [20], while lower than the self-reported SI incidence of 24% and commensurate with the SSV incidence of 2% in the past 12 months for VHA patients referred to primary care mental health services [21]. That rates of SSV in the current study were most commensurate with a sample of mental health treatment-seeking veteran patients may be due to the selection of patients with substance use disorders and similar matched patients, given high rates of comorbidity between substance use and mental health disorders. Indeed, 61% of patients in the current study had one or more mental health disorder diagnoses documented in the medical record in the year prior to opioid discontinuation. However, unlike prior studies that obtained patient self-reported SI and SSV, our estimates of SI and SSV were ascertained from medical record

Table 3
Multivariate correlates of new onset suicidal ideation or non-fatal suicidal self-directed violence in the year following discontinuation of long-term opioid therapy.

	Model 1	Model 2	Model 3
Demographic characteristics			
Age	0.98 (0.95–1.01)	0.98 (0.94–1.01)	0.97 (0.94–1.01)
Male gender	1.07 (0.23–4.93)	0.83 (0.17–4.03)	0.72 (0.15–3.57)
Race			
White, non-Hispanic	Reference	Reference	Reference
Black, non-Hispanic	1.18 (0.46–3.02)	1.19 (0.44–3.21)	1.15 (0.42–3.15)
Hispanic	10.69 (2.76–41.34)*	17.69 (4.03–77.61)*	16.49 (3.71–73.35)*
Other/unknown	0.96 (0.27–3.35)	1.14 (0.31–4.13)	1.06 (0.28–3.93)
Clinical diagnoses and medical comorbidities			
Elixhauser Medical Comorbidity Score	–	0.67 (0.44–1.03)	0.70 (0.46–1.07)
Any VHA Service Connected Disability	–	0.55 (0.24–1.28)	0.56 (0.24–1.31)
Mental health diagnoses			
Depressive disorder	–	0.91 (0.37–2.24)	0.93 (0.38–2.31)
Bipolar disorder	–	0.30 (0.04–2.43)	0.28 (0.03–2.37)
PTSD	–	3.61 (1.37–9.55)*	3.78 (1.41–10.14)*
Other anxiety disorders	–	1.09 (0.44–2.65)	1.06 (0.43–2.60)
Psychotic-spectrum disorders	–	6.51 (1.71–24.75)*	6.72 (1.73–26.17)*
Substance use disorder diagnosis	–	0.92 (0.43–2.00)	0.86 (0.39–1.87)
Tobacco use disorder diagnosis	–	0.82 (0.37–1.79)	0.74 (0.33–1.67)
Chronic pain diagnoses			
Muskuloskeletal pain	–	1.24 (0.42–3.70)	1.24 (0.41–3.75)
Neuropathic pain	–	0.87 (0.11–7.00)	1.09 (0.13–9.06)
Migraine headache	–	0.52 (0.13–2.04)	0.49 (0.12–1.96)
Sleep disorder diagnosis	–	1.05 (0.26–4.24)	1.14 (0.28–4.60)
Clinical care			
Prescribed benzodiazepine in the year prior to discontinuation	–	–	0.73 (0.21–2.59)
Average MEDD in the year prior to discontinuation	–	–	1.00 (1.00–1.01)
Reason for discontinuation of opioid therapy			
Aberrant behaviors	–	–	1.89 (0.70–5.13)
Patient safety concerns	–	–	0.89 (0.18–4.44)

Results presented as adjusted odds ratios (95% confidence intervals). The analytic sample comprised 34 patients with new onset SI/SSV and 450 patients without SI/SSV in the year following discontinuation of opioid therapy.

Demographic characteristics, clinical diagnoses, medical comorbidities, and prescription information were obtained for the year prior to discontinuation of opioid therapy. Substance use disorder diagnosis category includes alcohol use disorder diagnoses and excludes tobacco use disorder diagnoses.

MEDD = Morphine Equivalent Daily Dose; PTSD = Post-traumatic Stress Disorder; SI = Suicidal Ideation, SSV = Non-fatal Suicidal Self-directed Violence, VHA = Veterans Health Administration.

* $p < 0.05$.

documentation only. It is likely that we underestimated the actual proportion of patients who experienced SI or SSV in the year following discontinuation of opioid therapy. Within VHA, patients receiving mental health services are routinely asked about current suicidal ideation. Our findings suggest that asking these questions of patients who discontinue long-term opioid therapy may help identify patients in this population with SI, at which point intervening actions and safety planning can occur before patients engage in self-harm behaviors [22].

To our knowledge, ours is the first study to examine correlates of SI and SSV subsequent to discontinuation of long-term opioid therapy in patients with chronic pain. A prior study examined correlates of SI and SSV in a sample of patients with chronic pain prescribed opioid therapy for at least six weeks [23]. The strongest predictors of past 12 months reported SI was a diagnosis of depression and a lifetime suicide attempt. Pain-related factors, such as specific pain diagnoses, severity of pain, and physical functioning were unrelated to SI. The authors concluded that patient samples comprising people prescribed opioid therapy for chronic pain may represent those whose pain is more severe, and pain-related variables thus have less of an association with SI/SSV [23]. Findings from our study corroborate the finding that mental health diagnoses (PTSD and psychotic disorders in our sample) are more strongly associated with SI/SSV than pain-related factors and extend this finding to patients who discontinue opioid therapy.

Substance use disorder diagnoses in general were unrelated to SI/SSV in the current study. Among veterans, substance use disorder diagnoses have been shown to be unrelated to suicide outcomes after controlling for mental health variables [16]. One possible explanation of this finding is that while substance use can lead to behavioral

impulsivity and disinhibition, it must be paired with acute negative mood to elicit suicidal thoughts and self-directed violent behaviors [24]. Substance use in the absence of negative mood states may be insufficient to precipitate these suicidal thoughts and behaviors. An exception in the current study was the finding that a diagnosis of sedative use disorder was associated with SI/SSV in bivariate analyses, suggesting that some specific substance use disorders may be more strongly associated with SI/SSV than others. However, having a benzodiazepine prescription was unrelated to SI/SSV. It is notable that we identified six patients with documented suicide attempts via drug overdose and four of these attempts involved benzodiazepines. These data suggest that benzodiazepines by themselves may not be related to suicidality unless benzodiazepine misuse is present, as is the case for patients with sedative use disorders. In addition to monitoring patients for SI subsequent to opioid discontinuation, it may be particularly important for clinicians to pay close attention to patients with sedative use disorders who may have access to potentially lethal doses of their “drug of choice” in benzodiazepines, even when not prescribed these medications.

An unexpected finding was the association between Hispanic ethnicity, relative to non-Hispanic whites, and SI/SSV. This finding contradicts the preponderance of evidence synthesized in systematic reviews that has found Hispanic ethnicity to be unrelated to SI [16,25]. In our study, point estimates for the likelihood of having SI/SSV for Hispanic patients are bracketed by wide confidence intervals, likely due to the small number of Hispanic patients in this sample—only 11 patients (2.2%) out of 509 self-identified with Hispanic ethnicity, and nearly half of these patients (5 of 11) had some form of SI documented

in the medical record in the 12 months following discontinuation of opioid therapy. Additional research is needed to further explore the relationship between Hispanic ethnicity and SI following discontinuation of long-term opioid therapy. Particular attention should be given to identifying Hispanic ethnicity subgroups (e.g., Puerto Rican, Cuban, Mexican) and levels of acculturation, as these factors may account for differences in prevalence of mental health disorders and SI within the Hispanic population [25].

4.1. Limitations

Findings from this study should be considered in light of its limitations. First, the study sample comprised VHA patients with substance use disorder diagnoses in the year prior to discontinuation of opioid therapy and a matched sample without substance use disorder diagnoses. Results may not generalize to the general population of VHA or non-VHA patients. Second, we excluded patients who died in the year following discontinuation of opioid therapy. Our sample may thus underestimate the proportion of patients that experience SI/SSV following opioid discontinuation, as those who died by suicide in the year following discontinuation of opioid therapy would have been excluded. Third, we did not review pre-discontinuation chart notes for the presence SI/SSV for the 450 patients with no SI/SSV documented post-discontinuation. As a result, we were unable to determine baseline rates of SI/SSV in this sample prior to discontinuation of opioid therapy. Fourth, sample size limitations precluded an examination of demographic, medical comorbidity, and other clinical variables associated with SSV alone. Finally, SI/SSV was ascertained based solely on medical chart review, which likely underestimates actual rates of SI/SSV in this population.

4.2. Conclusions

A substantial proportion of patients with substance use disorder diagnoses and similar matched patients experience SI or SSV following discontinuation of long-term opioid therapy by opioid-prescribing clinicians, most of whom represent new onset cases. As in the general suicide and chronic pain-specific literature, mental health diagnoses appear to be more strongly correlated with SI and SSV relative to pain-specific factors. Primary care clinicians and allied mental health providers should pay extra attention to safety when patients are discontinued from long-term opioid therapy, particularly patients with PTSD or psychotic disorders.

Disclaimer

The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the U.S. Department of Veterans Affairs or U.S. Government.

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