ORIGINAL RESEARCH

Substance Use Disorder Treatment Following Clinician-Initiated Discontinuation of Long-Term Opioid Therapy Resulting from an Aberrant Urine Drug Test

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BACKGROUND: It is unclear whether substance use disorder (SUD) treatment is offered to, or utilized by, patients who are discontinued from long-term opioid therapy (LTOT) following aberrant urine drug tests (UDTs).

OBJECTIVE: To describe the proportion of patients who were referred to, and engaged in, SUD treatment following LTOT discontinuation and to examine differences in SUD treatment referral and engagement based on the substances that led to discontinuation.

DESIGN: From a sample of 600 patients selected from a national cohort of Veterans Health Administration patients who were discontinued from LTOT, we used manual chart review to identify 169 patients who were discontinued because of a UDT that was positive for alcohol, cannabis, or other illicit or non-prescribed controlled substances.

MAIN MEASURES: We extracted sociodemographic, clinical, and health care utilization data from patients' electronic medical records.

KEY RESULTS: Forty-three percent of patients (n = 73) received an SUD treatment referral following LTOT discontinuation and 20% (n = 34) engaged in a new episode of SUD treatment in the year following discontinuation. Logistic regression models controlling for sociodemographic and clinical variables demonstrated that patients who tested positive for cannabis were less likely than patients who tested positive for non-cannabis substances to receive referrals for SUD treatment (aOR = 0.44, 95% CI = 0.23–0.84, p = 0.01) or engage in SUD treatment (aOR = 0.42, 95% CI = 0.19–0.94, p = 0.04). Conversely, those who tested positive for cocaine were more likely to receive an SUD treatment referral (aOR = 3.32, 95% CI = 1.57–7.06, p = 0.002) and engage in SUD treatment (aOR = 2.44, 95% CI = 1.00–5.96, p = 0.05) compared to those who did not have a cocaine-positive UDT.

CONCLUSIONS: There may be substance-specific differences in clinician referrals to, and patient engagement in, SUD treatment. This suggests a need for more standardized implementation of clinical guidelines that recommend SUD care, when appropriate, following LTOT discontinuation.

KEY WORDS: long-term opioid therapy; chronic pain; substance use treatment; physician referral.
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INTRODUCTION

Up to 30% of Americans live with chronic pain conditions,[1] with as many as 11% experiencing daily pain of clinical significance.[2] Many individuals living with chronic pain are treated with opioid therapy.[3] To reduce opioid-related misuse and adverse events such as overdose and death, clinical guidelines recommend close monitoring of patients for aberrant behaviors using tools such as urine drug tests (UDTs) or querying state prescription drug-monitoring databases.[4,5] Evidence of high-risk behaviors, such as UDTs that are positive for illicit or non-prescribed controlled substances, may lead to discontinuation of long-term opioid therapy (LTOT).[6]

Among a national sample of patients who were discontinued from LTOT, 37% were discontinued because of an aberrant UDT.[7] While current recommendations suggest tapering or discontinuing opioid therapy and considering substance use treatment when indicated,[8] data about the care patients receive following LTOT discontinuation are limited. Among patients who are discontinued from LTOT following a positive UDT for alcohol, cannabis, other illicit substances, or non-prescribed controlled substances, little is known about whether follow-up substance use disorder (SUD) treatment is offered or utilized.

Furthermore, clinicians' treatment recommendations may differ based on the type of substance for which a patient tests positive. Cannabis is among the most common substances to be detected on a UDT among chronic pain patients prescribed LTOT.[6,7] More than half of the US and the District of Columbia (DC) have passed legislation to allow medical

cannabis use, and eight of these states and DC also allow recreational cannabis use.[8] These trends suggest a growing public acceptance of cannabis, despite limited evidence for effective pain management for most chronic pain conditions.[9,10] Thus, the likelihood of clinician referrals to, and patient engagement in, SUD treatment for cannabis use following LTOT discontinuation may differ from patients who are using non-cannabis substances.

This study aimed to (1) describe the proportion of patients who were referred to, and engaged in, SUD treatment following LTOT discontinuation for an aberrant UDT and (2) examine differences in SUD treatment referrals and engagement based on the type of substance for which patients were discontinued. We hypothesized that patients who were discontinued for cannabis, relative to alcohol or other illicit and non-prescribed controlled substances, would be less likely to receive a referral for, or engage in, SUD treatment.

METHODS

Data Source and Sample Selection

Study procedures were approved by the VA Portland Health Care System Institutional Review Board. A more detailed description of the research methods has been previously described.[7] The VA Corporate Data Warehouse (CDW) is a collection of multiple relational databases containing comprehensive and aggregated VA patient electronic medical record data, including demographic characteristics, diagnoses, treatment utilization, pharmacy, laboratory chemistry, and other data. We used the CDW to identify a national cohort of VA patients who were prescribed LTOT for the entire year of 2011. From this cohort, we identified patients who subsequently discontinued LTOT for at least 12 consecutive months, beginning in 2012. This duration was chosen to ensure that discontinuation was not due to circumstantial reasons that would inhibit the renewal of an active opioid prescription (e.g., geographic relocation or extended inpatient hospitalization). We defined the "index date" as the date of the last opioid fill. Because this study focused on LTOT for chronic non-cancer pain, we excluded patients whose only opioid therapy was provided through an opioid agonist treatment program, had a cancer diagnosis (other than non-melanoma skin cancer), were enrolled in hospice or long-term care, or had surgery in the year prior to the index date for which opioids may have been prescribed for post-surgical acute pain.

To identify a sample of patients at risk for discontinuation of LTOT due to aberrant behaviors, we randomly selected 300 patients with an SUD diagnosis in the year prior to LTOT discontinuation, who were matched using propensity scores to 300 patients without an SUD diagnosis, but who were otherwise similar in terms of demographic and clinical characteristics of SUD patients. Propensity scores were created using sociodemographic and clinical/pain variables. A more detailed description of the propensity matching process and variables included in propensity models has been previously described.[7]

From this sample of 600 patients, we identified 223 patients who were discontinued from LTOT because of an aberrant UDT. Thirty-one of these patients were discontinued solely because of testing negative for a prescribed opioid, leaving 192 patients who tested positive for alcohol, cannabis, other illicit substances, or a non-prescribed controlled substance. Because this study focused on new episodes of SUD treatment, we excluded 23 patients who had documentation of SUD treatment in the year prior to discontinuation, as post-discontinuation SUD treatment for these individuals may have represented an ongoing treatment episode. Our final analytic sample thus included 169 patients. Figure 1 details sample selection and the number of patients meeting each exclusion criterion.

Chart Review

A detailed explanation of the development and reliability testing of the chart review coding tool has been published elsewhere.[7] Briefly, following sample selection, four clinicians with expertise in chronic pain and SUD developed, pilot tested, and further refined a chart review coding tool. A research assistant (RA) with prior experience reviewing medical charts for similar studies received extensive training on the coding tool. The RA subsequently reviewed and coded the 600 charts from the patient sample. To ensure ongoing fidelity to the coding scheme, the study principal investigator double-coded 60 randomly selected charts (10%) from the analytic sample and discussed coding discrepancies with the RA. Fidelity, as indicated by high intercoder reliability, to the coding scheme was maintained over the course of the study. The average kappa in the study phase was 0.85 across all variables (average percent simple agreement = 98%). All variables reported in this study met our a priori standard of acceptable reliability (e.g., kappa $\geq$0.70 or simple agreement $\geq$95% for binary variables).[11]

Study Variables

Administrative Data Abstraction. Data abstracted from the CDW included demographic characteristics (age, gender, race/ethnicity) and clinical diagnoses in the year prior to discontinuation, including SUD, mental health, and pain diagnoses. Electronic medical record data were gathered about patients' utilization of SUD treatment in the year following discontinuation of opioid therapy, which we defined as documentation of one or more treatment encounters designated as SUD treatment—comprising psychosocial individual or group SUD treatment, as well as medication-assisted therapies such as buprenorphine and methadone maintenance.

Electronic Medical Record. Manual review of patients' electronic medical records identified the reason(s) for

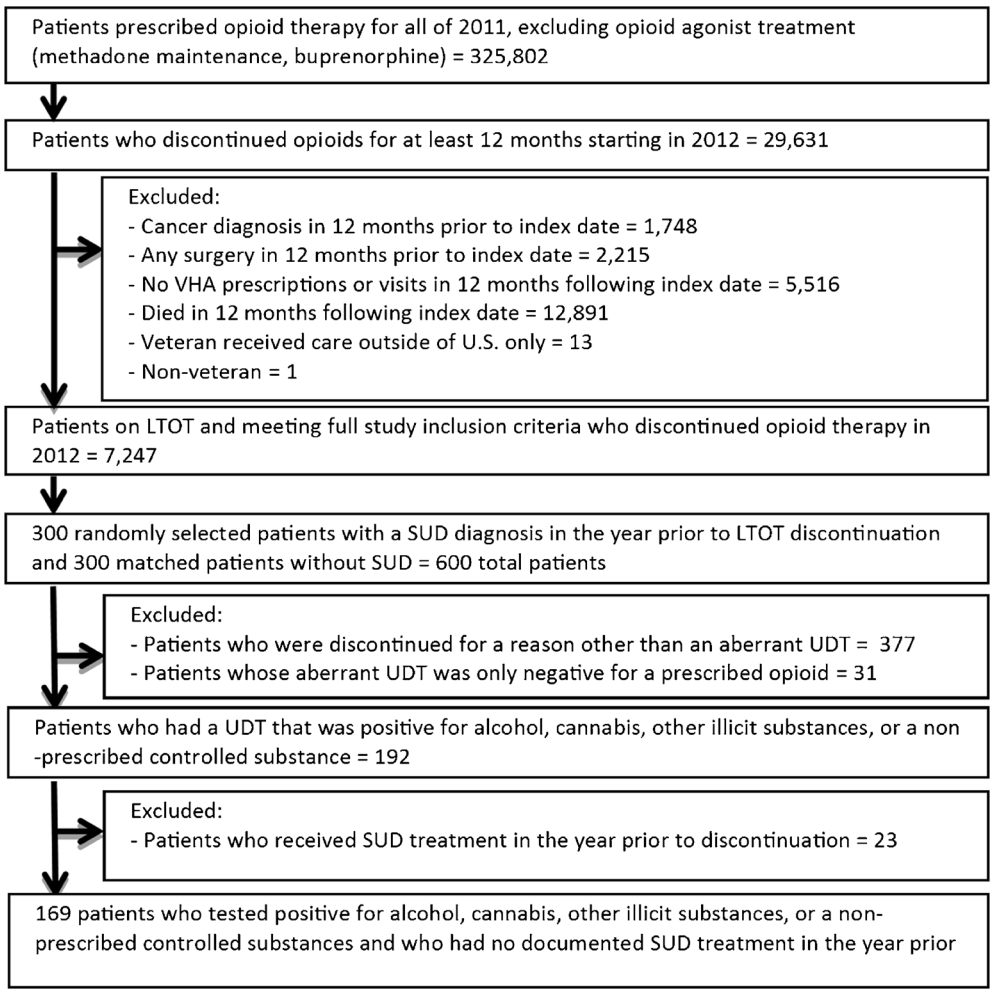

Fig. 1 Sample selection for patients who discontinued long-term opioid therapy (LTOT).

discontinuation of LTOT, including aberrant UDTs. These data were used to identify the study sample. Positive UDT categories included alcohol, cannabis, non-prescribed opioids, non-prescribed sedatives/hypnotics (including benzodiazepines), cocaine, amphetamines, and hallucinogens. Patients could test positive for more than one substance. The chart review also captured whether a referral had been made for SUD treatment at the time of, or following, LTOT discontinuation. SUD treatment referrals included referrals made by the opioid-prescribing primary care provider, other non-opioid-prescribing clinicians (e.g., inpatient providers), or patient self-referrals.

Statistical Analysis

Prior to conducting analyses, data were checked for completeness and accuracy. Descriptive data were summarized for sociodemographic and clinical variables. Unadjusted logistic regression models next examined the association of each specific substance that resulted in LTOT discontinuation (e.g., alcohol, cannabis, cocaine, amphetamine) with each dichotomous dependent variable (e.g., post-discontinuation SUD treatment referral and post-discontinuation SUD treatment engagement). Next, logistic regression models adjusted for age, gender, race, the presence of a pre-opioid discontinuation mental health diagnosis, and the presence of a pre-opioid discontinuation SUD diagnosis. All covariates were determined a priori based on previous literature suggesting that sociodemographic characteristics (age, gender, race) and clinical variables (presence of a mental health or SUD diagnosis) are associated with receipt of SUD treatment.[12,13] An alpha = 0.05 and two-tailed significance tests were used for all inferential analyses.

RESULTS

The study sample comprised 169 patients who were discontinued from LTOT because of testing positive on a UDT for alcohol, cannabis, other illicit substances, or a non-prescribed controlled substance. Sociodemographic and clinical characteristics of the sample are provided in Table 1. Patients were on average 55 years of age and predominantly male (97%). The majority (66%) of patients identified as White and of Non-Hispanic origin and lived in urban locations

Table 1 Sample Characteristics of Patients Discontinued from LTOT for an Aberrant UDT

Variable	Overall sample (*N* = 169)
Sociodemographic characteristics, % (N)	
Age (M ± *SD*)	54.8 ± 9.3
Gender	97.0% (164)
Race/ethnicity	
White, Non-Hispanic	66.3% (112)
Black, Non-Hispanic	20.1% (34)
Hispanic	2.4% (4)
Other/unknown	11.2% (19)
Clinical characteristics, % (N)	
Pre-discontinuation mental health diagnosis	59.8% (101)
Pre-discontinuation SUD diagnosis	49.7% (84)
Referred for SUD treatment following discontinuation of opioid therapy	43.2% (73)
Engaged in SUD treatment in the year following discontinuation of opioid therapy	20.1% (34)
Median number of post-discontinuation SUD encounters in the year following discontinuation of opioid therapy (IQR) †	24 (8–50)
Reasons for discontinuation of opioid therapy, % (N)	
Cannabis	56.8% (96)
Cocaine	26.0% (44)
Non-prescribed opioids	11.8% (20)
Amphetamines	11.2% (19)
Non-prescribed benzodiazepine	5.3% (9)
Alcohol	4.7% (8)

**IQR Interquartile range, SUD substance use disorder, UDT urine drug test*
†Median and IQR presented for patients with at least one SUD treatment encounter in the year following discontinuation of opioid therapy (n = 34)

(72%). Most (82%) were diagnosed with musculoskeletal pain, followed by migraine headaches (10%), neuropathic pain (6%), and other pain (2%). Approximately 60% of patients had a mental health diagnosis in the year prior to LTOT discontinuation. The most prevalent mental health diagnoses included post-traumatic stress disorder (30%), mood disorders (27%), and other non-trauma anxiety disorders (21%). Among patients with an SUD diagnosis in the year prior to LTOT discontinuation, the most common was alcohol use disorder (21%), followed by cocaine use disorder (9%), cannabis use disorder (8%), opioid use disorder (5%), and sedative use disorder (1%). Tobacco use disorder (not included in the above proportion of SUD diagnoses) was present in 48% of patients in the study sample.

Forty-three percent of patients (n = 73) were referred to SUD treatment following discontinuation of LTOT. The majority (90%, n = 66) were referrals made by the opioid-prescribing primary care clinician. One patient was referred by an inpatient psychiatrist, one by an opioid agonist treatment program that required concurrent engagement in psychosocial SUD treatment, two were patient self-referrals, and three were referred to SUD treatment for reasons not documented in the electronic medical record. Forty-seven percent of referred patients (n = 34) had one or more encounters in an SUD treatment setting in the year following LTOT discontinuation and these patients had a median of 24 treatment encounters (IQR = 8–50) (Table 1). Among the 39 patients who were referred for SUD treatment, but ultimately did not engage, 56% (n = 22) declined SUD treatment, 21% (n = 8) failed to attend a scheduled SUD treatment appointment, 21% (n = 8) were referred but never attempted to engage in SUD treatment, and 1 patient transferred care to a new VA and did not engage in SUD treatment following relocation of care.

Table 2 provides results of unadjusted and adjusted logistic regression analyses that examined the likelihood of SUD treatment referral and engagement based on the type of substance for which LTOT was discontinued. In both the unadjusted and adjusted models, those with a UDT positive for cannabis were less likely to receive a referral for SUD treatment (aOR = 0.44, 95% CI = 0.23–0.84, p = 0.01) and less likely to engage in SUD treatment in adjusted models (aOR = 0.42, 95% CI = 0.19–0.94, p = 0.04) compared to those with a UDT positive for substances other than cannabis. Those who tested positive for cocaine were more likely to be referred to SUD treatment in unadjusted and adjusted models (aOR = 3.32, 95% CI = 1.57–7.06, p < 0.01) and more likely to engage in SUD treatment in adjusted models (aOR = 2.44, 95% CI = 1.00–5.96, p = 0.05) compared to those who did not have a UDT positive for cocaine. There were no other associations between the type of substance that led to LTOT discontinuation and SUD treatment referral or engagement (Table 2).

Sensitivity Analyses

We conducted two sensitivity analyses. The first examined odds of SUD treatment referral and engagement in patients with UDT-positive tests for cannabis *only* versus substances other than cannabis. Of the 169 patients with a positive UDT, 77 tested positive for cannabis only, 73 tested positive for one or more non-cannabis substances, and 19 tested positive for cannabis and at least one other substance. For this analysis, we

Table 2 Association of Substance-Specific Discontinuation Reason with SUD Treatment Referral and Engagement Post-opioid Therapy Discontinuation (*N* = 169)

Substance leading to discontinuation	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Association with SUD treatment clinician referral		
Cannabis	**0.53 (0.28–0.98)**	**0.44 (0.23–0.84)**
Cocaine	**2.73 (1.35–5.53)**	**3.32 (1.57–7.06)**
Non-prescribed opioids	0.53 (0.19–1.44)	0.59 (0.21–1.63)
Amphetamines	1.95 (0.74–5.13)	2.38 (0.88–6.42)
Non-prescribed benzodiazepine	0.64 (0.16–2.66)	0.72 (0.17–3.04)
Alcohol	1.33 (0.32–5.52)	1.53 (0.36–6.51)
Association with SUD treatment engagement		
Cannabis	0.53 (0.25–1.13)	**0.42 (0.19–0.94)**
Cocaine	1.76 (0.78–3.94)	**2.44 (1.00–5.96)**
Non-prescribed opioids	1.38 (0.46–4.10)	1.24 (0.50–4.71)
Amphetamines	1.07 (0.33–3.45)	1.28 (0.38–4.30)
Non-prescribed benzodiazepine	0.48 (0.58–3.98)	0.60 (0.07–5.15)
Alcohol	1.34 (0.26–6.97)	1.43 (0.26–7.78)

**Adjusted models controlled for age, gender, race, pre-discontinuation mental health diagnosis, and pre-discontinuation SUD diagnosis. Bold text indicates a statistically significant finding at p < 0.05*
†The reference group for each OR is a UDT that is negative for that specific substance (e.g., cannabis-positive UDT compared to cannabis-negative UDT)

excluded the 19 patients who tested positive for both cannabis and another substance and conducted covariate-adjusted analyses described previously for the dependent variables SUD treatment referral and engagement. Patients with a UDT positive for cannabis only were less likely to receive a referral for SUD treatment than patients who tested positive for any substance other than cannabis (aOR = 0.46, 95% CI = 0.24–0.93, $p = 0.03$). Likelihood of treatment engagement trended in the direction of lower engagement for patients who tested positive for cannabis only (aOR = 0.43, 95% CI = 0.18–1.03, $p = 0.06$).

The second sensitivity analysis examined referrals for SUD treatment made specifically by the opioid-prescribing primary care provider. As noted previously, seven patients were referred to SUD treatment by someone other than the opioid-prescribing primary care provider. We re-analyzed the data for the dependent variable of SUD treatment referrals excluding these seven patients, yielding an analytic sample of $N = 162$. Results of all adjusted models were unchanged.

DISCUSSION

Overall, our data show 43% of patients discontinued by clinicians from LTOT because of a positive UDT were referred for SUD treatment in the year following opioid discontinuation. This is encouraging given that clinical practice guidelines recommend referral to SUD treatment, when indicated, for patients on LTOT and for those who discontinue LTOT.[4,14] It is unclear what proportion of the patients who were not referred for SUD treatment (1) would have benefitted from a referral, (2) were deemed by their clinicians not to need this treatment, or (3) received some SUD treatment within the primary care setting. These data suggest that there may be opportunities to improve rates of SUD treatment referral following LTOT discontinuation.

Fewer than half of SUD treatment-referred patients in this sample engaged in SUD treatment subsequent to the referral. Although we were unable to ascertain reasons for patients' non-engagement, documentation in patients' medical records suggested some patients declined SUD treatment at the time of referral (56%), while others accepted a referral but ultimately did not attend SUD treatment (21%). Non-engagement following referrals may be due to patient perceptions that SUD treatment is not needed,[15] patient frustrations about undertreated pain following LTOT discontinuation,[16] and difficulties accessing SUD treatment.[15,17] Although access to specialty SUD treatment has improved recently in the wake of reports of long wait times in the VA health care system (average inpatient SUD treatment admission wait times are currently 16 days), this study predated these findings.[18] The movement toward embedding SUD treatment into primary care clinics to co-locate pain and SUD services may address perceived access barriers.[19] These changes may further enhance coordination of care and facilitate engagement in SUD treatment among patients who are managing both chronic pain and SUD.[20] Moreover, the delivery of simultaneous SUD and chronic pain treatment has been shown to improve both pain functioning and SUD outcomes,[21,22] and brief clinician-delivered motivational interventions may enhance patients' willingness and readiness to engage in this treatment.[23]

As hypothesized, we identified differences in rates of clinician referrals to SUD treatment depending on the type of substance detected on the UDT. Specifically, those who were discontinued because of the presence of cannabis, which was detected in more than half our sample, were less likely than those who tested positive for substances other than cannabis to be referred for SUD treatment (36% vs. 52%). Conversely, those who were discontinued because of the presence of cocaine were more likely to be referred for SUD treatment (61%) compared to those who tested positive for a substance other than cocaine (36%). This difference may represent a belief among clinicians that cannabis is less harmful than other illicit substances or may be beneficial for some medical conditions[24] and therefore does not warrant follow-up SUD treatment. Alternatively, this finding may represent a reticence among clinicians to recommend SUD treatment given the growing number of states where cannabis is legal. In 2012, the year patients in the current study were discontinued from LTOT, the first 2 states had passed legislation allowing recreational cannabis use, while 16 states and the District of Columbia had legalized medical cannabis. Further research that elucidates the beliefs and practices among clinicians regarding SUD treatment referral, especially for patients using cannabis, is needed.

Similar to differences in SUD treatment referrals, substance-specific differences emerged in patients' SUD treatment engagement. Specifically, those who tested positive for cannabis were less likely to engage in SUD treatment, while those who tested positive for cocaine were more likely to engage in SUD treatment following LTOT discontinuation. Whereas SUD treatment referrals are often initiated by clinicians, engagement in SUD treatment is often predicated on patient motivation, and patients may not perceive cannabis use for chronic pain as problematic. Patients' perceptions of "allowable" uses of cannabis based on state laws may thus conflict with clinicians' assessments of the appropriateness of cannabis given the existing scientific evidence.[25] Yet evidence of the efficacy of cannabis for medical conditions, including chronic pain, has historically been limited.[9] This is due, in part, to federal restrictions on Schedule I substances that limit research on the efficacy of cannabis for various medical conditions.[26] Until additional research is conducted, patients' perceptions of the medical benefits of cannabis may, in many instances, differ from clinicians'.

There are several limitations that should be considered when interpreting these results. First, all patients received care within the Veterans Health Administration and results may not generalize to non-VHA patients who discontinue LTOT. Second, generalization may be further limited given the construction of the study sample. We purposefully sampled patients who were at an increased risk of LTOT discontinuation due to aberrant behaviors by randomly selecting patients with a diagnosed SUD in the year prior to opioid discontinuation, and propensity score matching non-SUD diagnosed patients. Third, conclusions about substance use disorder treatment referral and engagement following discontinuations due to urine drug tests positive for alcohol, amphetamines, and non-prescribed opioids and benzodiazepines may be limited given the small number of patients discontinued for these reasons. Future studies that examine substance-specific SUD treatment referral and engagement rates should include samples of sufficient size to detect clinically significant differences among patients using less commonly detected substances. Fourth, the data utilized were collected via an administrative data abstraction and retrospective electronic medical record review. Misclassifications common to all studies that utilize administrative data may be present in this study.

CONCLUSION

Findings from this study suggest that less than half of patients whose clinicians discontinue LTOT following a positive UDT are referred for SUD treatment. Moreover, there may be substance-specific differences in clinicians' practices of referring patients to SUD treatment as well as patients' engagement in SUD treatment. This may result in certain patients receiving inadequate clinical care and highlights the need for more standardized implementation of clinical guidelines that recommend SUD care, when indicated, following opioid discontinuation.

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Compliance with Ethical Standards:

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

Conflict of Interest: *The authors declare that they do not have a conflict of interest.*

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