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Guideline-Concordant Management of Opioid Therapy among HIV-Infected and Uninfected Veterans

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Abstract

Whether patients receive guideline-concordant opioid therapy (OT) is largely unknown and may vary based on provider and patient characteristics. We assessed the extent to which HIV-infected and uninfected patients initiating long-term (≥90-days) OT received care concordant with American Pain Society/American Academy of Pain Medicine and Department of Veterans Affairs/

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Department of Defense guidelines by measuring receipt of 17 indicators during the first 6 months of OT. Of 20,753 patients, HIV-infected patients (n= 6,604) were more likely than uninfected patients to receive a primary care provider (PCP) visit within 1-month (52.0% vs. 30.9%) and 6-months (90.7% vs. 73.7%) and urine drug tests (UDTs) within 1-month (14.8% vs. 11.5%) and 6-months (19.5% vs. 15.4%; all $p < .001$). HIV-infected patients were also more likely to receive OT concurrent with sedatives (24.6% vs. 19.6%) and an untreated substance use disorder (SUD; 21.6% vs. 17.2%). Among both patient groups, only modest changes in guideline-concordance were observed over time: UDTs and OT concurrent with untreated SUDs increased, while sedative co-prescriptions decreased (all p for trend < .001). Over a 10-year period, on average, patients received no more than 40% of recommended indicators. OT guideline-concordant care is rare in primary care, varies by patient/provider characteristics, and has undergone few changes over time.

Perspective—The promulgation of OT clinical guidelines has not resulted in substantive changes over time in OT management, which falls well short of the standard recommended by leading medical societies. Strategies are needed to increase the provision of OT guideline-concordant care for all patients.

Keywords

Opioid analgesics; practice guideline; quality of health care; chronic pain; HIV

Prescription opioids, medications once largely reserved for the treatment of severe acute pain and end-of-life cancer pain, are now routinely used by primary care physicians for the treatment of moderate to severe chronic non-cancer pain,[6, 8, 26, 41, 50] a trend that is increasingly controversial.[25, 26, 31, 45, 48] Rates of opioid-related serious adverse events, including unprecedented rates of addiction to prescription opioids as well as deaths from unintentional overdose, have risen in parallel with opioid prescribing.[5, 10, 11, 15, 17, 32, 40]

Partly in response to these trends, the American Pain Society (APS)/American Academy of Pain Medicine (AAPM) and the Department of Veterans Affairs (VA)/Department of Defense (DoD) have published guidelines and consensus statements over the past 17 years to assist clinicians in managing chronic pain with opioid therapy (OT).[1, 12, 39, 53, 54] These documents stipulate that initiation of long-term opioid therapy should be preceded by a risk assessment, followed by frequent monitoring.

Adherence to clinical guidelines varies by medical specialty, provider expertise, and patient population.[19, 24, 34, 43, 44] We hypothesize that HIV-infection, in particular, and its association with chronic pain and medical and psychiatric comorbidities, is likely to present obstacles to the receipt of guideline-concordant care for patients receiving long-term OT. Specifically, providers and patients must manage OT in the context of the competing demands of medical, psychiatric and substance use comorbidities, and accordingly, polypharmacy.[7, 14, 18, 30, 38, 42, 46] Moreover, military veterans, in general, suffer from a high prevalence of chronic pain, particularly veterans returning from Afghanistan and Iraq (i.e., Operation Enduring Freedom and Operation Iraqi Freedom, respectively).[46] To date, no studies have examined the provision of OT guideline-concordant care. The objective of this study is to examine the extent to which OT guideline-concordant care was provided in HIV-infected and uninfected veterans.

Materials and Methods

Study Overview

We conducted a retrospective analysis to examine the extent to which patient care was concordant with select APS/AAPM[1, 12] and VA/DoD[53, 54] OT recommendations among a large sample of patients receiving care in the VA healthcare system. Using electronic medical record (EMR) data, we examined receipt of OT guideline-concordant care among HIV-infected and uninfected patients initiating long-term OT as outpatients between fiscal years 1998 and 2010.

Data Source

EMR data, including administrative, clinical, laboratory, and pharmacy data, were obtained from the Veterans Aging Cohort Study-Virtual Cohort (VACS-VC), a prospective cohort of HIV-infected patients matched by age, sex, race, and VA site-of-care to uninfected controls.[20] Details regarding the VACS-VC are published elsewhere.[16, 21, 22]

The VACS-VC is HIPAA compliant and has received approval from the Review Boards for the VA Connecticut Healthcare System and the Yale School of Medicine; the requirement for informed consent was waived.

Study Population

Patients who initiated OT as outpatients between 1998 and 2010 were eligible for inclusion. The cohort was restricted to patients who received incident long-term OT to allow us to assess OT guideline-concordant care at the beginning of treatment, starting with the first prescription written for OT, and continuing until 6 months after OT initiation (patients not reaching 6 months of OT were followed through OT stop date); a follow-up period of 6 months was chosen because it represents a time of increased risk for adverse events, particularly for opioid naïve patients.[12]

Patients initiating OT were identified through the VA's Pharmacy Benefits Management (PBM) database. Long-term OT was defined as greater than or equal to 90 days of prescribed opioids (allowing for a 30-day window for prescription refills).[13, 15, 26] We included prescriptions for oral and transdermal opioids; methadone and buprenorphine prescribed for opioid dependence were excluded. We excluded patients who received an International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) code[9] for palliative/end of life care (V66.7) prior to OT initiation (n=99), those whose follow-up period extended beyond the end of 2010 (n=1,039), and those who died prior to receiving opioids for 90 days (n=328).

Demographic and Clinical Characteristics

Demographic characteristics were derived from the VA National Patient Care Database.[52] Clinical characteristics were based on ICD-9-CM codes and, when applicable, laboratory results (e.g., HIV/hepatitis C [HCV]). Variables reflecting current mental health, substance use disorder (SUD), and pain diagnoses were based on ICD-9-CM codes received between OT initiation and 6 months of follow-up (or OT stop date, when applicable); lifetime

prevalence was based on ICD-9-CM codes received any time prior to OT initiation. Medication variables were identified through PBM data; treatment/procedure variables were identified through administrative codes.

Guidelines and Indicators

Operational definitions for the OT guideline indicators (Fig. 1) were based on published national documents.[1, 12, 53, 54] Select indicators were chosen for study inclusion. We first identified the indicators thought to be the most important to patient safety: risk assessment, monitoring, care of high-risk patients, side-effects management, and chronic pain co-interventions. Within these indicators, we excluded those related to patient groups for which we would have insufficient power to assess guideline-concordant care (e.g., opioid use in pregnancy). We excluded indicators beyond the scope of routine care (e.g., driving and work safety) and those for which data were not contained in our databases (e.g., informal patient counseling).

Outcomes

Operational definitions (Table 1) for receipt of OT guideline indicators were operationalized a priori through consultation with the literature[35] and with practicing clinicians with expertise in Addiction Medicine, Clinical Epidemiology, Health-Services Research, HIV, Pain Management, and Primary Care. We based operational definitions on specific recommendations from the guidelines regarding how often patients should be seen or monitored. When these details were missing, we used consensus definitions based on a minimum standard of care. Unless otherwise noted, the follow-up period of interest is from OT start date through 6 months. With the exception of indicators related to urine drug tests (UDTs), all indicators were assessed from 1998 to 2010; UDT data were available starting in 2000.

Temporal Trends

Individual OT guideline-indicators—In addition to examining receipt of OT guideline indicators using pooled data (1998-2010), we examined temporal trends by categorizing yearly data into three distinct time periods: 1998-2003, 2004-2009, and 2010. These periods were chosen to allow for the implementation of new or updated guidelines.

Summary scores—To determine the proportion of patients receiving OT guideline-concordant care annually, we generated summary scores[27, 33, 47] by dividing the number of OT guideline indicators received per patient by the number of indicators for which the patient was eligible; scores were then multiplied by 100 and expressed as percentages. All indicators were assigned equal weight, as the association between OT guideline indicators and outcomes is unknown. For each year of data, a mean summary score was then calculated from these patient-specific scores (Fig. 2). As UDT data, a component of the summary score, were not available until 2000, summary scores were evaluated from 2000-2010.

Electronic Medical Record Review of PCP and Mental Health Visits

To provide insight into the extent to which PCP visits identified in the EMR addressed OT, two reviewers independently conducted chart reviews on a random sample of 100 patients (stratified by HIV status) receiving a PCP visit during the follow-up period. From the progress notes, reviewers cataloged whether opioids were listed (e.g. present on a computer generated medication list); commented on in the narrative notes; and/or assessed with respect to safety and/or efficacy. We repeated this process among patients receiving two or more outpatient mental health visits and cataloged whether chronic pain was commented on in the narrative notes, whether visits focused on chronic pain management, and whether psychotherapeutic interventions for chronic pain were provided.

Statistical Analyses

Frequencies, means, and proportions were used to characterize the sample at baseline (i.e., date of OT initiation) and to describe receipt of OT guideline indicators. Bivariate comparisons by HIV status were assessed with χ^2-tests and ANOVA, as appropriate. Nonparametric methods were used when indicated. Associations between HIV status and receipt of OT guideline indicators were quantified by odds ratios and corresponding 95% confidence intervals using unadjusted and multivariable logistic regression. Temporal trends in the receipt of OT guideline indicators were assessed using χ^2-tests for trend. Cohen's kappa (*k*) statistics were calculated to assess inter-rater agreement for the chart review. All analyses were performed using SAS software, version 9.2 (SAS Institute, Cary, NC). As a conservative measure, we chose to apply a Bonferroni correction to adjust for multiple comparisons. Specifically, a 2-sided statistical significance level of 0.001 was applied to all analyses.

Results

We identified 20,753 patients initiating long-term OT between 1998 and 2010, among whom 6,604 (31.8%) were HIV-infected (Table 2). We report key findings by HIV status below and in Figures 1 and 2. Multivariable associations are shown in Table 3.

Patient Monitoring

The median (interquartile range [IQR]) number of PCP visits over the 6 months of observation was 3.0 (2.0, 6.0) for HIV-infected patients compared to 2.0 (1.0, 3.0) for uninfected patients ($p<.001$). HIV-infected patients were more likely than uninfected patients to receive PCP visits within 1 month (52.0% vs. 30.9%) and 6 months (90.7% vs. 73.7%) and UDTs within 1 month (14.8% vs. 11.5%) and 6 months (19.5% vs. 15.4%) (all $p<.001$). Among patients prescribed methadone for chronic pain (n=397), electrocardiogram (ECG) receipt was similar for HIV-infected and uninfected patients within 1 month (3.9% vs. 8.6%; $p=.07$) and 6 months (12.3% vs. 14.0%; $p=.64$).

Co-Prescription of High-Risk Medications

HIV-infected patients were more likely to receive sedative co-prescriptions (24.6% vs. 20.0%; $p<.001$); ninety-two percent of these were for benzodiazepines (23.2% vs. 17.7%; $p<.001$). HIV-infected patients were also more likely to receive acetaminophen exceeding

daily-recommended doses (11.1% vs. 5.8%; $p<.001$). Among patients with liver injury (n=6,305), receipt of acetaminophen exceeding daily-recommended doses was similar for HIV-infected and uninfected patients (21.0% vs. 19.8%; $p=.23$).

Opioid Prescribing in High-Risk Patients

HIV-infected patients were more likely to have an active SUD (21.6% vs. 17.2%; $p<.001$). Among active SUD patients (n=3,855), HIV-infected patients were more likely to receive monthly PCP visits (33.6% vs. 14.4%; $p<.001$); there was no difference between groups in the percentage engaged in SUD treatment (51.2% vs. 51.0%; $p=.91$) or in receipt of monthly UDTs (15.9% vs. 15.7%; $p=.88$).

Management of Side Effects

HIV-infected patients were more likely than uninfected patients to be prescribed a bowel regimen (29.8% vs. 24.9%; $p<.001$).

Provision of Chronic Pain Co-Interventions

HIV-infected patients were more likely to be prescribed concurrent non-opioid pain pharmacotherapies (51.5% vs. 46.4%; $p<.001$) but less likely to receive physical rehabilitation therapies (i.e., physical, occupational, or rehabilitation therapies; 24.3% vs. 30.8%; $p<.001$). There was no difference according to HIV status in receipt of outpatient mental health care (30.9% vs. 33.1%; $p=.001$) at our previously established significance level.

Temporal Trends

Individual OT guideline-indicators—Over time, among both HIV-infected and uninfected patients, there was an increase in UDTs (p for trend <.001) and OT concurrent with active SUDs (p for trend <.001), while there was decrease in high-risk co-prescribing, including for benzodiazepines (all p for trend <.001). For HIV-infected patients there was an increase in physical rehabilitative therapies (HIV-infected, p for trend <.001). Among patients with an active SUD, there was a decrease in monthly PCP visits for HIV-infected patients ($p<.001$) and a decrease in SUD treatment engagement for uninfected patients (p for trend=.03). ECG receipt was not evaluated due to low frequency.

Summary scores—From 2000 to 2010, receipt of guideline-concordant care varied from 36.8% to 37.5% for HIV-infected patients ($p=.21$) and from 31.4% to 33.4% for uninfected patients ($p<.001$). (Fig. 2).

Multivariable Analyses

Results from the multivariable-adjusted logistic regression models support the majority of bivariate associations. After adjustment, however, there were no longer differences in receipt of UDTs within 1 month (AOR 1.07, 95% CI 0.96-1.18) or in receipt of OT concurrent with an active SUD (AOR 1.05, 95% CI 0.96-1.16). Models were not evaluated for ECGs due to the small number of outcome events relative to predictors.

Electronic Medical Record Review of PCP and Mental Health Visits

Opioids were listed in 45% of PCP visits reviewed (k=.92) and commented on in the narrative notes in 57% of visits (k=1.00). There was mention of safety or efficacy relative to opioids for 36% of visits (k=.92). For each of these measures, results were similar for HIV-infected and uninfected patients: listed (47% vs. 44%; p=.76), commented (59% vs. 55%; p=.66), safety/efficacy (31% vs. 41%; p=.27).

Pain was commented on in 44% of mental health visits (k=.90) and the focus of 27% of visits (k=.66). Psychotherapeutic interventions for pain were provided in 3% of visits (k=1.00). HIV-infected patients were less likely than uninfected patients to have pain commented on during a mental health visit (32% vs. 56%; p=.02). For the remaining measures, results were similar for HIV-infected and uninfected patients: focus (20% vs. 34%; p=.12), intervention (2% vs. 4%; p=.56).

Discussion

From 1998 to 2010, the majority of patients initiating long-term OT did not receive OT guideline-concordant care. This was true for all patients, regardless of HIV status, and evident across all domains. While HIV-infected patients were more likely than uninfected patients to receive guideline-concordant care for the majority of measures, patient care, overall, fell short of that recommended by the guidelines. For example, we found that at most 52% of patients had a primary care visit within 1 month of starting OT. Moreover, although we found that by 6 months the majority of patients had been seen in primary care, a review of the medical records of a subset of these patients suggests that only one-third were assessed for opioid-related safety and efficacy during such visits. In addition, the vast majority of patients did not undergo a UDT within the first 6 months of care.

We also found that among the 3,855 patients (approximately 20% of the sample) receiving long-term OT concurrent with an active SUD, only 51% were engaged in SUD treatment. According to the 2003 VA/DoD guidelines, OT in the presence of an active SUD is considered a “relative” contraindication for patients not engaged in SUD treatment; with the publication of the 2010 guidelines, it was deemed an “absolute” contraindication.[53, 54] Additionally, among all patients, we found that 25% of HIV-infected patients and 20% of uninfected patients were prescribed sedative medications (benzodiazepines primarily) concurrent with OT, increasing the risk for adverse outcomes, such as respiratory depression and overdose.[12, 53, 54]

Temporal trends in the receipt of OT guideline-concordant care suggest that clinicians are performing UDTs more frequently and prescribing benzodiazepines concurrent with OT less frequently. Less encouragingly, we found that timely PCP visits decreased over time among HIV-infected patients, while prescriptions for OT in the presence of an active SUD increased among both HIV-infected and uninfected patients. Moreover, mean summary scores indicate that over a 10-year period, patients received no more than 40% of recommended care.

Many of our findings run counter to our hypothesis that HIV-infected patients would be less likely to receive OT guideline-concordant care, possibly reflecting the complexities of caring for veterans in general. Similar to HIV-infected patients, 53% of uninfected patients had a history of mental illness and 35% a history of a SUD (Table 2). In addition, 21% of HIV-uninfected patients were HCV-infected and 33% had diabetes (Table 2). Thus, these patients presented to primary care with clinical challenges comparable to those of HIV-infected patients. Moreover, that HIV-infected patients were more likely to receive guideline-concordant care primarily for indicators related to monitoring (i.e., PCP visits/UDTs) is likely due to the increased frequency with which HIV-infected patients, in accordance with HIV guidelines, are seen in primary care.[51] Additionally, many of the differences that we found, due to our large sample size, while statistically significant, may not be clinically meaningful; conversely, our findings from the chart review, where we had a much smaller sample size, may reflect the opposite (i.e., clinically relevant differences in treatment). The important message from all of these findings, we believe, is that in both groups, patients received care that did not meet the standard set by the guidelines.

Although prior research has shown that for many conditions and patient populations, clinician adherence to clinical guidelines is suboptimal,[2, 4, 33, 43] this is the first study to present an extensive evaluation of longitudinal data on receipt of guideline-concordant OT. Three of the four studies that have been published in this area have focused on a subset of OT patients,[36, 37, 42] and all involved regional data.[28, 36, 37, 42] Consistent with our findings, these studies show deficiencies in the provision of OT across patient groups,[28, 36, 37, 42] with little evidence that high-risk patients are monitored more frequently.[36, 37, 49] Moreover, one study demonstrated that OT is often provided to those with untreated SUDs or with benzodiazepine co-prescriptions, and that few patients receive counseling regarding side-effects management, recommendations for nonpharmacological approaches to pain management, or mental health co-interventions.[36]

Our study has limitations. Specifically, we were unable to determine whether clinicians attempted to deliver OT guideline-concordant care but failed because patients did not adhere to prescribed treatments. And although we observed in a review of randomly sampled PCP and mental health visits that OT was infrequently addressed, it is possible that these issues were addressed but not documented. Additionally, for some indicators, such as adjunctive treatments, we were unable to determine whether some OT guideline indicators, such as adjunctive treatments, were provided specifically to address pain or for treatment of other comorbid conditions (e.g., rehabilitation following a stroke). Similarly, we lacked the data for this current study to determine what proportion of patients failed to receive any non-opioid interventions prior to beginning long-term OT. We also relied on ICD-9-CM data for defining co-morbidities, as a number of validation studies support the use of diagnostic codes for this purpose.[3, 22, 23, 29] For ICD-9-CM codes related to chronic pain, we found that HIV-infected patients were less likely to receive a chronic pain diagnosis; we postulate that these findings may reflect differences in coding practices between Infectious Disease vs. General Medicine providers, in particular differences in their approach to pain management, with Infectious Disease providers more likely to code for infectious or medical comorbidities.[13] Finally, our use of two OT guidelines, both of which were published and subsequently updated during the period of observation, would appear to present a challenge

to assessing guideline-concordant care. The VA/DoD guidelines, however, were modeled on the APS/AAPM document and a review of both reveals substantial overlap.[1, 12, 53, 54] Furthermore, the indicators we assessed did not vary substantively across documents and represent a minimum standard of care. In addition, by anchoring the assessment of temporal trends to one calendar year after major guideline publication dates, we were able to show that only modest changes in guideline-concordance occurred over time. The increased attention that long-term OT has received recently, however, may have resulted in more substantive changes in patient care in the time since our window of observation ended.

While our study has implications for research, policy, and clinical care, we caution against making comparisons between the observed quality of care within the VA and other medical settings. Limited information regarding OT guideline-concordant care outside of the VA exists to support such comparisons. In addition, efforts are underway in the VA to reduce harmful and ineffective care for patients receiving OT.[35] Future efforts should focus on educating clinicians in all settings on the risks associated with opioid prescribing, improving awareness of guideline recommendations, and implementing tools in the clinical practice setting, such as systems-based approaches and patient-centered medical homes, to facilitate safe and effective care for patients receiving long-term OT. In addition, research is needed to understand the barriers encountered by clinicians in delivering OT guideline-concordant care.[43] Importantly, research is also needed to improve the evidence-base from which the guidelines are drawn, specifically research that addresses associations between individual recommendations and patient outcomes. Only when such research is available will clinicians be able to prioritize recommended care and optimize safety and effectiveness.

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Highlights

- Opioid therapy in primary care falls short of guideline recommendations
- Substantive changes have not occurred in guideline-concordant care over time
- Strategies are needed to increase the provision of opioid therapy guideline-concordant care

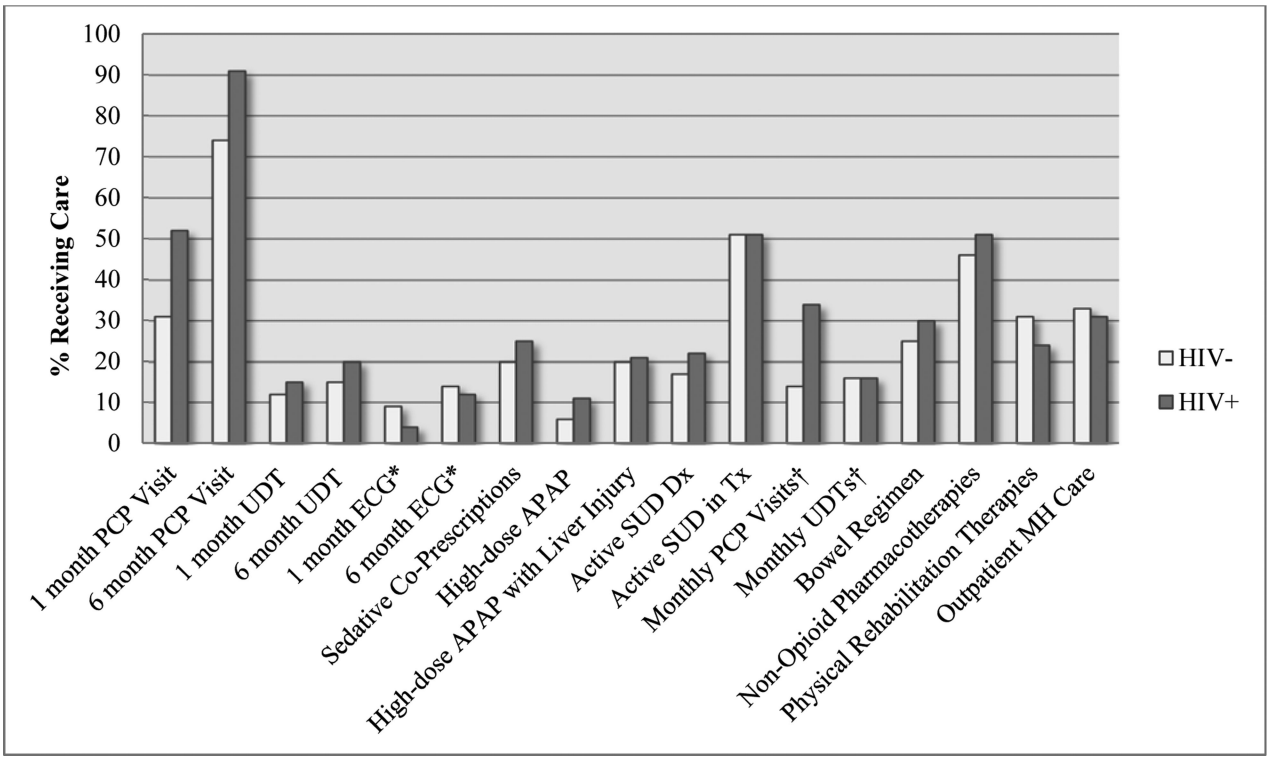

Figure 1. Receipt of OT Guideline-Concordant Care by HIV Status

Abbreviations: APAP, acetaminophen; Dx, diagnosis; ECG, electrocardiogram; MH, mental health; PCP, primary care provider; SUD, substance use disorder; Tx, treatment; UDT, urine drug test.

*Electrocardiograms measured only among patients receiving methadone for chronic pain.

†Monthly PCP Visits and UDTs measured only among those with an active SUD.

Differences in ECG receipt (1 month or 6 months), APAP with liver injury, active SUD treatment, and monthly UDTs were not significant ($P > .05$); MH care was significant at $P=.001$; all other indicators were significant at $P < .001$.

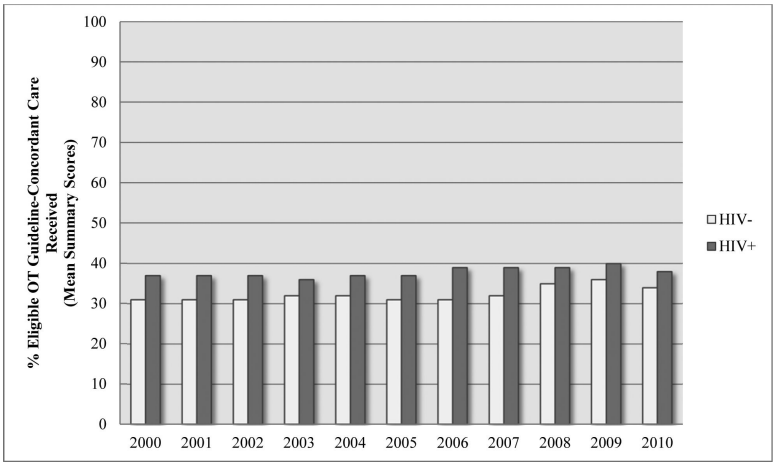

Figure 2. Temporal Trends in Receipt of OT Guideline-Concordant Care

Abbreviations: OT, opioid therapy.

HIV+: p=.27; HIV-: p <.001

Table 1

Opioid Therapy Guideline Indicators, Operational Definitions, and Sources

Guideline Indicators	Operational Definition(s)	Source
Monitoring		
Clinicians should conduct a follow-up visit within 2-4 weeks of OT initiation. This initial phase should be considered a therapeutic trial, for which opioid-naive patients[a] are particularly at risk.[b]	1. Any documented outpatient PCP visit (VA general medical or HIV-specialty clinic) between OT start date and end of 30-days of OT.	APS/AAPM, 1997[10] & 2009[11] VA/DoD 2003[12] & 2010[13]
As part of a comprehensive patient assessment, clinicians should obtain a UDT to assess for aberrant drug-related behaviors in all patients prior to initiating OT.	2. Laboratory documentation of UDT (i.e., toxicology) 30-days before or after OT start date.	APS/AAPM, 2009 VA/DoD 2003 & 2010
For patients receiving methadone for chronic pain, clinicians should obtain a pretreatment ECG to measure QTc interval before initiating OT.	**3.** ECG results obtained 30-days before or after OT start date.	VA/DoD 2003 & 2010
Clinicians should routinely reassess all patients on OT every 1 to 6 months for risks and benefits of treatment for duration of OT.[b]	4. Any documented outpatient PCP visit between OT start date and end of 180-days of OT (or OT stop date for patients on OT < 6 months).	APS/AAPM, 1997 & 2009 VA/DoD 2003 & 2010
Clinicians should routinely confirm adherence to OT plan of care in all patients through periodic UDTs.	5. Laboratory documentation of UDT between OT start date and end of 180-days of OT (or OT stop date).	APS/AAPM, 2009 VA/DoD 2003 & 2010
For patients receiving methadone for chronic pain, clinicians should obtain a follow-up ECG to measure QTc interval once methadone dose is stabilized.	6. ECG results for test(s) obtained between OT start date and end of 180-days of OT (or OT stop date).	VA/DoD, 2010
Co-Prescription of High-Risk Medications		
Clinicians should avoid co-prescription of sedatives and OT.	7. Pharmacy documentation that patient prescribed benzodiazepines (≥ 7-days so as to exclude prescriptions for acute indications [e.g., pre-operative sedation]), carisoprodol, or barbiturates between OT start date and end of 180-days of OT (or OT stop date).	VA/DoD, 2010
When using opioid combination products, clinicians should not exceed maximum recommended daily doses of prescribed acetaminophen.	8.Among all patients, pharmacy documentation that patient prescribed an average daily dose ≥ 4 grams/day[57] between OT start date and end of 180-days of OT (or OT stop date). 9.Among patients with liver injury (hepatitis C virus, end-stage liver disease, decompensated liver disease, or Fib-4 Index > 3.25), pharmacy documentation that patient prescribed an average daily dose ≥ 2 grams/day[58,59] between OT start date and end of 180-days of OT (or OT stop date).	VA/DoD 2003 & 2010
High-Risk Patients		
Clinicians may consider OT for patients with a history of SUD only if they are able to implement more frequent and stringent monitoring parameters.	10. Documentation of monthly VA PCP visits between OT start date and end of 180-days of OT (or OT stop date). 11. Documentation of monthly UDTs between OT start date and end of 180-days of OT (or OT stop date).	APS/AAPM, 1997 & 2009 VA/DoD, 2003 & 2010
Clinicians should initiate OT with caution in patients with a history of SUD and should never initiate OT in patients with an active disorder who are not in SUD treatment.	12. Examined by SUD treatment status: Documentation of any of following between OT start and end of 180-days of OT (or OT stop date): ICD-9-CM code for an alcohol or drug use disorder SUD treatment: 1 inpatient bed day or 1 outpatient SUD-specialty clinic visit Audit-C score ≥ 4	VA/DoD, 2003 & 2010
Side-Effects Management		
Clinicians should consider prescribing a bowel regimen to all OT patients.	13. Pharmacy documentation that patient prescribed stool softeners and/or laxatives between OT start date and end of 180-days of OT (or OT stop date).	APS/AAPM, 1997 & 2009 VA/DoD, 2003 & 2010
Chronic Pain Co-Interventions		

Guideline Indicators	Operational Definition(s)	Source
Clinicians should avoid relying exclusively on opioids for the management of chronic pain and should routinely take a multidisciplinary approach to pain management that includes the integration of non-opioid pharmacotherapies, rehabilitation or functional restoration, and psychotherapeutic interventions.	14.Non-Opioid Pharmacotherapies Pharmacy documentation that patient prescribed tricyclic antidepressants, gabapentin, or NSAIDs[c] between OT start date and end of 180-days of OT (or OT stop date). 15.Physical Rehabilitation Therapies Any documented outpatient visits to a VA physical therapy, occupational therapy, or rehabilitation clinic anytime between OT start date and end of 180-days of OT (or OT stop date). 16.Psychotherapeutic Co-Interventions Any two documented outpatient visits to a VA mental health clinic between OT start date and end of 180-days of OT (or OT stop date).	APS/AAPM, 1997 & 2009 VA/DoD, 2003 & 2010

Abbreviations: APS, American Pain Society; AAPM; American Academy of Pain Medicine; AUDIT-C, Alcohol Use Disorders Identification Test-Consumption; DoD, Department of Defense; ECG, electrocardiogram; ICD-9-CM, International Classification of Disease, Ninth Revision, Clinical Modification codes; NSAIDs, non-steroidal anti-inflammatory drugs; OT, opioid therapy; PCP, primary care provider; QTc, rate-corrected QT interval; SUD, substance use disorder; UDT, urine drug test; VA, Veterans Administration.

[a] All patients in this current study are considered opioid-naive (i.e., incident OT patients).

[b] Only the VA/DoD guidelines specify an exact time period.

[c] Does not include acetaminophen.

Table 2

Patient Demographic and Clinical Characteristics at OT Initiation: Overall and by HIV status (n=20,753)

	Overall (n=20,753)	HIV+ (n=6,604)	HIV-(n=14,149)	*P* Value*
Age, mean (SD), y	49.6 (9.2)	49.7 (8.9)	49.5 (9.4)	.42
Gender, n (%)				
Male	20,276 (97.7)	6,428 (97.3)	13,848 (97.9)	.02
Race/Ethnicity, n (%)				< .001
White	10,169 (49.0)	3,136 (47.5)	7,033 (49.7)	
Black	8,682 (41.8)	2,898 (43.8)	5,784 (40.9)	
Hispanic	1,333 (6.4)	376 (5.7)	957 (6.8)	
Other	569 (2.7)	194 (2.9)	375 (2.7)	
HCV-Infected, n (%)	6,002 (28.9)	2,971 (45.0)	3,031 (21.4)	< .001
Diabetes, n (%)	6,269 (30.2)	1,566 (23.7)	4,703 (33.2)	< .001
BMI, mean (SD)	28.4 (6.4)	25.6 (5.2)	29.6 (6.5)	< .001
Pain Comorbidities, n (%)[a]				
Chronic Pain[b]	11,836 (57.0)	3,129 (47.4)	8,707 (61.5)	< .001
Acute Pain[c]	2,700 (13.0)	936 (14.2)	1,764 (12.5)	< .001
No Pain Diagnosis	7,855 (37.9)	3,025 (45.8)	4,830 (34.1)	< .001
Any Mental Illness, n (%)[a]	7,126 (34.3)	2,185 (33.1)	4,941 (34.9)	<.01
Anxiety/Depression	4,564 (22.0)	1,520 (23.0)	3,044 (21.5)	.01
Serious Mental Illness[d]	4,138 (19.9)	1,114 (16.9)	3,024 (21.4)	<.001
History of Mental Illness[e]	11,164 (53.8)	3,693 (55.9)	7,471 (52.8)	<.001
Substance Use Disorder, n (%)[a]	3,439 (16.6)	1,279 (19.4)	2,160 (15.3)	<.001
Alcohol Use Disorder	2,177 (10.5)	729 (11.0)	1,448 (10.2)	.08
Drug Use Disorder	2,214 (10.7)	943 (14.3)	1,271 (9.0)	<.001
History of Substance Use Disorder, n (%)[e]	7,867 (37.9)	2,853 (43.2)	5,014 (35.4)	<.001
VACS Index, mean (SD)	25.0 (21.0)	36.9 (23.7)	18.2 (15.8)	<.001
CD4 count, median (IQR), cells/μL	---	386.5 (165, 543)	---	---
HIV-1 RNA, Log 10 Viral Load, < 500 copies/ml, n (%)	---	2,409 (54)	---	---
OT Duration, median (IQR), days	225 (139, 576)	235 (141, 605)	220 (138, 561)	.002

Abbreviations: BMI, body mass index; HCV, hepatitis C virus; IQR, interquartile range; OT, opioid therapy; PTSD, post-traumatic stress disorder; SD, standard deviation; TMJ, temporomandibular disorder; VACS, Veterans Aging Cohort Study.

*P values: t-test (or non-parametric equivalent) for continuous variables. c2-test for categorical variables.

[a]Current diagnosis: from OT index date through follow-up.

[b]Chronic pain: headache, TMJ, neck, back, extremity, arthritis, neuropathy, other.

[c]Acute pain: abdominal, chest fracture, or kidney stones.

[d] Serious Mental Illness: bipolar disorder, PTSD, schizophrenia, schizoaffective disorder, and psychosis.

[e] Lifetime prevalence.

Table 3

Odds Ratios for Receipt of Guideline-Concordant Care for HIV-infected vs. Uninfected Patients

Guideline Indicators	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
1 month PCP Visit	2.40 (2.26, 2.55)	2.49 (2.28, 2.70)
6 month PCP Visit	3.48 (3.18, 3.81)	5.94 (5.13, 6.87)
1 month UDT	1.33 (1.21, 1.46)	1.00 (0.88, 1.14)
6 month UDT	1.33 (1.22, 1.45)	1.12 (1.00, 1.27)
1 month ECG[ab]	0.43 (0.17, 1.09)	-----
6 month ECG[ab]	0.87 (0.47, 1.58)	-----
Sedative Co-Prescriptions	1.34 (1.25, 1.44)	1.56 (1.41, 1.73)
Benzodiazepines Co-Prescriptions	1.40 (1.31, 1.51)	1.57 (1.41, 1.74)
APAP Exceeding Recommended Doses	2.03 (1.83, 2.26)	1.45 (1.25, 1.69)
APAP Exceeding Recommended Doses Concurrent with Liver Injury	1.08 (0.95, 1.22)	1.06 (0.89, 1.25)
Opioids Concurrent with Active SUD	1.33 (1.23, 1.43)	0.92 (0.82, 1.04)
SUD Treatment[c]	1.01 (0.88, 1.14)	1.17 (0.96, 1.41)
Monthly PCP Visits[c]	3.14 (2.65, 3.70)	3.81 (3.03, 4.81)
Monthly UDTs[c]	1.05 (0.86, 1.29)	0.97 (0.74, 1.28)
Provision of Bowel Regimen	1.28 (1.20, 1.37)	0.78 (0.71, 0.86)
Provision of Non-Opioid Pharmacotherapies	1.22 (1.15, 1.30)	1.71 (1.57, 1.86)
Provision of Physical Rehabilitative Therapies	0.72 (0.67, 0.77)	0.82 (0.75, 0.91)
Provision of Outpatient Mental Health Care	0.90 (0.85, 0.96)	0.84 (0.76, 0.93)

Abbreviations: APAP, acetaminophen; ECG, electrocardiogram; OR, odds ratio, PCP, primary care provider; SUD, substance use disorder; UDT, urine drug test.

[a] Electrocardiograms measured only among patients receiving methadone for chronic pain.

[b] Adjusted models were not evaluated for ECGs due to the small number of outcome events relative to predictors.

[c] SUD treatment, monthly PCP Visits, and monthly UDTs measured only among those with an active SUD.