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Guideline-Concordant Management of Opioid Therapy Among Human Immunodeficiency Virus (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 human immunodeficiency virus (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/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 visit within 1 month (52.0% vs 30.9%) and 6 months (90.7% vs 73.7%) and urine drug tests 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 a current substance use disorder (21.6% vs 17.2%). Among both patient groups, only modest changes in guideline concordance were observed over time: urine drug tests and OT concurrent with current substance use disorders increased, whereas sedative coprescriptions decreased (all *P*s for trend <.001). Over a 10-year period, on average, patients received no more than 40% of recommended care. 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.***

Key words: *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 noncancer pain,[6,8,25,40,49] a trend that is increasingly controversial.[24,25,30,44,47] Rates

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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.[5,10,11,15,17,31,39]

Partly in response to these trends, the American Pain Society/American Academy of Pain Medicine 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).[1,12,38,52,53] These documents stipulate that initiation of long-term OT should be preceded by a risk assessment, followed by frequent monitoring.

Adherence to clinical guidelines varies by medical specialty, provider expertise, and patient population.[19,23,33,42,43] We hypothesized that human immunodeficiency virus (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.[7,14,18,29,37,41,45] Moreover, military veterans, in general, suffer from a high prevalence of chronic pain, particularly veterans returning from Afghanistan and Iraq (ie, Operation Enduring Freedom and Operation Iraqi Freedom, respectively).[45] To date, no studies have examined the provision of OT guideline–concordant care. The objective of this study was to examine the extent to which OT guideline–concordant care was provided in HIV-infected and uninfected veterans.

Methods

Study Overview

We conducted a retrospective analysis to examine the extent to which patient care was concordant with select American Pain Society/American Academy of Pain Medicine [1,12] and VA/DoD[52,53] 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, a prospective cohort of HIV-infected patients matched by age, sex, race, and VA site-of-care to uninfected controls.[20] Details regarding the Veterans Aging Cohort Study–Virtual Cohort are published elsewhere.[16,20,21]

The Veterans Aging Cohort Study–Virtual Cohort is HIPAA (Health Insurance Portability and Accountability Act of 1996) 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 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).[13,15,25] 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 before receiving opioids for 90 days (n = 328).

Demographic and Clinical Characteristics

Demographic characteristics were derived from the VA National Patient Care Database.[51] Clinical characteristics were based on ICD-9-CM codes and, when applicable, laboratory results (eg, HIV/hepatitis C virus). 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 Pharmacy Benefits Management 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.[1,12,52,53] 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 cointerventions. Within these indicators, we excluded those related to patient groups for which we would have insufficient power to assess guideline-concordant care (eg, opioid use in pregnancy). We excluded indicators beyond the scope of routine care (eg, driving and work safety) and those for which data were not contained in our databases (eg, informal patient counseling).

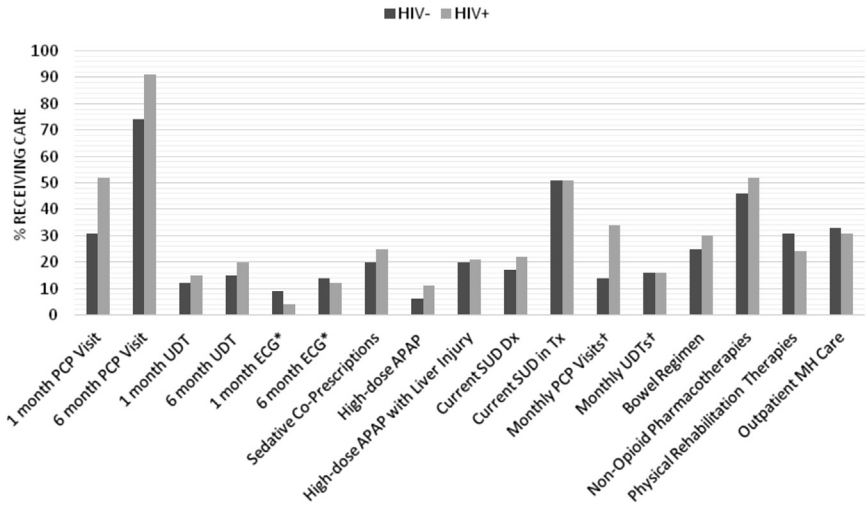

Figure 1. Receipt of OT guideline–concordant care by HIV status. Differences in ECG receipt (1 month or 6 months), APAP with liver injury, current SUD treatment, and monthly UDTs were not significant ($P > .05$); MH care was significant at $P = .001$; all other indicators were significant at $P < .001$. *ECGs measured only among patients receiving methadone for chronic pain. †Monthly PCP visits and UDTs measured only among those with a current SUD. Abbreviations: ECG, electrocardiogram; APAP, acetaminophen; Dx, diagnosis; Tx, treatment; MH, mental health; HIV−, HIV-uninfected; HIV+, HIV-infected.

Outcomes

Operational definitions (Table 1) for receipt of OT guideline indicators were operationalized a priori through consultation with the literature[34] 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 3 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[26,32,46] 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). Because UDT data, a component of the summary score, were not available until 2000, summary scores were evaluated from 2000 to 2010.

EMR Review of Primary Care Provider (PCP) and Mental Health Visits

To provide insight into the extent to which PCP visits identified in the EMR addressed OT, 2 reviewers (J.R.G. and E.J.E.) 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 (eg, present on a computer-generated medication list), were commented on in the narrative notes, and/or were assessed with respect to safety and/or efficacy. We repeated this process among patients receiving 2 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 (ie, date of OT initiation) and to describe receipt of OT guideline indicators. Bivariate comparisons by HIV status were assessed with χ^2 tests and analysis of variance, as appropriate. Nonparametric methods were used when indicated. Associations between HIV status and receipt of OT guideline indicators were quantified by odds ratios (ORs) and corresponding 95% confidence intervals (CIs) 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 (κ) statistics

Table 1. OT Guideline Indicators, Operational Definitions, and Sources

Guideline Indicators	*Operational Definition(s)*	*Source*
Monitoring		
Clinicians should conduct a follow-up visit within 2–4 wk of OT initiation. This initial phase should be considered a therapeutic trial, for which opioid-naïve patients* are particularly at risk.†	1. Any documented outpatient PCP visit (VA general medical or HIV specialty clinic) between OT start date and end of 30 d of OT	APS/AAPM[10,11] VA/DoD[12,13]
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 (ie, toxicology) 30 d before or after OT start date	APS/AAPM[11] VA/DoD[12,13]
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 d before or after OT start date	VA/DoD[12,13]
Clinicians should routinely reassess all patients on OT every 1–6 mo for risks and benefits of treatment for duration of OT†	4. Any documented outpatient PCP visit between OT start date and end of 180 d of OT (or OT stop date for patients on OT <6 mo)	APS/AAPM[10,11] VA/DoD[12,13]
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 d of OT (or OT stop date)	APS/AAPM[11] VA/DoD[12,13]
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 d of OT (or OT stop date)	VA/DoD[13]
Coprescription of high-risk medications		
Clinicians should avoid coprescription of sedatives and OT.	7. Pharmacy documentation that patient prescribed benzodiazepines (≥7 d so as to exclude prescriptions for acute indications [eg, preoperative sedation]), carisoprodol, or barbiturates between OT start date and end of 180 d of OT (or OT stop date)	VA/DoD[13]
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 g/d[54] between OT start date and end of 180 d 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 g/d[55,56] between OT start date and end of 180 d of OT (or OT stop date)	VA/DoD[12,13]
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 d of OT (or OT stop date) 11. Documentation of monthly UDTs between OT start date and end of 180 d of OT (or OT stop date)	APS/AAPM[10,11] VA/DoD[12,13]
Clinicians should initiate OT with caution in patients with a history of SUD and should never initiate OT in patients with a current disorder who are not in SUD treatment.	12. Patients were considered to have a current SUD if they had documentation of any of the following between OT start date and 180 d of OT (or OT stop date)§: a) ICD-9-CM code for an alcohol or drug use disorder b) SUD treatment: 1 inpatient bed day or 1 outpatient SUD specialty clinic visit c) AUDIT-C score ≥ 4	VA/DoD[12,13]

Table 1. Continued

Guideline Indicators	Operational Definition(s)	Source
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 d of OT (or OT stop date)	APS/AAPM[10,11] VA/DoD[12,13]
Chronic pain cointerventions		
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 nonopioid pharmacotherapies, rehabilitation or functional restoration, and psychotherapeutic interventions.	14. Nonopioid pharmacotherapies: Pharmacy documentation that patient prescribed tricyclic antidepressants, gabapentin, or NSAIDs‡ between OT start date and end of 180 d of OT (or OT stop date) 15. Physical rehabilitation therapies: Any documented outpatient visits to a VA physical therapy, occupational therapy, or rehabilitation clinic any time between OT start date and end of 180 d of OT (or OT stop date) 16. Psychotherapeutic cointerventions: Any 2 documented outpatient visits to a VA mental health clinic between OT start date and end of 180 d of OT (or OT stop date)	APS/AAPM[10,11] VA/DoD[12,13]

Abbreviations: VA, Veterans Administration; APS, American Pain Society; AAPM; American Academy of Pain Medicine; ECG, electrocardiogram; QTc, rate-corrected QT interval; ICD-9-CM, *International Classification of Disease, Ninth Revision, Clinical Modification* codes; AUDIT-C, Alcohol Use Disorders Identification Test–Consumption; NSAIDs, nonsteroidal anti-inflammatory drugs.

*All patients in this current study are considered opioid-naïve (ie, incident OT patients).

†Only the VA/DoD guidelines specify an exact time period.

‡Does not include acetaminophen.

§Patients meeting the criteria for current SUD were examined by SUD treatment status.

were calculated to assess interrater 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 .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 Figs 1 and 2. Multivariable associations are shown in Table 3.

Patient Monitoring

The median (interquartile range) 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 Ps < .001). Among patients prescribed methadone for chronic pain (n = 397), electrocardiogram 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%; $P = .64$).

Coprescription of High-Risk Medications

HIV-infected patients were more likely to receive sedative coprescriptions (24.6% vs 19.6%; $P < .001$); 92% of these were for benzodiazepines (23.2% vs 17.7%; $P < .001$). HIV-infected patients were also more likely to receive acetaminophen exceeding recommended daily doses (11.1% vs 5.8%; $P < .001$). Among patients with liver injury (n = 6,305), receipt of acetaminophen exceeding recommended daily 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 a current SUD (21.6% vs 17.2%; $P < .001$). Among current 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%; $P < .001$).

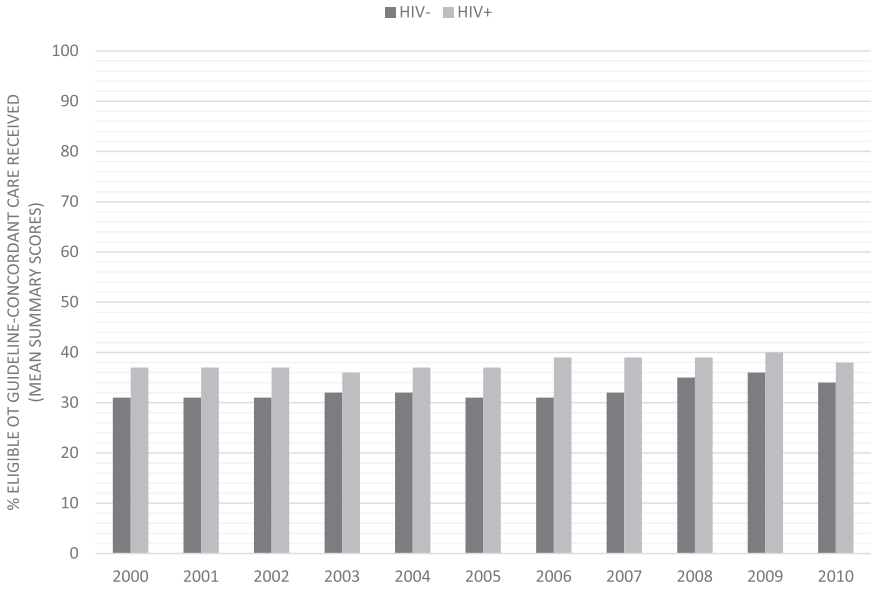

Figure 2. Temporal trends in receipt of OT guideline–concordant care. Abbreviations: HIV−, HIV-uninfected ($P < .001$); HIV+, HIV-infected ($P = .27$).

Provision of Chronic Pain Cointerventions

HIV-infected patients were more likely to be prescribed concurrent nonopioid pain pharmacotherapies (51.5% vs 46.4%; $P < .001$) but less likely to receive physical rehabilitation therapies (ie, 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 current SUDs (P for trend <.001), whereas there was decrease in high-risk coprescribing, 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 a current 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). Electrocardiogram receipt was not evaluated because of low frequency.

Summary Scores

From 2000 to 2010, receipt of guideline-concordant care varied from 36.8% to 37.7% for HIV-infected patients ($P = .21$) and from 31.4% to 33.6% 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 (adjusted OR = 1.00, 95% CI = .88–1.14.) or in receipt of OT concurrent with a current SUD (adjusted OR = .92, 95% CI = .88–1.04). Models were not evaluated for electrocardiograms because of the small number of outcome events relative to predictors.

EMR Review of PCP and Mental Health Visits

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

Pain was commented on in 44% of mental health visits ($\kappa = .90$) and the focus of 27% of visits ($\kappa = .66$). Psychotherapeutic interventions for pain were provided in 3% of visits ($\kappa = 1.00$). 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. Although 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

Table 2. Patient Demographic and Clinical Characteristics at OT Initiation: Overall and by HIV Status (N = 20,753)

Characteristics	Overall (n = 20,753)	HIV-Positive (n = 6,604)	HIV-Negative (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 (%)†				
Chronic pain‡	11,836 (57.0)	3,129 (47.4)	8,707 (61.5)	<.001
Acute pain§	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 (%)†	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‖	4,138 (19.9)	1,114 (16.9)	3,024 (21.4)	<.001
History of mental illness¶	11,164 (53.8)	3,693 (55.9)	7,471 (52.8)	<.001
SUD, n (%)†	3,855 (18.6)	1,424 (21.6)	2,431 (17.2)	<.001
Alcohol use disorder	2,432 (11.7)	790 (12.0)	1,642 (11.6)	.46
Drug use disorder	2,214 (10.7)	943 (14.3)	1,271 (9.0)	<.001
History of SUD, n (%)¶	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	—	338.0 (165, 543)	—	—
HIV-1 RNA, $\log_{10}$ viral load, <500 copies/mL, n (%)	—	2,409 (53.7)	—	—
OT duration, median (IQR), d	225 (139, 576)	235 (141, 605)	220 (138, 561)	.002

Abbreviations: SD, standard deviation; HCV, hepatitis C virus; BMI, body mass index; VACS, Veterans Aging Cohort Study; IQR, interquartile range.
*P values: t-test (or nonparametric equivalent) for continuous variables. χ^2 test for categorical variables.
†Current diagnosis: from OT index date through follow-up.
‡Chronic pain: headache, temporomandibular disorder, neck, back, extremity, arthritis, neuropathy, other.
§Acute pain: abdominal, chest, fracture, or kidney stones.
‖Serious mental illness: bipolar disorder, posttraumatic stress disorder, schizophrenia, schizoaffective disorder, and psychosis.
¶Lifetime prevalence.

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 a current SUD, only 51% were engaged in SUD treatment. According to the 2003 VA/DoD guidelines, OT in the presence of a current 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.[52,53] 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.[12,52,53]

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, whereas prescriptions for OT in the presence of a current 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 hepatitis C virus–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 (ie, PCP visits/UDTs) is probably due to the increased frequency with which HIV-infected patients, in accordance with HIV guidelines, are seen in primary care.[50] Additionally, because of our large sample size,

Table 3. ORs for Receipt of Guideline-Concordant Care for HIV-Infected Versus Uninfected Patients

Guideline Indicators	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
1-mo PCP visit	2.40 (2.26–2.55)	2.49 (2.28–2.70)
6-mo PCP visit	3.48 (3.18–3.81)	5.94 (5.13–6.87)
1-mo UDT	1.33 (1.21–1.46)	1.00 (.88–1.14)
6-mo UDT	1.33 (1.22–1.45)	1.12 (1.00–1.27)
1-mo ECG*†	.43 (.17–1.09)	—
6-mo ECG*†	.87 (.47–1.58)	—
Sedative coprescriptions	1.34 (1.25–1.44)	1.56 (1.41–1.73)
Benzodiazepines coprescriptions	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 (.95–1.22)	1.06 (.89–1.25)
Opioids concurrent with current SUD	1.33 (1.23–1.43)	.92 (.82–1.04)
SUD treatment‡	1.01 (.88–1.14)	1.17 (.96–1.41)
Monthly PCP visits‡	3.14 (2.65–3.70)	3.81 (3.03–4.81)
Monthly UDTs‡	1.05 (.86–1.29)	.97 (.74–1.28)
Provision of bowel regimen	1.28 (1.20–1.37)	.78 (.71–.86)
Provision of nonopioid pharmacotherapies	1.22 (1.15–1.30)	1.71 (1.57–1.86)
Provision of physical rehabilitative therapies	.72 (.67–.77)	.82 (.75–.91)
Provision of outpatient mental health care	.90 (.85–.96)	.84 (.76–.93)

Abbreviations: ECG, electrocardiogram; APAP, acetaminophen.
*ECGs measured only among patients receiving methadone for chronic pain.
†Adjusted models were not evaluated for ECGs because of the small number of outcome events relative to predictors.
‡SUD treatment, monthly PCP Visits, and monthly UDTs measured only among those with a current SUD.

many of the differences that we found, though 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 (ie, 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,[2,4,32,42] this is the first study to present an extensive evaluation of longitudinal data on receipt of guideline-concordant OT. Three of the 4 studies that have been published in this area have focused on a subset of OT patients,[35,36,41] and all involved regional data.[27,35,36,41] Consistent with our findings, these studies show deficiencies in the provision of OT across patient groups,[27,35,36,41] with little evidence that high-risk patients are monitored more frequently.[35,36,48] Moreover, 1 study demonstrated that OT is often provided to those with untreated SUDs or with benzodiazepine coprescriptions, and that few patients receive counseling regarding side effects management, recommendations for nonpharmacologic approaches to pain management, or mental health cointerventions.[35]

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. Also, 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 (eg, rehabilitation following a stroke). Similarly, we lacked the data for this current study to determine what proportion of patients failed to receive any nonopioid interventions prior to beginning long-term OT. We also relied on ICD-9-CM data for defining comorbidities, as a number of validation studies support the use of diagnostic codes for this purpose.[3,21,22,28] 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 and 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 2 OT guidelines,[1,12,52,53] 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 American Pain Society/American Academy of Pain Medicine document, and a review of both reveals substantial overlap.[1,12,52,53] 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 1 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.

Although 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 under way in the VA to reduce harmful and ineffective care for patients receiving OT.[34] 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.[42] 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.

References

1. American Pain Society/American Academy of Pain Medicine: The use of opioids for treatment of chronic pain. A consensus statement from the American Academy of Pain Medicine and the American Pain Society. Clin J Pain 13:6-8, 1997

2. Asch SM, Kerr EA, Keesey J, Adams JL, Setodji CM, Malik S, McGlynn EA: Who is at greatest risk for receiving poor-quality health care? N Engl J Med 354:1147-1156, 2006

3. Bebu I, Tate J, Rimland D, Mesner O, Macalino GE, Ganesan A, Okulicz JF, Bavaro M, Weintrob AC, Justice AC, Agan BK, Infectious Disease Clinical Research Program HIV Working Group: The VACS Index Predicts Mortality in a Young, Healthy HIV Population Starting Highly Active Antiretroviral Therapy. J Acquir Immune Defic Syndr 65:226-230, 2014

4. Berkenblit GV, Sosman JM, Bass M, Gebrekristos HT, Cofrancesco JJ, Sullivan LE, Cook RL, Edison M, Bashook PG, Korthuis PT: Factors affecting clinician educator encouragement of routine HIV testing among trainees. J Gen Intern Med 27:839-844, 2012

5. Bohnert AS, Valenstein M, Bair MJ, Ganoczy D, McCarthy JF, Ilgen MA, Blow FC: Association between opioid prescribing patterns and opioid overdose-related deaths. J Am Med Assoc 305:1315-1321, 2011

6. Braden JB, Fan MY, Edlund MJ, Martin BC, DeVries A, Sullivan MD: Trends in use of opioids by noncancer pain type 2000-2005 among Arkansas Medicaid and HealthCore enrollees: Results from the TROUP study. J. Pain 9: 1026-1035, 2008

7. Breitbart W, Rosenfeld BD, Passik SD, McDonald MV, Thaler H, Portenoy RK: The undertreatment of pain in ambulatory AIDS patients. Pain 65:243-249, 1996

8. Caudill-Slosberg MA, Schwartz LM, Woloshin S: Office visits and analgesic prescriptions for musculoskeletal pain in US: 1980 vs. 2000. Pain 109:514-519, 2004

9. Centers for Disease Control and Prevention: International Classification of Diseases, Ninth Revision, Clinical Modification. Hyattsville MD, National Center for Health Statistics, 2010

10. Centers for Disease Control and Prevention: Unintentional poisoning deaths—United States, 1999-2004. MMWR Morb Mortal Wkly Rep 56:93-96, 2007

11. Centers for Disease Control and Prevention: Vital signs: Overdoses of prescription opioid pain relievers—United States, 1999-2008. MMWR Morb Mortal Wkly Rep 60:1487-1492, 2011

12. Chou R, Fanciullo GJ, Fine PG, Adler JA, Ballantyne JC, Davies P, Donovan MI, Fishbain DA, Foley KM, Fudin J, Gilson AM, Kelter A, Mauskop A, O'Connor PG, Passik SD, Pasternak GW, Portenoy RK, Rich BA, Roberts RG, Todd KH, Miaskowski C, American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel: Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. J Pain 10: 113-130, 2009

13. Edelman EJ, Gordon K, Becker WC, Goulet JL, Skanderson M, Gaither JR, Brennan Braden J, Gordon AJ, Kerns RD, Justice AC, Fiellin DA: Receipt of opioid analgesics by HIV-infected and uninfected patients. J Gen Intern Med 28:82-90, 2013

14. Edelman EJ, Gordon KS, Glover J, McNicholl IR, Fiellin DA, Justice AC: The next therapeutic challenge in HIV: Polypharmacy. Drugs Aging 30:613-628, 2013

15. Edlund MJ, Steffick D, Hudson T, Harris KM, Sullivan M: Risk factors for clinically recognized opioid abuse and dependence among veterans using opioids for chronic non-cancer pain. Pain 129:355-362, 2007

16. Fultz SL, Skanderson M, Mole LA, Gandhi N, Bryant K, Crystal S, Justice AC: Development and verification of a "virtual" cohort using the National VA Health Information System. Med Care 44:S25-S30, 2006

17. Hall AJ, Logan JE, Toblin RL, Kaplan JA, Kraner JC, Bixler D, Crosby AE, Paulozzi LJ: Patterns of abuse among unintentional pharmaceutical overdose fatalities. J Am Med Assoc 300:2613-2620, 2008

18. Hansen L, Penko J, Guzman D, Bangsberg DR, Miaskowski C, Kushel MB: Aberrant behaviors with prescription opioids and problem drug use history in a community-based cohort of HIV-infected individuals. J Pain Symptom Manage 42:893-902, 2011

19. Jatulis DE, Meng YY, Elashoff RM, Schocket AL, Evans RM, Hasan AG, Legorreta AP: Preventive pharmacologic therapy among asthmatics: Five years after publication of guidelines. Ann Allergy Asthma Immunol 81: 82-88, 1998

20. Justice AC, Dombrowski E, Conigliaro J, Fultz SL, Gibson D, Madenwald T, Goulet J, Simberkoff M, Butt AA, Rimland D, Rodriguez-Barradas MC, Gibert CL, Oursler KA, Brown S, Leaf DA, Goetz MB, Bryant K: Veterans Aging Cohort Study (VACS): Overview and description. Med Care 44:S13-S24, 2006

21. Justice AC, Erdos J, Brandt C, Conigliaro J, Tierney W, Bryant K: The Veterans Affairs Healthcare System: A unique laboratory for observational and interventional research. Med Care 44:S7-S12, 2006

22. Justice AC, Lasky E, McGinnis KA, Skanderson M, Conigliaro J, Fultz SL, Crothers K, Rabeneck L, Rodriguez-Barradas M, Weissman SB, Bryant K, Team VP: Medical disease and alcohol use among veterans with human immunodeficiency infection: A comparison of disease measurement strategies. Med Care 44:S52-S60, 2006

23. Koethe JR, Moore RD, Wagner KR: Physician specialization and women's primary care services in an urban HIV clinic. AIDS Patient Care STDS 22:373-380, 2008

24. Korff MV: Long-term opioid therapy reconsidered. Ann Intern Med 155:325-328, 2011

25. Korff MV, Saunders K, Thomas Ray G, Boudreau D, Campbell C, Merrill J, Sullivan MD, Rutter CM, Silverberg MJ, Banta-Green C, Weisner C: De facto long-term opioid therapy for noncancer pain. Clin J Pain 24:521-527, 2008

26. Korthuis PT, Fiellin DA, Fu R, Lum PJ, Altice FL, Sohler N, Tozzi MJ, Asch SM, Botsko M, Fishl M, Flanigan TP, Boverman J, McCarty D, BHIVES Collaborative: Improving adherence to HIV quality of care indicators in persons with opioid dependence: The role of buprenorphine. J Acquir Immune Defic Syndr 56(Suppl 1):S83-S90, 2011

27. Krebs EE, Ramsey DC, Miloshoff JM, Bair MJ: Primary care monitoring of long-term opioid therapy among veterans with chronic pain. Pain Med 12:740-746, 2011

28. Lo Re V III, Lim JK, Goetz MB, Tate J, Bathulapalli H, Klein MB, Rimland D, Rodriguez-Barradas MC, Butt AA, Gibert CL, Brown ST, Kidwai F, Brandt C, Dorey-Stein Z, Reddy KR, Justice AC: Validity of diagnostic codes and liver-related laboratory abnormalities to identify hepatic decompensation events in the Veterans Aging Cohort Study. Pharmacoepidemiol Drug Saf 20:689-699, 2011

29. Lum PJ, Little S, Botsko M, Hersh D, Thawley RE, Egan JE, Mitty J, Boverman J, Fiellin DA, BHIVES Collaborative: Opioid-prescribing practices and provider confidence recognizing opioid analgesic abuse in HIV primary care settings. J Acquir Immune Defic Syndr 56(Suppl 1):S91-S97, 2011

30. Manchikanti L, Ailinani H, Koyyalagunta D, Datta S, Singh V, Eriator I, Sehgal N, Shah R, Benyamin R, Vallejo R, Fellows B, Christo PJ: A systematic review of randomized trials of long-term opioid management for chronic non-cancer pain. Pain Physician 14:91-121, 2011

31. Manchikanti L, Singh A: Therapeutic opioids: A ten-year perspective on the complexities and complications of the escalating use, abuse, and nonmedical use of opioids. Pain Physician 11:S63-S88, 2008

32. McGlynn EA, Asch SM, Adams J, Keesey J, Hicks J, DeCristofaro A, Kerr EA: The quality of health care delivered to adults in the United States. N Engl J Med 348:2635-2645, 2003

33. Meng YY, Leung KM, Berkbigler D, Halbert RJ, Legorreta AP: Compliance with US asthma management guidelines and specialty care: A regional variation or national concern? J Eval Clin Pract 5:213-221, 1999

34. Midboe AM, Lewis ET, Paik MC, Gallagher RM, Rosenberg JM, Goodman F, Kerns RD, Becker WC, Trafton JA: Measurement of adherence to clinical practice guidelines for opioid therapy for chronic pain. Transl Behav Med 2:57-64, 2012

35. Morasco BJ, Cavanagh R, Gritzner S, Dobscha SK: Care management practices for chronic pain in veterans prescribed high doses of opioid medications. Fam Pract 30: 671-678, 2013

36. Morasco BJ, Duckart JP, Dobscha SK: Adherence to clinical guidelines for opioid therapy for chronic pain in patients with substance use disorder. J Gen Intern Med 26:965-971, 2011

37. Morrison RE, Brint JM, Smith WR, Arheart KL, Wray D, Palte SB, Ackerman TF: Appropriate and inappropriate prescribing of narcotics for ambulatory HIV-positive patients. J Gen Intern Med 9:301-305, 1994

38. Nuckols TK, Anderson L, Popescu I, Diamant AL, Doyle B, Di Capua P, Chou R: Opioid prescribing: A systematic review and critical appraisal of guidelines for chronic pain. Ann Intern Med 160:38-47, 2014. http://dx.doi.org/10.7326/0003-4819-160-1-201401070-00732

39. Office of National Drug Control Policy: Epidemic: Responding to America's Prescription Drug Abuse Crisis. Washington, DC, Office of National Drug Control Policy, 2011

40. Olsen Y, Daumit GL, Ford DE: Opioid prescriptions by U.S. primary care physicians from 1992 to 2001. J Pain 7: 225-235, 2006

41. Önen NF, Barrette EP, Shacham E, Taniguchi T, Donovan M, Overton ET: A review of opioid prescribing practices and associations with repeat opioid prescriptions in a contemporary outpatient HIV clinic. Pain Pract 12: 440-448, 2012

42. Pronovost P: Enhancing physicians' use of clinical guidelines. J Am Med Assoc 310:2501-2502, 2013

43. Rosenblatt RA, Baldwin LM, Chan L, Fordyce MA, Hirsch IB, Palmer JP, Wright GE, Hart LG: Improving the quality of outpatient care for older patients with diabetes: Lessons from a comparison of rural and urban communities. J Fam Pract 50:676-680, 2001

44. Rosenblum A, Marsch LA, Joseph H, Portenoy RK: Opioids and the treatment of chronic pain: Controversies, current status, and future directions. Exp Clin Psychopharmacol 16:405-416, 2008

45. Seal KH, Shi Y, Cohen G, Cohen BE, Maguen S, Krebs EE, Neylan TC: Association of mental health disorders with prescription opioids and high-risk opioid use in US veterans of Iraq and Afghanistan. J Am Med Assoc 307:940-947, 2012

46. Shrank WH, Asch SM, Adams J, Setodji C, Kerr EA, Keesey J, Malik S, McGlynn EA: The quality of pharmacologic care for adults in the United States. Med Care 44:936-945, 2006

47. Silverberg MJ: Prescription long-term opioid use in HIV-infected patients. Clin J Pain 28:39-46, 2012

48. Starrels JL, Becker WC, Weiner MG, Li X, Heo M, Turner BJ: Low use of opioid risk reduction strategies in primary care even for high risk patients with chronic pain. J Gen Intern Med 26:958-964, 2011

49. Sullivan MD, Edlund MJ, Fan MY, Devries A, Brennan Braden J, Martin BC: Trends in use of opioids for noncancer pain conditions 2000-2005 in commercial and Medicaid insurance plans: The TROUP study. Pain 138: 440-449, 2008

50. Thompson MA, Aberg JA, Hoy JF, Telenti A, Benson C, Cahn P, Eron JJ, Gunthard HF, Hammer SM, Reiss P, Richman DD, Rizzardini G, Thomas DL, Jacobsen DM, Volberding PA: Antiretroviral treatment of adult HIV infection: 2012 recommendations of the International

Antiviral Society-USA panel. J Am Med Assoc 308:387-402, 2012

51. US Department of Veterans Affairs. US Department of Veterans Affairs National Patient Care Database (NPCD). Available at: http://www.virec.research.va.gov/NPCD/Overview.htm. Accessed December 18, 2013

52. US Department of Veterans Affairs/Department of Defense. Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. 2003

53. US Department of Veterans Affairs/Department of Defense. Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. 2010

54. US Food and Drug Administration. FDA drug safety communication: Prescription acetaminophen products to be limited to 325 mg per dosage unit; boxed warning will highlight potential for severe liver failure. 2011. http://www.fda.gov/Drugs/DrugSafety/ucm239821.htm. Accessed September 17, 2011

55. Chandok N, Watt KD: Pain management in the cirrhotic patient: The clinical challenge. Mayo Clin Proc 85:451-458, 2010

56. Edelman EJ, Gordon KS, Lo Re V III, Skanderson M, Fiellin DA, Justice AC; VACS Project Team: Acetaminophen receipt among HIV-infected patients with advanced hepatic fibrosis. Pharmacoepidemiol Drug Saf 22:1352-1356, 2013