POPULATION HEALTH MANAGEMENT
Volume 12, Number 4, 2009

DOI: 10.1089/pop.2009.0015

Original Article

High Rates of Inappropriate Drug Use in the Chronic Pain Population

Joseph E. Couto, PharmD., M.B.A.,[1] Martha C. Romney, M.S., J.D., M.P.H.,[1] Harry L. Leider, M.D., M.B.A., F.A.C.P.E.,[2] Smiriti Sharma,[3] and Neil I. Goldfarb[1]

Abstract

Chronic opioid treatment is a highly effective method to treat chronic pain; however, the prevalence of abuse of opioids can make treating patients with these agents difficult for clinicians. The objective of this study was to describe rates of inappropriate utilization, abuse, and diversion in a population of patients who were prescribed chronic opioids, as measured by urine drug testing in the clinical setting. A retrospective analysis was conducted of results from all urine drug tests conducted by Ameritox, Ltd. between January 2006 and January 2009, for patients whose physicians ordered the test in order to screen for noncompliance. Data from 938,586 patient test samples showed that 75% of patients were unlikely to be taking their medications in a manner consistent with their prescribed pain regimen. Thirty-eight percent of patients were found to have no detectable level of their prescribed medication, 29% had a nonprescribed medication present, 27% had a drug level higher than expected, 15% had a drug level lower than expected, and 11% had illicit drugs detected in their urine. Note that all categories add to a total greater than 100% as each category is not mutually exclusive, and a single patient could fall into multiple categories. The high observed rate of noncompliance demonstrates a significant clinical concern and confirms the importance of periodic urine drug screening for the population prescribed long-term opioid therapy. (*Population Health Management* 2009;12:185–190)

Chronic pain is a highly prevalent condition and various studies estimate its prevalence at 15% of the adult population.[1, 2] National consensus guidelines continue to support a major role for opioid agents in the management of patients with chronic moderate-to-severe pain,[3] however, the prevalence of abuse, diversion, and supplementation of these drugs is a growing problem and a major concern for both the clinicians who treat these patients and for our health care system.

According to the *2007 National Survey on Drug Use and Health*,[4] the number of Americans abusing prescription pain relievers is steadily increasing, with approximately 5% of Americans 12 years old and older using a prescription pain reliever for nonmedical purposes in 2007. The survey also reports that of individuals who had used pain relievers for nonmedical purposes, nearly 70% obtained the medication from a friend or relative for free, for money, or without the individual knowing. Another study showed that the increase of abuse of the 2 most common opiates, hydrocodone and oxycodone, rose 116% and 166%, respectively, from 1994 to 2000.[5]

For patients who abuse opiates, there has been considerable focus on individuals who see multiple physicians to obtain opiates, often referred to as "doctor shopping." In fact, in 2007 fewer than 3% of individuals who used pain relievers for nonmedical purposes obtained narcotics in this manner. Most patients who did not obtain their medication through a relative obtained their medication from a single prescriber, with nearly 20% of opioid abusers reporting they obtain narcotics from 1 prescriber.[4] With over 2.3 million Americans who abuse opioids obtaining their pain reliever directly from a clinician, and another 8 million obtaining their opioid from a friend or relative, there exists a significant opportunity and imperative for practitioners to reduce abuse and diversion of opioids.

Concurrent use of illicit drugs is a significant problem in individuals who abuse opiates. The work of Manchikanti and colleagues demonstrated that individuals who have a history of controlled substance abuse also have higher rates of illicit drug use when compared to patients without evidence of controlled substance abuse. The authors showed

[1]Jefferson School of Population Health, Thomas Jefferson University, Philadelphia, Pennsylvania.
[2]Ameritox, Ltd., Baltimore, Maryland.
[3]Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania.

that 14% of patients without a history of controlled substance abuse tested positive for marijuana or cocaine, whereas 34% ($P = 0.0095$) of the patients with a previous history of controlled substance abuse tested positive for 1 of these substances. This study demonstrates how prominent illicit drug use is in this patient population.[6]

Several studies have been conducted over the years to identify populations in which inappropriate opioid utilization is more likely to occur. Some of these studies had similar results, while others provide conflicting data. A retrospective cohort study found that age, a lifetime history of substance abuse, and the number of medical conditions a patient has are all associated with opioid abuse.[7] Comparable results were seen in a prospective cohort study, which found that age, past alcohol use, past cocaine use, and a previous driving under the influence or drug conviction are all predictors of opioid misuse.[8]

Two studies have been identified and impart conflicting results. The first study, conducted in 1997, found no differences between chronic opioid users and abusers with regard to a history of alcohol abuse, a history of drug abuse, and psychosocial testing.[9] However, the second study, performed in 2007, noted an association between psychiatry morbidity and opioid misuse. This study divided patients into 2 groups, a "high psych" morbidity group and a "low psych" morbidity group. They found that patients in the high-psych group were younger, reported a greater impact of their pain on social relationships, took opioids for a longer period of time, and had a higher frequency of abnormal urine toxicology tests as well as higher scores on the drug misuse index.[10]

Regardless of the cause of opiate abuse, the costs associated with it are considerable. White et al determined average direct health care costs, including outpatient and inpatient costs, are more than 8 times higher for opioid abusers than for a control group of non-abusers ($15,884 vs. $1,830) in 2003 dollars. The authors reported a prevalence of hospital inpatient admissions of opioid abusers were more than 12 times higher than non-abusers. Moreover, mean drug costs for opioid abusers are more than 5 times higher than for nonabusers.[11]

In the United States, the production and prescribing of opiates are regulated at the federal and state levels. Pharmaceutical products must be approved by the federal Food and Drug Administration (FDA) prior to marketing and distribution in the United States. However, the FDA does not regulate the prescribing of approved medications. Due to the recognized danger resulting from the misuse, abuse, diversion, and unmonitored use of certain pharmaceuticals, Congress enacted the Controlled Substances Act (CSA) to regulate access to these products.[12] The CSA is enforced by the Drug Enforcement Administration to control misuse of designated classes of drugs, including opiates, without interfering with clinical practice. The CSA requires registration by those who prescribe, dispense, distribute, and manufacture controlled substances.[12]

State practice acts and other laws regulate the practice of medicine. State requirements for the prescribing of controlled substances vary from jurisdiction to jurisdiction and may include special forms, licenses, informed consent, and prescribing restrictions.[12] Physicians may face allegations of overprescribing, underprescribing, as well as inadequate prescribing. Therefore it is not surprising that many physicians have concerns about governmental investigation or professional disciplinary actions that can result in loss of licensure, or civil and criminal liability. This fear of professional liability creates barriers to medical decision making and the prescribing of opioids for the treatment of chronic pain.

One of the more effective methods of detecting misuse of opioids is through the use of urine drug testing (UDT) as part of a comprehensive patient monitoring program.[13] Katz et al determined that UDT was most effective when coupled with behavioral monitoring when trying to identify "problem" patients. The authors found that in a population of non-cancer pain patients treated chronically with opioids, 29% of patients had a UDT that was positive for an illicit drug, a non-prescribed controlled drug, or ethanol. However of the 71% of patients with a negative UDT, 14% had 1 or more behavioral issues that have been described as being suggestive of inappropriate drug-seeking behaviors. Thus the authors concluded that while UDT is a powerful tool in the detection of opioid misuse, abuse, and diversion in patients being treated for non-cancer pain, it should be a component of a comprehensive patient monitoring program that also includes behavioral monitoring.[14] Behavioral monitoring of patients on chronic opioid therapy, through formal screening instruments such as the PADT[15,16] and COMM,[7] is recommended in the latest expert panel clinical pain guidelines issued by the American Pain Society (APS). These tools are deemed by the expert panel to have strong content, face validity, and construct validity.[3] However, these tools have not been fully validated for their ability to predict or identify actual abuse or diversion, and therefore some experts feel they should not be used in isolation or argue for routine UDT as part of "universal precautions."[13,18]

The *Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain (2009)*[3] also recommend periodically obtaining urine drug screens from patients at high risk for misuse, abuse, and diversion. The guidelines recommend that clinicians also consider UDT for patients who are not at high risk of misuse, abuse, or diversion. While the literature suggests that UDT is already standard in the addiction treatment setting, UDT appears to be underutilized by primary care physicians (PCPs) who prescribe opioids for chronic pain patients.[19,20] Bhamb and colleagues conducted a survey of 248 PCPs and reported that only 6.9% conducted UDT on their patients prior to initiation of opioid therapy, and that only 15% of these PCPs used UDT routinely for patients already undergoing chronic opioid therapy. Little data is available about the frequency of use of UDT by a growing group of physicians who primarily practice pain medicine. These low levels of utilization indicate clinicians are not using all of the tools available to them in order to combat misuse, abuse, and diversion of controlled substances.[20]

Methods

Data were collected on 938,586 urine toxicology tests conducted during routine patient clinic visits from January 2006 to January 2009. These data were retrospectively abstracted and, because a patient's course of treatment was not altered by this abstraction, no patient consent was required.

Urine screening was performed using Ameritox Ltd.'s RxGuardian testing process, which consists of 2 distinct phases. The first phase uses enzyme immunoassay or fluorescent polarization immunoassay testing as a screen for

opiates, benzodiazepines, illicit drugs, and other related medications. If positive, these immunoassays are then followed by gas chromatography-mass spectrometry or liquid chromatography-tandem mass spectrometry confirmatory testing, which provides additional accuracy and specificity in detecting the absence or presence of the patient's prescribed medication(s), as well as the presence of nonprescribed or illicit medications.[19,20]

The second phase of testing involves using patient demographic data, UDT results, urine pH, and specific gravity to calculate a normalized patient result using a proprietary methodology offered by Ameritox, Ltd. This normalized patient result is then compared to a set of expected ranges developed from tests of known compliant patients to help the patient's treating physician determine whether the patient is likely to be taking his or her medication in a manner consistent with the dose and frequency prescribed.[22,23] Expected ranges have been developed for the following medications: hydrocodone, morphine, codeine, methadone, oxycodone, oxazepam, lorazepam, alprazolam, and diazepam.

Demographic information on patient gender, age, primary insurance, and primary diagnosis was collected for 99.84% of patients included in the study. Patients were assigned to the following categories based on UDT results and analysis: illicit drug(s) present, nonprescribed medication(s) present, prescribed medication not present, prescribed medication level lower than expected, prescribed medication level higher than expected, and compliant (eg, having none of the prior test abnormalities and likely to be taking the medications as prescribed by their physician). Patients could have multiple types of abnormal results. Patients having at least 1 illicit drug present were further placed into 1 or more of the following categories: nonprescribed medication(s) present, prescribed medication not present, prescribed medication level lower than expected, and prescribed medication level higher than expected. All results were compared using chi-square statistics, where P values <0.001 were considered statistically significant.

Results

A total of 938,586 urine toxicology tests from patients chronically treated with opiates and/or benzodiazepines were identified during the study period. The urine tests were obtained more often from female patients, with the bulk of patients falling into the 35–50 year old age range. The majority of patients in this study had private insurance designated as their primary payor and had a primary diagnosis of back pain or "therapeutic drug monitoring" (Table 1). Figure 1 presents the results across all 938,586 tests, with 11.1% (n = 103,846) of patients testing positive for at least 1 illicit substance, 29.4% (n = 275,563) testing positive for at least 1 nonprescribed medication, and 38.4% (n = 360,347) with no detectable level of the medication prescribed by the physician. When applying the expected ranges offered by Ameritox, Ltd., 15.2% (n = 142,754) of patients had a level of the prescribed medication that was below the expected range for that medication, 26.6% (n = 249,882) of patients had a level of the prescribed medication that was higher than the expected range, and 25.5% (n = 238,940) had no evidence of abnormal drug use. The results of all UDTs stratified by demographic categories are presented in Table 2. Pearson's chi-squares were performed to test associations between demographics and test results.

TABLE 1. DEMOGRAPHIC PROFILE OF PATIENTS ADMINISTERED URINE DRUG SCREENING USING RXGUARDIAN TESTING (JANUARY 2006–JANUARY 2009)

Demographics	*Number (n)*	*Percent (%)*
Total patient samples	938,586	
Gender		
Female	518,212	55.2%
Male	420,208	44.8%
Age		
12–21	8,555	~1.0%
21–35	143,942	15.3%
35–50	399,183	42.5%
50–65	306,914	32.7%
65+	78,523	8.4%
No specified age	1,469	~0.2%
Primary insurance		
Private insurance	426,284	46.7%
Medicare	224,394	24.6%
Medicaid	78,510	8.6%
Workers' compensation	89,907	9.9%
Other	93,650	10.3%
Unknown payor	25,841	2.8%

In the 103,846 patients who tested positive for at least 1 illicit substance, 38.7% (n = 40,178) also tested positive for at least 1 nonprescribed medication, and 44.9% (n = 46,620) had no detectable level of the medication prescribed by the physician. Of the 834,740 patients who had tested negative for an illicit substance, 20.6% (n = 171,717) tested positive for at least 1 nonprescribed medication, and 37.6% (n = 313,727) had no detectable level of the medication prescribed by the physician (Fig. 2). Using Pearson's chi-squares, both comparisons yielded significant associations with $P < 0.0001$. This comparison demonstrates the heightened awareness that clinicians should have when treating patients who test positive for at least 1 illicit substance, as their rates of testing positive for at least 1 nonprescribed medication or having no detectable level of the medication prescribed by the physician are higher than their counterparts.

Discussion

This descriptive study of over 900,000 UDTs ordered by physicians to monitor their patients' appropriate use of opioids found alarmingly high rates of potential problems: approximately 11% of screens detected an illicit drug, 29% found nonprescribed medications, 38% found that a prescribed medication was not present, 15% found opioid levels lower than the RxGuardian expected ranges, and 27% found opioid levels higher than expected. It is important to note that urine samples can fall into multiple categories, and thus patient sample result categories add to greater than 100%. Of the total samples screened, 75% had 1 or more of these problems. While this rate of problematic tests is considerably higher than that found by Katz and colleagues (46%), Katz did not consider the absence of prescribed opioid in the urine a "problem" test result, whereas a considerable number of patients (38%) fit into this category in the current study.[24]

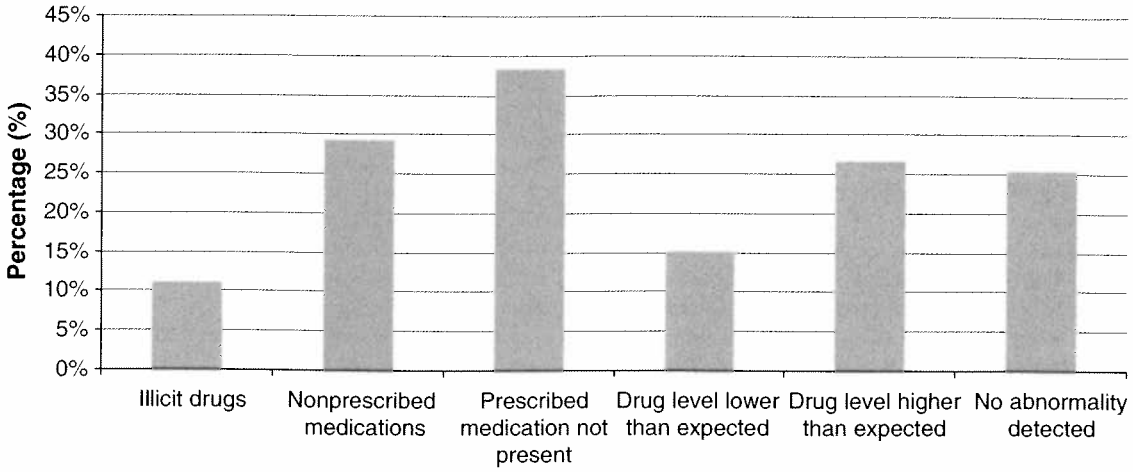

FIG. 1. Aggregate test results of patients administered urine drug screening using RxGuardian testing (January 2006–January 2009). Note that all categories add to a total greater than 100% as a single patient can fall into more than 1 category. $N = 938,420$.

These results clearly confirm that physicians and health plans should be vigilant in periodically screening patients who are prescribed long-term opioid therapy.

Finding that 75% of patients were unlikely to be taking their medications in a manner consistent with their prescribed pain regimen is alarming, although not surprising given the propensity for misuse, abuse, and diversion associated with these medications. Vermeire et al reported that up to 50% of patients are nonadherent to their chronic medication regimens, regardless of disease, prognosis, or setting.[25]

Although the amount of demographic and clinical information available for this analysis was limited, the study

TABLE 2. TEST RESULTS BY DEMOGRAPHIC OF URINE DRUG SCREENING USING RXGUARDIAN TESTING (JANUARY 2006–JANUARY 2009)

Demographics	*Illicit substances*	*Nonprescribed medication(s) present*	*Prescribed medication not present*
Gender			
Male	59,197 (14.9%)	121,058 (28.8%)	157,131 (37.4%)
Female	44,632 (8.6%)	154,450 (29.8%)	203,163 (39.2%)
Pearson's chi-square*	7068.41	110.85	321.75
df	1	1	1
P	<0.0001	<0.0001	<0.0001
Age			
12–21	2,129 (24.9%)	2,553 (29.8%)	2,726 (31.9%)
21–35	24,023 (16.7%)	47,790 (33.2%)	57,203 (39.7%)
35–50	52,725 (13.2%)	119,840 (30.0%)	162,214 (40.6%)
50–65	23,669 (7.7%)	85,700 (27.9%)	114,279 (37.2%)
65+	1,121 (1.4%)	19,245 (24.5%)	23,431 (29.8%)
Pearson's chi-square	19072.87	2305.61	3716.62
df	4	4	4
P	<0.0001	<0.0001	<0.0001
Primary insurance			
Private insurance	43,304 (10.2%)	123,176 (28.9%)	270,479 (36.6%)
Medicaid	13,185 (16.8%)	25,985 (33.1%)	42,602 (45.7%)
Medicare	20,610 (9.2%)	66,563 (29.7%)	136,965 (39.0%)
Workers' compensation	9,566 (10.6%)	20,371 (22.7%)	55,648 (38.1%)
Other	14,431 (15.4%)	31,683 (33.8%)	56,195 (40.0%)
Pearson's chi-square	5588.47	34.34	2536.07
df	4	4	4
P	<0.0001	<0.0001	<0.0001

*Pearson's chi-squares were performed to test associations between demographics and test results.

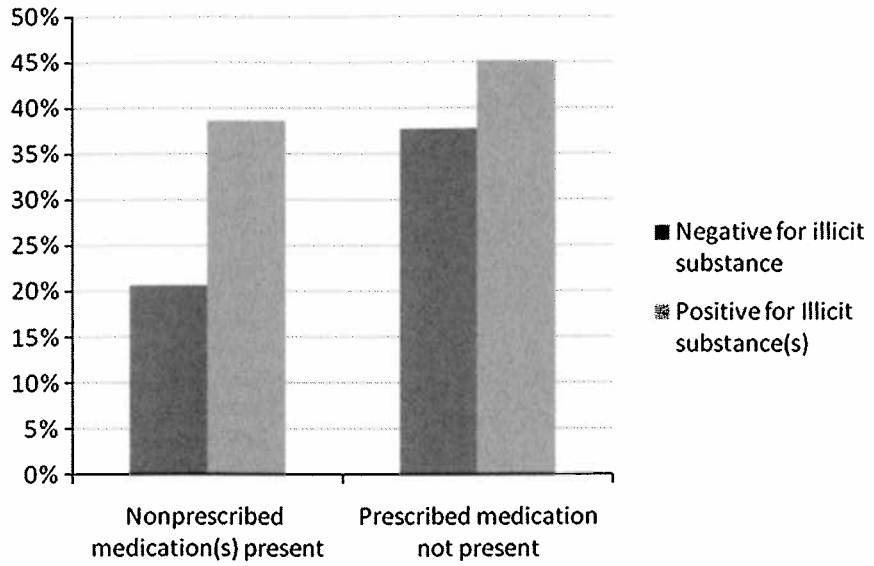

FIG. 2. Urine test results in patients testing positive or negative for illicit substance(s). The rates of both nonprescribed medication(s) present and prescribed medication not present between individuals testing positive or negative for illicit substance(s) were found to be statistically significant using Pearson's chi-squares with $P < 0.0001$.

confirms previously reported findings that "inappropriate" drug use spans all demographic groups, although to different degrees. While males were approximately 75% more likely to have an illicit drug detected, in comparison with females, gender differences for other categories of findings were not observed. Age differences with respect to illicit substances detected were quite pronounced, with illicit drug use nearly twice as likely in patients between the ages of 12–21 as patients between the ages of 35–50. A reverse pattern was observed in individuals who had no prescribed medication present, with patients ages 35–50 years being over 30% more likely than patients ages 12–21 years to have no prescribed medication detectable in their urine. While patients who had Medicaid designated as their primary payor were observed to have higher rates of apparent misuse, abuse, and diversion, it was surprising to the authors that their rates of nonprescribed medication(s) present and prescribed medications not present were only a few percentage points higher than their counterparts. Future multivariate analysis is needed to identify which, if any, of these characteristics appears to drive potentially inappropriate use. This in turn will help guide development of risk stratification models and characteristic-specific screening schedules.

There are many possible explanations for the findings in this study, which can be classified around the concepts of potential misuse, abuse, or diversion. As shown in Table 3, test findings do not align cleanly with just 1 of these problems. Detection of illicit drugs is most likely associated with abuse; however, interpretation is less clear for other test findings. For example, the presence of nonprescribed medications may result from a lack of pharmacotherapeutic coordination across various providers a patient is seeing, incorrect documentation, or patient misunderstanding or confusion. However, abuse is also a possibility. Where prescribed medications are not detected or low levels of opioids are detected, diversion may be suspected; however, there are several other potential explanations (eg, underuse of medication due to misunderstanding of dosing frequency or fear of dependency, temporary clinical abatement of pain associated with a chronic condition, incorrect documentation of the drug and/or dose). Similarly, where opioid levels are higher than expected, abuse is a possibility, but patient misunderstanding, incorrect documentation, uncontrolled pain, or other factors may also need to be explored before labeling the patient as an abuser. As with many tests conducted in clinical practice, physicians therefore need to interpret findings from UDT in combination with their knowledge of patient demographic and clinical characteristics, and use knowledge, intuition, and experience to determine how best to proceed based on the findings.

Several limitations to the study should be pointed out. First, the results may overstate the extent of the inappropriate use problem due to selection bias (ie, physicians may be more likely to order UDT for patients in whom they suspect a problem). The data source used for this analysis did not

TABLE 3. IMPLICATIONS OF URINE TEST RESULTS ON MISUSE, ABUSE, AND DIVERSION

	Misuse	*Abuse*	*Diversion*	*Incorrect documentation*
Illicit drug detected		X		
Nonprescribed medications present	X	X		X
Prescribed medications not present	X		X	X
Opioid levels lower than expected	X		X	X
Opioid levels higher than expected	X	X		X

identify the reason for screening—whether a routine monitoring test or a test specifically ordered to confirm or rule out a suspected problem. Nonetheless, the prevalence of identified issues confirms that periodic UDT for patients prescribed long-term opioid therapy should be a standard part of clinical practice, as is suggested by the APS.[3]

This is especially true given that it is also possible that the results understate the extent of problems, because some patients may refuse, or passively not complete, an ordered drug screen, or may defer the screen until they believe their system has cleared any illicit or nonprescribed drugs. Another limitation of the present descriptive analysis is that it is primarily univariate and bivariate. Further knowledge about patterns of inappropriate utilization and development of risk strata for conducting periodic UDT will undoubtedly be gained by conducting multivariate analyses; further research is needed in this area. However, the descriptive results alone demonstrate a significant clinical concern and confirm the importance of periodic UDT for the population prescribed long-term opioid therapy.

Disclosures

Dr. Leider is the Chief Medical Officer and an employee of Ameritox, Ltd. Funding for this study and manuscript have been provided to the Jefferson School of Population Health by Ameritox, Ltd. Dr. Couto and Ms. Romney, Ms. Sharma, and Mr. Goldfarb have no conflicts of interest or financial ties to disclose.

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Address correspondence to:
Joseph E. Couto, PharmD., M.B.A.
Jefferson School of Population Health
Thomas Jefferson University
1015 Walnut Street, Suite 115
Philadelphia, PA 19107

E-mail: joseph.couto@jefferson.edu