Published in final edited form as:

Clin J Pain. 2019 January ; 35(1): 1–6. doi:10.1097/AJP.0000000000000652.

Clinician Response to Aberrant Urine Drug Test Results of Patients Prescribed Opioid Therapy for Chronic Pain

Benjamin J. Morasco, PhD^{1,2}, Erin E. Krebs, MD, MPH^{3,4}, Melissa H. Adams, MA^{1,2}, Stephanie Hyde, MA^{1,2}, Janet Zamudio, MS¹, and Steven K. Dobscha, MD^{1,2}

¹Center to Improve Veteran Involvement in Care, VA Portland Health Care System

²Department of Psychiatry, Oregon Health & Science University

³Center for Chronic Disease Outcomes Research, Minneapolis VA Health Care System

⁴Department of Medicine, University of Minnesota Medical School

Abstract

Objective: Urine drug testing (UDT) is recommended for patients who are prescribed opioid medications, but little is known about the various strategies clinicians use to respond to aberrant UDT results. We sought to examine changes in opioid prescribing and implementation of other risk reduction activities following an aberrant UDT.

Methods: In a national cohort of VA patients with new initiations of opioid therapy through 2013, we identified a random sample of 100 patients who had aberrant positive UDTs (results positive for non-prescribed/illicit substance), 100 who had aberrant negative UDTs (results negative for prescribed opioid), and 100 who had expected UDT results. We examined medical record data for opioid prescribing changes and risk reduction strategies in the 12 months following UDT.

Results: Following an aberrant UDT, 17.5% of clinicians documented planning to discontinue or change the opioid dose and 52.5% initiated another strategy to reduce opioid-related risk. In multivariate analyses, variables associated with a planned change in opioid prescription status were having an aberrant positive UDT (OR=30.77, 95% CI=5.92–160.10) and higher prescription opioid dose (OR=1.01, 95% CI=1.01–1.02). The only variable associated with implementation of other risk reduction activities was having an aberrant positive UDT (OR=0.29, 95% CI=0.16–0.55).

Discussion: The majority of clinicians enacted some type of opioid prescribing or other change to reduce risk following an aberrant UDT, and the action depended on whether the result was an aberrant positive or aberrant negative UDT. Experimental studies are needed to develop and test strategies for managing aberrant UDT results.

Correspondence regarding this manuscript should be addressed to: Benjamin Morasco, Ph.D., VA Portland Health Care System (R&D99), 3710 SW US Veterans Hospital Road, Portland, OR 97239, Telephone: 503-220-8262 x57625, Facsimile: 503-273-5367, benjamin.morasco@va.gov.

Conflicts of Interest

No author reports having any potential conflict of interest with this study.

Introduction

Opioid prescribing guidelines for chronic pain recommend urine drug testing (UDT) [1,2]. This is encouraged as part of a universal precautions approach to opioid treatment, as one screening strategy to determine if patients are adhering to opioid medication as prescribed and not taking other non-prescribed or illicit substances [3]. The Centers for Disease Control and Prevention recommends UDT be conducted at the initiation of treatment and at least annually for all patients who remain prescribed opioids; patients at higher risk for opioid-related harm may be evaluated more frequently [1]. When administered to all patients, aberrant UDT results may be identified in up to 40–50% of patients with non-cancer pain [4] and cancer-related pain [5].

Although UDT is consistently recommended, prior research indicates that the evidence for effectiveness of UDT to reduce or prevent prescription opioid misuse is limited [6], and some have questioned whether the use of standard UDT should be continued [7]. There are several potential reasons for the limited effectiveness of UDT. First, rates of UDT have historically been low [8,9], even among individuals at increased risk for prescription opioid misuse [10,11]. Potential barriers to implementation of UDT have been described, including issues related to testing methods and interpretation, lack of standardized protocol, patient and provider factors, institutional barriers, and financial/reimbursement issues [12]. Second, opioid prescribing clinicians may not adequately use UDT results to modify or inform care [13–15]. Third, clinicians may have concerns about negatively impacting the clinician-patient relationship [16–18]. Fourth, clinicians may also determine that the benefits of ongoing opioid therapy outweigh the potential risks of adverse effects.

Prior studies provide important data about the ways in which clinicians respond to UDT results. However, studies have been limited by small sample sizes, recruitment from a single setting, or lack of an adequate comparison group. In the current study, we attempt to account for some limitations in prior research by examining the clinical care received for 12 months after a UDT among a national sample of patients prescribed opioids for pain. In this study, we identified 100 patients in each of three groups: those with an aberrant positive UDT, an aberrant negative UDT, or a UDT result that was expected. We examined planned changes in opioid prescribing and implementation of other risk reduction activities following the aberrant UDT result.

Methods

This is a retrospective cohort study of patients receiving treatment in Department of Veterans Affairs (VA) facilities nationwide. All data collected as part of this study were extracted from the electronic health record. The Institutional Review Board at the VA Portland Health Care System provided approval for this study.

Procedure

The Corporate Data Warehouse (CDW) provides comprehensive information contained in electronic health records for all VA patients. We identified a cohort of patients who had been engaged in VA care for at least one year, had no opioid prescriptions in 2012, and had new

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initiations of opioid therapy in 2013. Patients were included if there was a documented diagnosis of musculoskeletal pain, neuropathy, and/or migraine headache, and they received prescription opioids daily from the VA for 90 or more consecutive days. To be included in the sample, patients also had to be prescribed an opioid agent that could be identified in the standard UDT panel: morphine, hydrocodone, hydromorphone, codeine, methadone, and/or oxycodone. Patients could additionally receive fentanyl, buprenorphine, or tramadol but these are not routinely tested for in standard UDTs so we did not include patients if their only prescription was for one of these opioids. Patients were excluded if they had recent opioid prescriptions from a non-VA source (indicating this was not a new initiation of opioid therapy), a diagnosis of cancer any time in the prior year, had surgery in the prior year, were enrolled in hospice or long-term care, received care in a VA opioid substitution program, or died in the following year.

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After identifying a national cohort of potentially-eligible patients, we reviewed UDT data to identify 100 patients for each of three different groups for chart review. We compared 100 patients with an aberrant positive UDT, 100 patients with an aberrant negative UDT, and 100 patients with an UDT result that was expected. To be included in the study, the UDT result must have occurred on a day that overlapped with the timing of the prescription opioid dispense period.

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For this review, an aberrant positive UDT was defined as the presence of an illicit substance (e.g., marijuana, cocaine) or a non-prescribed medication (i.e., different opioid than prescribed, presence of benzodiazepine or stimulant in a patient without a prescription in the past three months). An aberrant negative UDT was defined as occurring when the UDT was negative for the prescribed opioid, or negative for at least one prescribed opioid in instances where patients received multiple agents. An expected UDT was a result which was positive for the prescribed opioid and negative for other non-prescribed or illicit substances. We considered cross-reactivity and metabolism of other opioids when interpreting UDT results, which included a comprehensive evaluation of all medications prescribed at the time of UDT and a review of potential UDT outcomes (e.g., a patient could be prescribed oxycodone and have a positive opiate screen). When confirmatory UDT was conducted, these results superseded the initial screening immunoassay for a given substance.

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For each patient, we enrolled the earliest UDT that was administered following initiation of prescription opioids. We reviewed all clinical notes in the medical record for the 12 months after UDT, to examine any changes in care following the UDT result. The medical record review included notes from the opioid prescriber, other medical specialties, emergency room, inpatient notes, and other outpatient visits. A chart review tool was augmented based on our prior research [14]. Our primary outcomes were (1) planned changes in opioid prescribing and (2) implementation of other risk reduction activities. Potential changes in opioid prescribing included plans to discontinue opioids, decrease or increase the opioid dose, or transition to a different prescription opioid. Additional records were reviewed to determine if the clinician followed through on any planned change in opioid prescribing. To evaluate if a clinician implemented another risk reduction activity, we examined if there was more frequent urine drug testing, more frequent primary care appointments or medication

fills, referrals to mental health or addictions treatment, completion of an opioid treatment agreement, or some other risk reduction strategy.

Medical record reviews were conducted by four highly trained research staff. Initial training consisted of a summary of the empirical literature on this topic, education about reviewing UDT results and laboratory data, summary of relevant clinical issues, and review of best practices in abstracting medical record data. Medical records were initially double-reviewed for 10 patients. If research staff achieved Kappa ≥ 0.80 they were permitted to code independently. If consistency rating was not achieved, a minimum of 5 additional charts were coded. To ensure ongoing fidelity and to prevent drift, after research staff coded 10 charts independently, an additional five charts were double-coded. All research staff were required to maintain Kappa ≥ 0.80 to code independently. In total, 182 out of 300 charts were double-coded.

Demographic, Diagnostic, and Pharmacy Data

Demographic and clinical data were extracted from the CDW. Demographic characteristics that were assessed included age, gender, race/ethnicity, marital status and VA service-connected disability status. Pharmacy data included prescriptions for opioids, benzodiazepines, and stimulant medications. All prescription opioids were converted to an average daily dose in morphine equivalents (using a formula of quantity divided by days supply issued multiplied by an opioid conversion factor) [19]. In instances where patients received multiple agents, a total daily morphine equivalent was calculated for all prescribed opioids. Participants were coded as having a pain-related, mental health, or other diagnosis based on ICD-9-CM codes documented within one year of the study index date.

Statistical Analyses

Participants were placed into one of three groups based on UDT results and comparisons were made across groups using the UDT result categories described above. We compared demographic and clinical characteristics among groups using chi-square tests for categorical data and analysis of variance for linear data; follow-up pairwise comparisons were conducted with Scheffe post-hoc tests.

Two multivariate models were conducted. The first examined variables that were associated with having any planned change in opioid prescribing (i.e., discontinuation, dose modification, or transition to another opioid). The second multivariate model examined variables associated with any other planned risk reduction activity (i.e., more frequent UDT, more frequent appointments, referrals to mental health or addictions, or “other” activity). Variables included in these models were age, gender, race, prescription opioid dose, depression diagnosis, substance use disorder diagnosis, and UDT group categorization (Aberrant Positive, Aberrant Negative, or Expected Result).

Results

Among patients in the Aberrant Positive group, the most common substances detected were THC/cannabinoids (48%), non-prescribed benzodiazepine (29%), non-prescribed opioid (22%), non-prescribed/illicit amphetamine (9%), barbiturates (9%) and cocaine (4%). Of

patients with a UDT positive for a non-prescribed opioid, the most common opioids detected were oxycodone (40.9%) and methadone (18.2%). Among patients in the Aberrant Negative group, the most common prescribed opioids that were absent in the UDT were hydrocodone (57%), oxycodone (39%), methadone (4%), and morphine (3%).

Table 1 shows characteristics of patients in the three respective UDT results groups. The most common pain-related diagnoses were back pain (63.3%), arthritis (31.0%), and other neck/joint pain (56.3%). Forty-three percent of patients were diagnosed with depression and 22.3% were diagnosed with posttraumatic stress disorder. The only pain-related or mental health diagnosis that significantly differed among groups was a substance use disorder, which was more common ($p = 0.002$) in the Aberrant Positive group (22% vs 9% in the Aberrant Negative group and 7% in the Expected Result group).

Patients in the Aberrant Positive group were younger (52.0 years) than those in the Expected Result (56.9 years) group, and not significantly different in age from patients in the Aberrant Negative group (54.7 years). The average daily opioid dose significantly differed among groups ($p = 0.022$). Patients in the Aberrant Negative group were prescribed a significantly lower average daily dose (43.7 mg) than participants in the Expected Result group (68.6 mg). Patients from the Aberrant Positive group were more likely than those in the Expected Result group to have a documented discussion of the UDT result with their clinician (35% vs 16%, $p = 0.002$).

Planned Changes in Opioid Prescribing

Table 2 presents a comparison of planned opioid prescribing changes and implementation of other risk reduction activities among the three groups. Patients in the Aberrant Positive group (22%) and the Aberrant Negative group (4%) had higher rates of planned opioid discontinuations than patients in the Expected Result group (0%). Clinicians of patients in the Aberrant Positive group were also more likely to report a plan for transitioning patients to an alternative opioid medication, compared with patients in the Expected Result group (9% vs 0%). Of patients whose clinician planned to make a change in opioid prescribing, the change was successfully implemented in 81.1% of cases. The likelihood of a clinician following through on any planned opioid prescribing change did not significantly differ among the three groups (23 of 29 patients in the Aberrant Positive group, 6 of 6 in the Aberrant Negative group, and 1 of 2 in the Expected Result group).

A multivariate analysis was conducted to examine variables significantly associated with a patient having any planned change in opioid prescribing. Variables included in this analysis were age, gender, race, prescription opioid dose, depression diagnosis, substance use disorder diagnosis, and UDT result. The overall model was significant ($\chi^2 = 48.4$, $df = 9$, $p < 0.001$). The only variables that were significantly associated with planning a change in opioid prescribing were prescription opioid dose (OR = 1.01, 95% CI = 1.01 – 1.02) and having an Aberrant Positive UDT (OR = 30.77, 95% CI = 5.92 – 160.10).

Other Risk Reduction Strategies

Patients in the Aberrant Positive group (29%) and Aberrant Negative group (36%) were less likely than patients in the Expected Result group (51%) to have one or more follow-up

UDTs. Those in the Expected Result group (60%) were also more likely to have an “Other” risk reduction strategy, relative to patients in the Aberrant Positive group (28%). In 85% of cases, the “Other” risk reduction activity involved having the patient complete an opioid treatment agreement or engage with the opioid prescriber in a discussion about taking opioids safely.

A multivariate analysis was conducted to examine variables significantly associated with having any documented change in non-opioid risk reduction activity. Variables included in this analysis were age, gender, race, prescription opioid dose, depression diagnosis, substance use disorder diagnosis, and UDT result. The overall model was significant ($\chi^2 = 23.1$, $df = 9$, $p = 0.006$). The only variable that was significantly associated with having any documented change in other risk reduction activities was having an Aberrant Positive UDT; compared with those in the Expected Result group, the Aberrant Positive group had a decreased likelihood of any planned risk reduction activity (OR = 0.29, 95% CI = 0.16 – 0.55).

Sensitivity Analyses Related to Cannabis

Sensitivity analyses for both multivariate analyses were conducted removing the patients who had aberrant UDTs due to cannabis. The statistically significant results identified in the multivariate analyses were similar when patients with aberrant UDT results due to cannabis were removed.

Chi-square analyses were also conducted comparing patients who tested positive for cannabis ($n=48$) versus patients who tested positive for other non-prescribed or illicit substance ($n=52$) (patients who had tests positive for both cannabis and another aberrant substance were classified in the cannabis group). There were no differences between groups in the likelihood of having a planned change in opioid prescribing (33.3% in the cannabis group versus 25.0% in the “other substance” group; $\chi^2 = 0.842$, $p = 0.359$) or experiencing any other risk reduction strategy (50.0% versus 42.3%; $\chi^2 = 0.595$, $p = 0.441$).

Discussion

In this retrospective cohort study of a national sample of patients prescribed opioid medications for non-cancer pain, we found that 29% of clinicians of patients who had an Aberrant Positive UDT and 6% of patients who had an Aberrant Negative UDT planned a change in their opioid prescriptions following the UDT. The variable most strongly associated with a planned change in opioid prescribing was having a UDT result that was positive for a non-prescribed or illicit substance. In prior research conducted at a single setting, among patients with an aberrant positive UDT, we observed that prescribers documented an intent to change the opioid prescribing practice in 52% of patients, but the planned changes were implemented in only 24% of cases [14]. In the current study, while the overall rate of planned changes in opioid prescribing was lower (29% in the Aberrant Positive group), the likelihood of the clinician implementing the change was higher (81%). This increase in changes to opioid prescribing plans is likely due to increased awareness about potential adverse effects [20] associated with prescription opioids, as well as emerging

VA and other national recommendations and guidance about strategies for monitoring patients who are prescribed opioids.

Nearly one-half of the aberrant positive UDT results identified in this study were for cannabis. While the data to support the efficacy of cannabis for chronic pain are weak [21], prior research demonstrates that up to 39% of patients prescribed long-term opioid therapy report co-occurring use of cannabis [22–23]. As cannabis is now legal for medical use in 29 states, and legal for recreational use in eight of these states, clinicians are likely to increasingly encounter patients with co-occurring cannabis and prescription opioid use. Unfortunately, empirically-based data are not available about the long-term benefits and harms associated with the dual use of opioid medications and cannabis, and clinicians may be unsure of the best strategies to respond to patients with co-occurring use [24]. Clinicians also have differing opinions about potential benefits and harms associated with the co-occurring use of prescription opioids and cannabis [25]. In sensitivity analyses, we did not identify differences in the likelihood of changes in opioid prescribing or other risk reduction strategy based on aberrant UDT result to cannabis or other non-prescribed or illicit substances. Data from the present study suggest that most clinicians who respond to the dual use of prescription opioids and cannabis will implement additional UDT or talk with patients about risk of harms, while in 22% of cases clinicians planned to discontinue the opioid. However, because cannabis is a Schedule 1 controlled substance, VA clinicians may have different responses to cannabis compared with clinicians outside the VA or in states where cannabis is legal. Future research is needed about best strategies for managing chronic pain and potential substance use disorder in situations of co-occurring prescription opioid and cannabis use.

Little empirical data are available about clinician response to potential diversion of prescription opioids [26]. In the present study, we observed low (4%) instances of planned opioid discontinuation following an aberrant negative UDT result. These results suggest that clinicians may have been using UDT primarily as a strategy to screen for potential use of illicit or non-prescribed substances, as opposed to confirming the presence of the prescribed substance. However, because of the retrospective nature of data collection, we do not know if the observed rate of opioid cessation was due to beliefs that the medication would not have been detected via UDT [27], lack of concern about the negative UDT result, or some other factor. The observed rates may also reflect accurate interpretation of the UDT in instances of intermittent patient use or if the UDT was not sensitive for the medication/dose prescribed. Among patients who are discontinued from opioids, retrospective research indicates that approximately one-quarter of discontinuations are due to an aberrant negative UDT result [26]. Future prospective work is needed to understand the factors that precipitate prescription opioid discontinuation among patients with an aberrant negative UDT result.

Clinical recommendations suggest that a patient who is no longer taking the prescribed opioid should be discontinued from opioid therapy [1]. However, before this treatment plan is enacted, clinicians should conduct confirmatory testing of the aberrant result and follow-up directly with the patient. In some cases, the aberrant negative result could have occurred due to a missed dose (potentially due to adverse effects, inadequate analgesia, or other

factors). If the opioid is continued, or an alternative opioid is initiated, follow-up UDT (potentially at random intervals) would be indicated to confirm opioid use.

There is no consensus on best strategies for responding to an aberrant positive UDT. In instances of a patient using co-occurring cannabis, at minimum, clinicians should evaluate for potential substance use disorder, as well as the benefits and harms associated with use [24]. Patients with a co-occurring substance use disorder may be referred for specialty addictions treatment. Data suggest that integrated treatments for chronic pain and substance use disorder can be effective in reducing pain, improving function, and reducing symptoms of addiction [28–30].

A second multivariate analysis examined variables associated with implementation of other risk reduction strategies. After controlling for demographic and clinical variables, an aberrant positive UDT was associated with a significantly decreased likelihood of implementation of other risk reduction strategies. This appears to have occurred as patients in the Expected Result group experienced a host of additional risk reduction strategies, such as more frequent UDT and signing an opioid treatment agreement. However, it is unclear why patients in the Aberrant Positive group would not also have had more evaluations for prescription opioid misuse/abuse or other risk reduction strategies. One explanation may be that, as patients in the Aberrant Positive group were more likely to experience changes in opioid prescribing (such as change in dose or discontinuation), clinicians may have considered the issue adequately addressed and were less likely to implement additional risk reduction strategies. Additional data are needed about the effectiveness of these strategies to mitigate risk, while not having a negative impact on the clinician-patient relationship or pain-related outcomes.

The current study attempted to account for some limitations in prior research studies conducted on this topic. Notably, we recruited a random national sample of patients, included patients with aberrant negative and expected UDT results, and had adequate statistical power to conduct analyses. However, limitations remain. All data for this study were retrospective and obtained from the medical record, which may be limited by clinical documentation [31]. Related to this, we reviewed medical record data through 2013; new opioid treatment guidelines have been published since this time and the medical culture related to prescription opioid safety continues to evolve. There was not a standard UDT protocol at each facility and not all UDT results had follow-up confirmatory testing; as a result, test results may be subject to false negatives, false positives, or potential cross-reactivity. Finally, the sample was predominantly white and male, and all patients were receiving care in Department of Veterans Affairs medical centers; results may not generalize to patients or clinical practices in other settings.

Results from the present study indicate that, among patients who are newly initiated on prescription opioids, clinicians are predominately responding to UDT results by implementing additional risk reduction strategies, the most common being follow-up UDT and completing opioid treatment agreements. We observed a plan to discontinue opioid therapy in 22% of patients with an aberrant positive UDT, and in 4% of patients with an aberrant negative UDT. The empirical base for making recommendations about strategies for

modifying opioid prescribing practices following an aberrant UDT is limited. Prospective and experimental studies are needed to examine the efficacy of different strategies for responding to aberrant UDT results, with a focus on improving quality of life and minimizing treatment-related harms.

Acknowledgments

Source of Funding

Research reported in this manuscript was supported by awards from the U.S. Food & Drug Administration (FD004508) and from the National Institute on Drug Abuse (034083). The work was also supported by resources from the VA Health Services Research and Development-funded Center to Improve Veteran Involvement in Care at the VA Portland Health Care System (CIN 13-404). The content of this manuscript is solely the responsibility of the authors and does not represent the official views of the Department of Veterans Affairs, U.S. Food & Drug Administration, or the National Institute on Drug Abuse.

References

1. Dowell D, Haegerich TM, Chou R. CDC Guideline for prescribing opioids for chronic pain – United States, 2016. *JAMA* 2016;315:1624–1645. [PubMed: 26977696]
2. VA/DoD Clinical Practice Guideline: Management of Opioid Therapy for Chronic Pain [2010]. Department of Veterans Affairs, Department of Defense. <https://www.healthquality.va.gov/guidelines/Pain/cot/>. Accessed August 11, 2017.
3. Gourlay DL, Heit HA, Almahrezi A. Universal precautions in pain medicine: A rational approach to the treatment of chronic pain. *Pain Med* 2005;6:107–112. [PubMed: 15773874]
4. Katz NP, Sherburne S, Beach M, Rose RJ, Vielguth J, Bradley J, Fanciullo GJ. Behavioral monitoring and urine toxicology testing in patients receiving long-term opioid therapy. *Anesthesia & Analgesia* 2003;97:1097–1102. [PubMed: 14500164]
5. Arthur JA, Edwards T, Lu Z, Reddy S, Hui D, Wu J, Liu D, Williams JL, Bruera E. Frequency, predictors, and outcomes of urine drug testing among patients with advanced cancer on chronic opioid therapy at an outpatient supportive care clinic. *Cancer* 2016;122:3732–3739. [PubMed: 27509305]
6. Starrels JL, Becker WC, Alford DP, Kapoor A, Williams AR, Turner BJ. Systematic review: Treatment agreements and urine drug testing to reduce opioid misuse in patients with chronic pain. *Ann Int Med* 2010;152:712–720. [PubMed: 20513829]
7. Turner JA, Saunders K, Shortreed SM, Rapp SE, Thielke S, LeResche L, Riddell KM, Von Korff M. Chronic opioid therapy risk reduction initiative: Impact on urine drug testing rates and results. *J Gen Intern Med* 2014;29:305–311. [PubMed: 24142119]
8. Bhamb B, Brown D, Hariharan J, Anderson J, Balousek S, Fleming MF. Survey of select practice behaviors by primary care physicians on the use of opioids for chronic pain. *Curr Med Res Opin* 2006;22:1859–1865. [PubMed: 16968589]
9. Boulanger A, Clark AJ, Squire P, Cui E, Horbay GLA. Chronic pain in Canada: have we improved our management of chronic noncancer pain? *Pain Res Manage* 2007;12:39–47.
10. Morasco BJ, Duckart JP, Dobscha SK. Adherence to clinical guidelines for opioid therapy for chronic pain in patients with substance use disorder. *J Gen Int Med* 2011;26:965–971.
11. 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 Int Med* 2011;26:958–964.
12. Bair MJ, Krebs EE. Why is urine drug testing not used more often in practice? *Pain Pract* 2010;10:493–496. [PubMed: 21040440]
13. Gupta A, Patton C, Diskina D, Cheattle M. Retrospective review of physician opioid prescribing practices in patients with aberrant behaviors. *Pain Physician* 2011;14:383–389. [PubMed: 21785482]

14. Morasco BJ, Krebs EE, Cavanagh R, Hyde S, Crain A, Dobscha SK. Treatment changes following aberrant urine drug test results for patients prescribed chronic opioid therapy. *J Opioid Manage* 2015;11:45–51.
15. Stammet MM, Spradley SS. Evaluation of treatment changes following electronic consultation to a pharmacist-run urine drug testing service in a veterans healthcare system. *J Opioid Manage* 2016;12:389–395.
16. Barry DT, Irwin KS, Jones ES, Becker WC, Tetrault JM, Sullivan LE, Hansen H, O'Connor PG, Schottenfeld RS, Fiellin DA. Opioids, chronic pain, and addiction in primary care. *J Pain* 2010;11:1442–1450. [PubMed: 20627817]
17. Kilaru AS, Gadsden SM, Perrone J, Paciotti B, Barg FK, Meisel ZF. How do physicians adopt and apply opioid prescription guidelines in the emergency department? A qualitative study. *Ann Emerg Med* 2014;64:482–489.
18. Matthias MS, Parpart AL, Nyland KA, Huffman MA, Stubbs DL, Sargent C, Bair MJ. The patient-provider relationship in chronic pain care: Providers' perspectives. *Pain Med* 2010;11:1688–1697. [PubMed: 21044259]
19. Morasco BJ, Yarborough BJ, Smith NX, Dobscha SK, Deyo RA, Perrin NA, Green CA. Higher prescription opioid dose is associated with worse patient-reported pain outcomes and more health care utilization. *J Pain* 2017;18:437–445. [PubMed: 27993558]
20. Chou R, Turner JA, Devine EB, Hansen RN, Sullivan SD, Blazina I, Dana T, Bougatsos C, Deyo RA. The effectiveness and risks of long-term opioid therapy for chronic pain: A systematic review for a National Institutes of Health Pathways to Prevention workshop. *Ann Intern Med* 2015;162:276–286. [PubMed: 25581257]
21. Nugent SM, Morasco BJ, O'Neil ME, Freeman M, Low A, Kondo K, Elven C, Zakher B, Motu'apuaka M, Paynter R, Kansagara D. The effects of cannabis among adults with chronic pain and an overview of general harms: A systematic review. *Ann Intern Med* 2017;167:319–331. [PubMed: 28806817]
22. Degenhardt L, Lintzeris N, Campbell G, Bruno R, Cohen M, Farrell M, Hall WD. Experience of adjunctive cannabis use for chronic non-cancer pain: findings from the Pain and Opioids IN Treatment (POINT) study. *Drug Alcohol Depend* 2015;147:144–150. [PubMed: 25533893]
23. Reisfield GM, Wasan AD, Jamison RN. The prevalence and significance of cannabis use in patients prescribed chronic opioid therapy: a review of the extant literature. *Pain Med* 2009;10:1434–41. [PubMed: 19793342]
24. Savage SR, Romero-Sandoval A, Schatman M, Wallace M, Fanciullo G, McCarberg B et al. Cannabis in pain treatment: Clinical and research considerations. *J Pain* 2016;17:654–668. [PubMed: 26961090]
25. Carlini BH, Garrett SB, Carter GT. Medicinal cannabis: A survey among health care providers in Washington State. *Am J Hosp Palliat Care* 2017;34:85–91. [PubMed: 26377551]
26. Lovejoy TI, Morasco BJ, Demidenko MI, Meath THA, Frank JW, Dobscha SK. Reasons for discontinuation of long-term opioid therapy in patients with and without substance use disorders. *Pain* 2017;158:526–534. [PubMed: 28192376]
27. Reisfield GM, Salazar E, Bertholf RL. Rational use and interpretation of urine drug testing in chronic opioid therapy. *Ann Clin Lab Sci* 2007;37:301–314. [PubMed: 18000286]
28. Ilgen MA, Bohnert AS, Chermack S, Conran C, Jannausch M, Trafton J, Blow FC. A randomized trial of a pain management intervention for adults receiving substance use disorder treatment. *Addiction* 2016;111:1385–93. [PubMed: 26879036]
29. Morasco BJ, Greaves DW, Lovejoy TI, Turk DC, Dobscha SK, Hauser P. Development and preliminary evaluation of an integrated cognitive-behavior treatment for chronic pain and substance use disorder in patients with the Hepatitis C virus. *Pain Med* 2016;17:2280–2290. [PubMed: 28025362]
30. Morasco BJ, Gritzner S, Lewis L, Oldham R, Turk DC, Dobscha SK. Systematic review of prevalence, correlates, and treatment outcomes for chronic non-cancer pain in patients with comorbid substance use disorder. *Pain* 2011;152:488–497. [PubMed: 21185119]
31. Krebs EE, Bair MJ, Carey TS, Weinberger M. Documentation of pain care processes does not accurately reflect pain management delivered in primary care. *J Gen Intern Med* 2010;15:194–199.

Table 1.

Comparison of Demographic and Clinical Variables among Groups.

	Aberrant Positive (n= 100)	Aberrant Negative (n= 100)	Expected Result (n= 100)	p- value
Age	52.0 (12.8)	54.7 (10.8)	56.9 (10.7) [*]	0.012
Male gender	89%	97%	95%	0.054
Marital status				0.139
Single	15%	6%	11%	
Married	34%	42%	50%	
Divorced/Separated	46%	46%	33%	
Widowed	5%	6%	6%	
Race				0.095
White	79%	79%	82%	
Black	10%	16%	6%	
Other	11%	5%	12%	
Average daily morphine equivalent opioid dose	52.3 (51.8)	43.7 (52.9)	68.6 (83.1) ⁺	0.022
Back pain	60%	66%	64%	0.669
Arthritis	32%	25%	36%	0.745
Other neck/joint pain	50%	65%	54%	0.086
Depression	48%	41%	42%	0.558
Posttraumatic stress disorder	22%	19%	26%	0.491
Other anxiety disorder	25%	18%	19%	0.417
Alcohol use disorder	18%	17%	17%	0.977
Other substance use disorder	22%	9%	7%	0.002

^{*} *Note.* = The Aberrant Positive group differed significantly from the Expected Result group in post-hoc testing.

⁺ = The Aberrant Negative group differed significantly from the Expected Result group in post-hoc testing.

Table 2.

Comparison of Planned Opioid Prescribing Changes and Risk Reduction Activities among Groups.

	Expected Result (n= 100)	Aberrant Positive (n= 100)	<i>p</i> -value	Aberrant Negative (n= 100)	<i>p</i> - value
Planned changes in opioid prescribing					
Discontinue opioids	0	22%	< 0.001	4%	0.043
Decrease opioid dose	2%	3%	0.651	0	0.155
Increase opioid dose	0	3%	0.081	1%	0.316
Transition to a different opioid	0	9%	0.002	2%	0.155
Any planned changes in opioid prescribing *	2%	29%	< 0.001	6%	0.149
Risk reduction strategies					
More frequent urine drug testing	51%	29%	0.001	36%	0.032
More frequent appointments/fills	0	3%	0.081	0	1.000
Referred patient to mental health	6%	10%	0.297	5%	0.756
Referred patient to addictions treatment	1%	5%	0.097	4%	0.174
Other risk reduction strategy	49%	26%	0.001	39%	0.154
Any implemented risk reduction strategy *	74%	46%	< 0.001	59%	0.025

* Note. = The percentages listed in these rows are not an addition of prior rows, as some patients may have had more than one planned change in opioid prescribing or risk reduction strategy. Chi-square *p*-values reported in Table 2 use the Expected Result group as controls. Column 3 is the comparison of differences between the Aberrant Positive and Expected Result groups; Column 5 is the comparison of differences between the Aberrant Negative and Expected Result groups.