Healthcare system-wide implementation of opioid-safety guideline recommendations: the case of urine drug screening and opioid-patient suicide- and overdose-related events in the Veterans Health Administration

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Abstract

This study provides an example of how healthcare system-wide progress in implementation of opioid-therapy guideline recommendations can be longitudinally assessed and then related to subsequent opioid-prescribed patient health and safety outcomes. Using longitudinal linear mixed effects analyses, we determined that in the Department of Veterans Affairs (VA) healthcare system ($n = 141$ facilities), over the 4-year interval from 2010 to 2013, a key opioid therapy guideline recommendation, urine drug screening (UDS), increased from 29 to 42 %, with an average within-facility increase rate of 4.5 % per year. Higher levels of UDS implementation from 2010 to 2013 were associated with lower risk of suicide and drug overdose events among VA opioid-prescribed patients in 2013, even after adjusting for patients' 2012 demographic characteristics and medical and mental health comorbidities. Findings suggest that VA clinicians and healthcare policymakers have been responsive to the 2010 VA/Department of Defense (DOD) UDS treatment guideline recommendation, resulting in improved patient safety for VA opioid-prescribed patients.

Keywords

Treatment guideline implementation, Opioid therapy safety, Urine drug screening, Suicide, Drug overdose

INTRODUCTION

Pain treatment with prescription opioids has increased dramatically over the last two decades [1, 2]. Concomitant with this, there has been a sharp upswing in adverse medical events associated with opioid use, including drug-related suicide attempts, which increased by more than 50 % between 2005 and 2007 [3], and overdose with opioids, rates of which tripled from 1999 to 2006 [4]. Since 2006, rates of these adverse medical events have continued to grow [4–6].

This growth has prompted patient-, provider-, and healthcare system-focused interventions to prevent opioid misuse and to improve opioid treatment safety [4, 7]. In this regard, the Department of Veterans Affairs (VA) took the lead in 2003 in joining the Department of Defense (DOD) to formulate specific

Implications

For researchers, this study provides an example of how healthcare system-wide electronic patient treatment data can be used to operationalize and measure patient treatment guideline implementation and the use of a longitudinal linear mixed effects statistical approach to determine associations between implementation metrics and patient health and safety outcomes. For clinicians, this study contributes to the evidence base for urine drug screening as a promising tool for improving opioid-prescribed patient safety. For healthcare providers and policy makers, results of studies such as this can help guide clinical practices and healthcare system resource allocations that better balance the desire to provide patients with accessible, effective relief for pain with evidence-based practices that protect them from adverse medical events associated with opioid therapy.

clinical practice guidelines on healthcare provider- and facility-level practices to maximize safe use of opioid treatments for chronic pain [8]. Building upon this and others' work [9], VA/DOD updated and revised these recommendations in 2010 [10]. Soon thereafter, Midboe and the VA Opioid Metric Development Team [7] used expert consensus procedures and national VA electronic patient treatment data to generate a panel of metrics that define and measure the implementation of the main recommendations of the 2010 VA/DOD clinical practice guidelines for opioid therapy for pain. These metrics tap a total of eight recommendation domains (e.g., postprescription clinical follow-up, avoidance of opioid-only pain treatments), and include the recommendation to *order appropriate lab tests, including urine drug screens (UDS), for all opioid-prescribed pain patients*.

We focus here on the extent and effects of implementation of the VA/DOD UDS recommendation because although this practice continues to be among the top strategies advocated by opioid-management experts (e.g., 11), there still is a dearth of research evidence on the relationship between the use of

UDS and patient outcomes, including opioid-prescribed patient safety [12, 13].

A strong clinical rationale underlies the VA/DOD UDS recommendation: urine drug screens help clinicians detect use of illicit drugs by their opioid-prescribed patients and to monitor their adherence to prescribed medication regimens. They guide clinicians' ongoing opioid therapy decision making, enhance clinician-patient communication about the risks and benefits of opioids, and contribute to clinicians' satisfaction, confidence, and sense of mastery as opioid treatment providers [14–16]. In contrast, almost nothing is known about the effects of UDS on opioid-prescribed patients' health outcomes, including the risk of suicide- and overdose-related events. In part, this may be because very large, longitudinal samples are required to determine links between healthcare facility-level UDS practices and relatively low incidence suicide-related and drug overdose events among opioid-prescribed patients [13]. A recent large study [17] showed that VA opioid-prescribed patients treated in VA facilities ordering more UDS were at lower risk of suicide attempts than were those in facilities ordering fewer UDS. However, this study was cross-sectional and confined to data from 2010, which is the first year that VA/DOD opioid-therapy guidelines were widely disseminated across the national VA healthcare system.

In each year since 2010, the metrics described in Midboe et al. [7], including facility adherence to the UDS recommendation, have been calculated for the overall VA healthcare system. The resulting data provide an opportunity to assess levels of implementation of the VA/DOD UDS recommendation and variation in these levels, among VA facilities nationwide since 2010, when the VA/DOD treatment guidelines were first disseminated across the VA healthcare system. They also provide an opportunity to determine the within-facility rate at which VA facilities have improved their implementation of the UDS recommendation since 2010 and variability among VA facilities in this within-facility implementation rate. Moreover, these cross-time metrics afford examination of the question of how average levels and rates of change in UDS implementation in VA facilities in the 4 years spanning 2010 to 2013 influence risk of suicide and drug overdose events among opioid-prescribed patients during the fourth year (2013) after initial dissemination of the VA/DOD opioid treatment guidelines.

Here, we avail ourselves of these opportunities to provide an example of how healthcare systems can longitudinally measure their progress in implementing specific opioid therapy guideline recommendations, such as increased use of UDS, and relate this progress to subsequent opioid patient health and safety outcomes, such as suicide- and overdose-related events. Accordingly, the purpose of this study is to determine (a) the level and rate of change in VA healthcare system-wide implementation of UDS over 4 years (2010–2013) following first dissemination of the 2010

VA/DOD opioid therapy guideline recommendations and (b) predictive associations between these and VA opioid-prescribed patients' risk of suicide- and overdose-related events in the fourth year (2013) after initial VA/DOD guideline dissemination.

METHOD

Sample

The facility-level population for this study comprised the 141 VA healthcare facilities in the nationwide VA healthcare system. The patient-level sample for this study was identified using the Veterans Health Administration's (VHA) managerial cost accounting (MCA; formerly decision support system) inpatient and outpatient pharmacy benefits files. It comprised the 484,241 individuals prescribed a long-acting opioid (methadone, morphine, oxycodone, fentanyl, hydromorphone, oxymorphone) and/or engaged in chronic, short-acting opioid use (i.e., prescribed at least a 90-day supply of a short-acting opioid (codeine, morphine, propoxyphene, levorphanol, oxycodone, meperidine, hydromorphone, dihydrocodeine, butorphanol, pentazocine, fentanyl, hydrocodone, oxymorphone, tapentadol) while a VA patient during 2012 who also had one or more inpatient or outpatient encounters in the VA healthcare system during 2013.

Measures

Facility-level data—For each of the 141 VA healthcare facilities, at each of the 4 years (2010–2013), we calculated from VHA MCA pharmacy and laboratory data the facility-level urine-screening implementation metric described in Midboe et al. [7]. Specifically, this metric is defined as *the facility percentage of opioid (long acting and/or chronic, short acting)-prescribed patients who obtained one or more urine drug screenings during the year in question*.

Patient-level data—From the VA National Patient Care Data (NPCD) files, we obtained information about the 484,241 opioid-prescribed patients' demographic and medical characteristics in 2012. We used the 2012 values of these characteristics as covariates in our model for the following two reasons: (1) the temporal proximity of these characteristics to the opioid-prescribed patients' 2013 suicide/overdose events and (2) temporal precedence, that is, their occurrence in 2012 made it clear that they preceded, and were not a consequence of, the 2013 suicide/overdose event outcomes in our model.

Opioid-prescribed patients' *demographic characteristics* included their 2012 values for *age*, *gender* (0 = male, 1 = female), *race* (0 = white, 1 = nonwhite), and *marital status* (0 = unmarried, 1 = married). Patients' medical and mental health comorbidities were determined by International Classification of Diseases–Ninth Revision (ICD-9 [18]) diagnostic codes in the NPCD data files. ICD-9 codes are used to record patients' medical and mental health conditions at their healthcare treatment encounters. To calculate a dichotomous measure

of *medical comorbidities* (0=no, 1=yes), we examined patients' 2012 NPCD records to determine whether they had been assigned one or more of the ten ICD-9 diagnostic codes (e.g., AIDS, cardiac arrhythmia, heart failure, hypertension, diabetes, cancer, obesity, weight loss) shown by Elixhauser et al. [19] to be strongly associated with high hospital resource use and mortality.

To create a dichotomous measure of patients' *mental health comorbidities* (0=no, 1=yes), we determined whether they had been assigned ICD-9 codes that included alcohol abuse or dependence, drug abuse or dependence, PTSD, depression, bipolar disorder, or schizophrenia. We chose these diagnoses to represent mental health comorbidity because of their known associations with elevated risk of suicide and overdose [20, 21].

VA MCA laboratory procedure data were used to determine whether patients had been provided *one or more urine drug screens* (0=no, 1=yes) during their 2012 VA healthcare service use [7]. The MCA laboratory procedure codes used to identify urine drug screens and details on their extraction from VA patient treatment files are documented in Appendix 4, Im et al. [17].

To determine patients' suicide and overdose events, their 2013 NPCD records were scanned for ICD-9 codes (E850.0–E850.2; E850.4; E851–E852; E853.0; E853.2; E853.8–E853.9; E935.0–E935.2; E935.4; E939.4–E939.5; E937.0; E937.8; E938.0; E939.1–E939.2; E950.0–E959.9; E958.0; E980.0–E980.3; E980.8; E981.0–E984.9; E988; E965.0, 965.4, 967.0, 967.8, 968.0, 969.1–969.5) indicative of *suicide- and drug overdose-related events*, i.e., self-inflicted injury or poisoning by opioids, sedatives, tranquilizers, or other CNS depressants during 2013. Note that these ICD-9 codes record only occurrence of self-inflicted injury or poisoning events; they do not indicate whether the event was intentional or resulted in death.

Analytic approach

We used the lme4 package for mixed effects models [22] in R statistical programming language [23] to analyze our data. A mixed effects or multilevel modeling approach is the most appropriate to use when data are organized at more than one level of analysis; for example, when repeated measures of UDS screening and opioid-prescribed patients' outcomes are nested within VA healthcare facilities [24, 25].

To review, we first wanted to describe VA healthcare system-wide levels and rates of change in UDS in the 4 years following first dissemination of the 2010 VA/DOD opioid therapy clinical practice guidelines. Accordingly, we first determined the average level of UDS in the VA healthcare system overall in each of the years 2010 through 2013 with descriptive statistical analyses. Next, we conducted multilevel regression to generate an unconditional growth model describing the average within-facility levels and linear rates of

increase in UDS use in VA medical centers over the interval 2010–2013.

Second, we wanted to know whether within-facility levels and rates of change in implementation of the VA/DOD UDS recommendation from 2010 to 2013 would influence risk of suicide- and overdose-related events among VA opioid-prescribed patients in the last of the 4 years following guideline dissemination (i.e., 2013). Accordingly, we conducted conditional multilevel regressions in which facility-level intercepts and slopes, obtained from our earlier unconditional growth modeling, were predictors of suicide and drug overdose risk among VA opioid-prescribed patients in 2013. Opioid-prescribed patients' age, gender, marital status, presence of medical comorbidities, presence of mental health comorbidities, and urine drug screening receipt in 2012 were also included as covariates in the model. We chose the 2012 values as covariates due to their occurrence prior and in close proximity to opioid-prescribed patients' risk of suicide or overdose events in 2013. Thus, our overall model estimates *prospective* effects of urine drug screening practices in the VA healthcare system from 2010 to 2013 on opioid-prescribed patients' suicide/overdose risk in 2013, independent of their 2012 demographic characteristics and medical and mental health comorbidities.

RESULTS

Sample characteristics

As shown in Table 1, the average age of the opioid-prescribed patient sample in 2012 was 60 years (SD = 12.4); the sample was 7 % women, 19 % non-white, and comprised almost 50 % unmarried individuals. About one third (29 %) of these opioid-prescribed patients had one or more medical comorbidities and more than one half (55 %) had a mental health comorbidity. Almost 37 % of these patients had obtained one or more urine drug screens during 2012.

Implementation of the UDS guideline recommendation

As shown in Fig. 1, VA facilities nationwide increased overall in implementation of the 2010 VA/DOD opioid-therapy UDS recommendation from 2010 to 2013. Over this interval, the percentage of opioid-prescribed patients who received urine drug screens from their VA healthcare facilities increased from an average of almost 29 % in 2010 to an average of about 42 % in 2013.

Table 2 describes the average within-facility level and rate of change in implementation of the urine drug screening guideline. As indicated by the intercept value of 34.68, the average within-facility level of implementation across the 2010–2013 time frame was almost 35 %; there was statistically significant ($p < .01$) variance (SD = 16.02) among the facilities in this level of implementation. As indicated by the slope value of 4.46, the average within-facility rate of increase in UDS implementation was about 4.5 % per year. Again, there was statistically significant variance (SD = 3.44)

Table 1 | Sample characteristics of VA opioid-prescribed patients

Demographic and health characteristics (2012)	
Age (mean, SD)	60.2 (12.4)
Gender (% female)	6.8 %
Race/ethnicity (% non-white)	19.1 %
Marital status (% married)	49.5 %
Medical comorbidities (% one or more)	28.8 %
Mental health comorbidities (% one or more)	55.4 %
Received urine drug screening (% once or more)	36.7 %
Outcome (2013)	
Suicide- or overdose-related events (% yes)	2.0 %

Notes. "VA opioid-prescribed patients" is defined as patients receiving long-acting opioid (methadone, morphine, oxycodone, fentanyl, hydromorphone, oxymorphone) or 90+ days' supply of short-acting opioid (codeine, morphine, propoxyphene, levorphanol, oxycodone, meperidine, hydromorphone, dihydrocodeine, butorphanol, pentazocine, fentanyl, hydrocodone, oxymorphone, tapentadol) prescriptions in 2012 who also had a VA inpatient or outpatient encounter in 2013, $n = 484,241$

among the facilities in this rate of increase; the range was one of slight decline (-1.1%) to marked increase (almost 12%) in yearly rate of UDS recommendation implementation. Figure 2 depicts the variation in within-facility levels and rates of change in percentage of opioid-prescribed patients provided urine drug screens in the VA healthcare system. The dark line near the center of the graph shows the average level and rate of change within facilities in percentage patients provided screenings for the VA healthcare system overall; the gray lines show dispersion of VA facilities' implementation trajectories around this average trajectory.

Predicting 2013 suicide/overdose risk from UDS implementation

As expected, independent of facility-level UDS guideline implementation, VA opioid-prescribed patients who were younger, non-white, and unmarried in 2012 were at elevated risk of suicide or overdose events in 2013 (Table 3). Opioid-prescribed patients in poorer physical and mental health, as reflected by having one or more medical or mental health comorbidities in 2012, also were at elevated risk for these adverse medical events. Moreover, opioid-prescribed patients who received one or more urine drug screens in 2012, indicating care providers' efforts to monitor their drug use that year, were twice as likely as non-

screened opioid-prescribed patients to have a suicide- or overdose-related event in 2013.

Results in Table 3 show that, independent of these patient-level risk factors, the facility-level characteristic of having higher average levels of UDS over the interval 2010–2013 predicted a statistically significant reduction in risk of suicide- and overdose-related events in 2013 among VA opioid-prescribed patients. Parameter estimates shown in Table 3 suggest that for every additional 1% of opioid-prescribed patients monitored by a facility using urine drug screening, there is as much as a 1% reduction in patient-level risk of a suicide or overdose event.

DISCUSSION

In earlier research, Midboe and the VA Opioid Metric Development Team [7] demonstrated how VA/DOD opioid therapy and clinical treatment guidelines can be operationalized and measured using VA electronic patient treatment records. Here, we show how these metrics can be used to track healthcare system-wide progress in implementing practices aimed at improving opioid-prescribed patient safety and to ascertain whether this progress is associated with a reduction of adverse medical events, including suicide- and overdose-related events, among opioid-prescribed patients.

Fig 1 | Average annual percentage of opioid-prescribed patients provided with urine drug screening (UDS) in the VA healthcare system

Table 2 | Within-facility levels and rates of change in implementation of UDS in the VA healthcare system

	Estimate	(SD)
Fixed Effects		
Intercept	34.68**	(16.02)
Rate of change (slope)	4.46**	(3.44)
Random Effects		
Variance intercept	253.98	(15.91)
Variance slope	8.66	(2.94)
Residual	15.91	(3.99)
Model Fit		
-2LL	-1964.0	
AIC	3839.0	
BIC	3965.0	

Notes. $N = 141$

SD = standard error, $-2LL$ = log likelihood criterion, AIC = Aikake Information Criteria, BIC = Bayesian Information Criteria

** $p < .01$

Our findings show that since 2010, when the VA/DOD opioid-therapy guidelines were first widely disseminated in VA, levels of concordance between the VA/DOD UDS recommendation and facility practice have been moderate but have clearly increased. Among VA facilities nationwide, the average level of drug-screening coverage of opioid-prescribed patients increased from about 29 % to almost 42 %. Buscaglia and colleagues [26] found considerable variability among VA facilities in implementing the VA/DOD UDS recommendation in 2010. Similarly, we found a wide range of adherence to the VA/DOD UDS recommendation in VA facilities from 2010 to 2013. For example, our findings show that in 2010 and 2013, the percentage of VA opioid-prescribed patients who received UDS was 2 to 6 % in facilities with the lowest UDS coverage and exceeded 75 % in facilities with the highest UDS coverage.

The availability of healthcare system-wide longitudinal data on implementation of the UDS recommendation allowed us to determine variation in 4-year *within-facility* rates of change in the delivery of UDS to VA opioid-prescribed patients. We found that between 2010 and 2013, the average within-facility increase in UDS use has been about 4.5 % per year but with considerable variability among the facilities in this implementation rate.

The moderate rates of urine drug screening among VA opioid-prescribed patients may reflect clinical decision making based on perceived patient risk and doubts about the effectiveness of UDS, as well as facility-level barriers to UDS implementation. That patients chosen to receive UDS in 2012 were at elevated risk of subsequent suicide and overdose events suggests that clinicians selectively use UDS with patients they recognize as higher risk. The moderate overall level of implementation of UDS may reflect the fact that clinicians judge relatively few opioid-prescribed patients as warranting UDS as a component of monitoring to prevent drug misuse, suicide attempts, and unintentional overdose. In addition, because the VA/DOD guideline's UDS recommendation was based solely on expert consensus and not on research evidence, clinicians may not be convinced of the value of UDS outside of the context of suspected substance misuse or medication diversion. Facility-level barriers, such as limited laboratory capacity to process UDS results, and variation in clinicians' skills at interpreting them, may also contribute to incomplete implementation of the UDS recommendation [27]. Nonetheless, the system wide and within-facility increases in implementation of the UDS recommendation found here reflect responsiveness of VA facilities nationwide to this specific VA/DOD clinical treatment guideline recommendation. However, we note that the considerable and consistent variability among VA facilities in implementing this recommendation suggests that there is room for VA clinicians and

Fig 2 | Within-facility levels and rates of change in percentage opioid-prescribed patients provided UDS

Table 3 | Effects of implementation of urine drug screening on opioid-prescribed patients' risk of suicide- or overdose-related events

	Est	SE	OR	CI	z value	p value
Predictors						
Facility-Level						
Average level implementation	−0.01	0.002	0.992	(0.988, 0.995)	−4.3	.00 **
Rate of change in implementation	−0.01	0.019	0.991	(0.967, 1.23)	−0.8	.45 ns
Individual-Level						
Age	−0.35	0.010	0.707	(0.692, 0.722)	−31.9	.00 **
Gender	0.02	0.03	1.02	(0.951, 1.09)	0.5	.30 ns
Race	0.17	0.02	1.19	(1.29, 1.25)	6.7	.00 **
Marital status	−0.41	0.02	0.666	(0.638, 0.695)	−18.8	.00 **
Medical comorbidities	0.45	0.02	1.57	(1.50, 1.64)	20.1	.00 **
Mental health comorbidities	1.46	0.03	4.31	(4.05, 4.58)	46.7	.00 **
Received UDS 2012	0.74	0.02	2.10	(2.01, 2.19)	33.0	.00 **
Model Fit						
−2LL				−43615		
AIC				87252		
BIC				87374		

Notes. Est = estimate, SE = standard error, OR = odds ratio, CI = confidence interval, −2LL = log likelihood criterion, AIC = Akaike Information Criteria, BIC = Bayesian Information Criteria

***p* < .01

policy makers to adopt practices that will encourage increased adherence to this VA/DOD opioid treatment recommendation to enhance opioid-prescribed patients' safety.

Our findings contribute much needed evidence regarding UDS as a method of enhancing opioid therapy safety. Although UDS has been shown to have positive effects on clinicians' confidence and comfort in opioid prescribing [14–16], there is almost no research evidence [12, 13] demonstrating the effects of UDS on health and safety of opioid-prescribed patients. Our findings suggest that, even after controlling for key patient-level risk factors, receiving opioid treatment in a facility with higher levels of UDS implementation over the interval 2010–2013 was associated with reduced risk of suicide and overdose events among opioid-prescribed patients in 2013. This result should be interpreted with caution. On the one hand, our study reproduced the effect found in the Im et al. cross-sectional investigation of a 2010 VA patient sample, using a prospective longitudinal research design, which had the strengths of temporal precedence (facility UDS practices and patient risk factors preceded patients' suicide/overdose risk period) and statistical control over confounding patient risk factors. Moreover, we report what appears to be a clinically significant finding, that is, the estimated effect in our multilevel regression model suggests that for each 1 % increment in facility-level UDS use, there is a 1 % reduction in patient-level risk of suicide- or overdose-related events. Thus, even modest boosts in UDS at the facility-level pay off in some subsequent reduction of suicide and overdose events at the patient level. This is an important outcome given that suicide and overdose are arguably the most serious adverse medical events associated with opioid therapy. On the other hand, the obtained effect may be statistically significant in part due to our large patient sample size,

and we cannot rule out alternative explanations for it. For example, higher UDS levels may be more readily attainable in medical centers that have more abundant laboratory and other clinical resources; thus, this wealth of resources and associated healthcare practices and policies, rather than UDS implementation *per se*, may account for the effect we found. We emphasize that we cannot infer from our findings that UDS *alone* predicts subsequent suicide/overdose risk. Information in Buscaglia et al. [26] suggests that there is some overlap between UDS practices and other VA/DOD opioid treatment guideline-concordant efforts in VA medical centers. The additive effects of multiple guideline-concordant activities in VA facilities, or related elevations in their overall quality improvement efforts, rather than UDS practices alone, may account for the reduced risk of suicide and overdose events observed here.

Several other limitations of this study should be considered in interpreting our findings. Our data comprise metrics based on VA electronic patient treatment data on patients' pharmacy and clinic use. Although there is good evidence for the reliability and validity of healthcare metrics based on VA electronic medical record-keeping [28], we acknowledge that our data may not be completely accurate because we cannot be certain of patients' opioid prescription compliance. MCA pharmacy data only indicate whether a patient has filled an opioid prescription and not his or her opioid use. Moreover, this data source does not inform us of opioid-prescribed patients' medical treatments and adverse health events occurring outside the VA healthcare system. Finally, we do not know whether findings reported here are generalizable to non-VA healthcare systems or to non-VA opioid-prescribed patients. Further studies that examine the extent and effects of opioid treatment guideline implementation in large, non-VA healthcare

settings are needed to determine the generalizability of our findings.

Our findings suggest several avenues for future research. Further research is needed to determine whether the levels and rates of change in implementation of the UDS recommendation in VA from 2010 to 2013 generalize to the seven other VA/DOD 2010 clinical guideline domains outlined by Midboe et al. [7]. We suspect that there has been increased implementation of many of the other 2010 VA/DOD recommendations due to recent national, regional, and local VA efforts to address opioid safety. Thanks to the foundational work of Midboe and colleagues [7], it is now possible to examine empirically the levels and rates of implementation from 2010 to present of each of the individual recommendations outlined in Midboe et al. and to determine whether there are prospective links between these and subsequent opioid-prescribed patient health and safety outcomes. Knowledge of which opioid treatment recommendations can be most broadly, quickly, and sustainably implemented within healthcare facilities, and which have the greatest preventive impact on adverse medical outcomes, can help healthcare systems planners to better specify procedures and allocate quality-improvement resources to improve opioid treatment safety in their facilities.

Further research also should aim to identify clinician- and healthcare facility-level factors that pose barriers to or predict faster and more thorough implementation of VA/DOD opioid therapy guideline recommendations. This information can support the formulation of clinician- and facility-level interventions to support faster and more complete implementation of VA/DOD clinical treatment guidelines to facilitate safer opioid therapy for pain patients.

Notwithstanding its limitations, this study makes two important contributions to research on opioid treatment safety. First, it adds promising new findings to the evidence base for implementation of urine drug screening as a means of preventing what are among the worst adverse medical events for opioid-prescribed patients, suicide and drug overdose events. Second, it is responsive to recent recommendations by the National Action Plan for Adverse Drug Event Prevention (ADE) [29] to improve opioid therapy safety in demonstrating that opioid treatment guidelines can be operationalized and measured, as done by Midboe and the VA Opioid Metric Development Team [7], then prospectively examined in relation to specific opioid-prescribed patient outcomes. Further research responsive to the ADE Action Plan is needed. Specifically, it is important to determine the rates with which other VA/DOD opioid treatment guidelines have been adopted by VA healthcare facilities since 2010, to identify facility-level predictors of more complete and faster opioid treatment guideline implementation, and to demonstrate which guideline recommendations are most important to implement to ensure enhanced safety of opioid therapy. This information can help guide clinical practices and healthcare system resource allocation that better balance the desire to provide

patients with accessible, effective relief for pain with evidence-based practices that protect them from adverse medical events associated with opioid therapy.

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Conflict of Interest: The authors declare that they have no conflicts of interest.

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