Outcomes Associated With a Multidisciplinary Pain Oversight Committee to Facilitate Appropriate Management of Chronic Opioid Therapy Among Veterans

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The implementation of an opioid management initiative increased appropriate monitoring and led to better management of high-risk chronic opioid therapy.

he use of opioids to treat chronic noncancer pain (CNCP) has become increasingly common over the previous 2 decades. The Office of National Drug Control Policy (ONDCP) reported that from 1997 to 2007, there was a 4-fold increase in the mg per person per year sale of prescription opioids, from 74 mg to 369 mg.¹ The number of opioid prescriptions dispensed by pharmacies also has increased by 48% from 2000 to 2009.² Within the VA population, about half of the 1.44 million patients with a diagnosis of pain (excluding cancer pain) received opioids during 2011, and 57% of these patients received chronic opioid therapy (COT), which is at least 90 days of opioid use in a year.³

Despite this increased use of opioids, data regarding the efficacy of long-term opioid use for noncancer pain remain limited.^{1,4-8} Instead, there is a growing body of evidence describing potential adverse effects (AEs) of long-term opioid use at even relatively modest doses, including sexual dysfunction, hyperalgesia, and altered brain structure.9-11 Additionally, increases in the misuse and abuse of opioids as well as mortality associated with opioid toxicity have been observed.12-14 Opioid pain relievers were involved in nearly 17.000 deaths in the U.S. in 2010, which represents a 3-fold increase since 1999. This number also represents 75% of all deaths that were attributed to prescription drug poisoning in 2010.13 Unfortunately, this alarming trend parallels the aforementioned increases in the utilization of prescription opioids for CNCP.

Given this accumulating data

regarding the profound risks and limited benefit of COT, many organizations have advocated a reassessment of the upward trajectory of opioid utilization. In 2009, the American Pain Society (APS) in partnership with the American Academy of Pain Medicine (AAPM) released clinical guidelines for the use of COT in CNCP.⁶ In this guideline, the authors advocate a balanced approach to opioid use: Clinicians consider both the legitimate medical need for opioids in some patients with CNCP as well as the serious public health problem of abuse, addiction, and diversion.6 In 2011, the FDA, Drug Enforcement Agency (DEA), and ONDCP enacted the Prescription Drug Abuse Prevention Plan, which focused on 4 major areas: education, prescription monitoring, proper medication disposal, and law enforcement.4

In March 2016, the CDC released a new guideline for prescribing opioids for chronic pain

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that included 12 recommendations based on 3 key principles. First, nonopioids are preferred for chronic pain in all settings except for active cancer, palliative, and end-of-life care. Next, when opioids are used for chronic pain, they always should be prescribed at the lowest possible effective dose to reduce the risk of opioid use disorder and overdose. Finally, clinicians should exercise caution when prescribing opioids and monitor all patients closely for opioid-related risk.¹⁵

Recently, an August 2016 FDA review found that the combined use of opioids and benzodiazepines (BZDs) resulted in serious AEs, including respiratory depression and death. Based on these findings, the FDA requires that updated boxed warnings be added to the labeling of prescription opioid and BZDs.¹⁶

The VHA also has been at the forefront of this national movement to promote the appropriate use of opioids. In 2009, the VHA released a pain management directive that highlighted the risks of COT and required adoption of a stepped-care approach to opioid prescribing that focused on quality of life as the primary determinant of treatment quality.¹⁷ In 2010, the VHA released its guideline on opioid therapy for chronic pain, which also included tools for providers, such as a sample opioid therapy agreement, equivalent potency tables, and a urine drug screening guide.¹⁸ In 2014, the VHA released the Opioid Safety Initiative (OSI), which advocates for a team-based approach to reduce the use of opioids for veterans through a focus on alternate methods to alleviate pain.

At the Ralph H. Johnson VAMC (RHJVAMC) in Charleston, South Carolina, a multidisciplinary pain oversight committee (POC) was

tasked with assisting in achieving the goals set forth in the VHA OSI. To reach these goals, the POC sought to develop and implement a population-based initiative targeting modifiable factors that are known to increase the risk of opioid-related toxicity and overdose. These factors included patient utilization of multiple prescribers or multiple pharmacies, high-dose COT (defined in the APS/AAPM guidelines as a morphine equivalent daily dose [MEDD] > 200 mg⁶), and use of concomitant central nervous system-active medications, chiefly BZDs.¹⁹⁻²³ The POC consisted of the RHIVAMC chiefs of mental health. primary care, and pharmacy; a physician specializing in pain and addiction medicine; a pharmacist specializing in pain and palliative care; quality management personnel; a patient advocate; and multiple physicians from the mental health and primary care departments.

Previous studies have described the successful implementation of opioid management initiatives in a variety of health care settings.^{2,21,24-27} However, most of this work focused only on strategies to decrease prescribing of high-dose and longacting opioid formulations. The study presented here sought to add to the existing body of knowledge through evaluation of an initiative aimed at increasing appropriate monitoring as a tool to decrease opioidrelated patient risk. The primary aim of this study was to describe the types of interventions implemented by the POC during the study period. The secondary aim was to evaluate the effect of these interventions on the appropriate monitoring of COT as well as the appropriate management of high-risk COT > 200 mg MEDD.

METHODS

This study involved a qualitative description of individual POC interventions as well as a retrospective data analysis that examined the clinical impact of these interventions during the study period from April 1, 2012 to September 30, 2015. This study was reviewed and approved by the Medical University of South Carolina Institutional Review Board and the RHJVAMC Research and Development Committee.

200 mg Morphine ²⁹			
Opioid Drugs	Morphine Equivalent Daily Dose		
Codeine	1,333 mg		
Fentanyl	50 mcg/h every 72 h		
Hydrocodone	200 mg		
Hydromorphone	50 mg		
Methadone	25 mg/30 mg (varies depending on conversion tool) ^a		
Oxycodone	133 mg		

Table 1 Conversion Dosages Equivalent to

^aOpioid Conversion Calculator, accessed from http://www.globalrph.com/opioidconverter2.cgi, used for methadone due to more conservative nature for methadone.

Settina

The RHJVAMC is a tertiary care teaching hospital with primary and specialized outpatient services that are provided at the main medical center in Charleston, South Carolina, and at 6 community-based outpatient clinics (CBOCs) located throughout southeastern South Carolina and parts of Georgia. Primary care is delivered by patient aligned care teams (PACTs) based on the patient-centered medical home model.28 The PACT consists of a primary care provider (PCP) who is aided by dedicated nursing, pharmacy, and mental health care providers. In most cases, COT is prescribed and managed in the PACT setting. At the time of this initiative, a broad range of specialty services were available, including a multidisciplinary pain management team, orthopedics, and physical medicine and rehabilitation. In 2012, about 55,000 patients were enrolled and received care at RHIVAMC. The POC interventions were carried out at all clinic sites.

Patients

The study population included all patients prescribed COT at RHJVAMC

during the study period. A patient was considered to be prescribed COT if at least 1 opioid-containing medication was dispensed to the patient in a selected fiscal quarter during the study period and the total cumulative supply of opioid-containing medications was \geq 90 days for both the selected quarter and the prior quarter.

Furthermore, a high-risk COT subpopulation included any patient who satisfied either of the following criteria: (1) Receipt of outpatient prescription(s) for opioid-containing medication(s) (including tramadol) and a benzodiazepine derivative in the same fiscal quarter; patients were included in this subpopulation regardless of whether they met COT criteria; (2) Receipt of outpatient prescription(s) for opioidcontaining medication(s) with at least 1 instance in which the MEDD was \geq 200 mg in the designated quarter (Table 1). The MEDD was calculated for each fill in the fiscal quarter using the following equation:

Strength x Quantity x

Equivalence Conversion = MEDD Day supply for each month in the fiscal quarter

If medication fills were within 3 days of each other, the prescriptions were considered to be taken together and the MEDD was summed.

Intervention Descriptions

The primary aim of this study was to qualitatively describe each intervention implemented by the POC. The POC monthly meeting minutes were recorded and reviewed for the study period, and descriptive information regarding each intervention was extracted. Extracted information included implementation date(s), the responsible POC member, and a general description of each intervention. Interventions were then categorized as informatics tool, targeted patient intervention, provider education, or patient education.

Impact of Interventions on Monitoring

In order to characterize the impact of POC interventions on appropriate monitoring of COT, the electronic medical record (EMR) of each patient satisfying COT criteria was queried for the presence of an annual urine drug screen (UDS) result and a note in the chart signaling that a prescription drug monitoring program (PDMP) review had been performed. The authors defined appropriate UDS monitoring and PDMP review as the presence of a UDS result and a PDMP review note in the EMR in the year prior to the query date.

Prior to the start of the POC interventions, 4.1% of RJVAMC patients had an annual PDMP review and 47.8% had an annual UDS. Although more frequent UDS results and PDMP reviews are appropriate in most cases, yearly monitoring was considered by the POC to be a reasonable initial goal. The percentage of veterans receiving COT who had received appropriate monitoring for each measure was collected for each fiscal quarter during the study

Table 2. Opioid and Benzodiazepine Combination Risk Assessment Tool ^a				
Patient Assessment/Monitoring	Response	Comments		
Is the patient stable on current mental health regimen or therapy?	Yes/No			
Assess and document the level of risk for the patient	Low/Med/High			
Has the patient had any adverse reactions to BZDs/opioids/combination in the past 2 years? If so, does risk of ADR(s) still exist that warrants discontinuation?	Yes/No			
Can a plan be developed to taper the patient off the BZD(s)? If not, why?	Yes/No	Why?		
Near absolute contraindications to the concomitant use of BZDs and opioids				
Active misuse, abuse, or addiction to BZD(s), opioids, alcohol, and/or other CNS depressants	Yes/No			
Use of > 1 BZD	Yes/No			
Strong relative contraindications to concomitant use				
History of any substance use disorder; stronger contraindications apply to patients with shorter periods of remission, absent or poor substance abuse recovery programs, and histories of substance use disorders involving BZDs, opioids, alcohol, or other CNS depressants	Yes/No			
Unstable mood, anxiety, or thought disorders	Yes/No			
Personality disorders, particularly 'Cluster B' disorders characterized by combinations of affective instability, impulsivity, failure to conform to social norms, disregard for safety, and suicidality	Yes/No			
Relevant medical comorbidities, including morbid obesity, sleep-disordered breathing, COPD, and hepatic or renal dysfunction	Yes/No			
Older adults and others at elevated fall risk	Yes/No			
If there is no choice but to leave the patient on this medication the provider must:				
Discuss risks and benefits of using opioids and BZDs with the patient; document in chart	Yes/No			
Document indication for BZD use and justification for concomitant use in chart	Yes/No			
Document in chart that the lowest effective dose is being prescribed				
Consider consulting the primary care provider about any concerns regarding concomitant opioid therapy	Yes/No			

Abbreviations: ADRs, adverse drug reactions; BZD, benzodiazepine; CNS, central nervous system; COPD, chronic obstructive pulmonary disease. ^aSource: Reisfield GM, Webster LR. *Pain Med*. 2013;14(10):1441-1446.

period. In addition, the difference between the initial and final fiscal quarter during the study period was calculated for each measure.

Impact of Interventions on High-Risk Opioid Prescribing

To assess the impact of POC inter-

ventions on appropriate management of high-dose COT, clinical variables were collected for patients who were prescribed high-dose COT and received targeted intervention in the form of a pain clinic e-consult. These variables were MEDD, presence of annual UDS, presence of annual PDMP review, and active BZD prescription. Each variable was assessed on the date of intervention (e-consult submission) and at 6 months postintervention. Changes in each clinical variable between baseline and at 6 months postintervention were then evaluated.

MANAGING CHRONIC OPIOID THERAPY



Figure 2. Patients on Chronic Opioid Therapy With Annual Prescription Drug Monitoring Plan



Abbreviation: PDMP, prescription drug monitoring program.

Data Sources

All patient data were obtained from the VHA Corporate Data Warehouse (CDW). The CDW contains extracts from VHA clinical and administrative systems that contain complete clinical data from October 1999 to the present. Population-level data were obtained from the Opioid Safety Initiative Master Dashboard National Report where available. Data not contained in this national dashboard were obtained through local data extractions from the CDW.

Informatics Tool

In September 2014, an e-consult tool was created to enable PCPs to efficiently consult the RHJVAMC pain clinic for advice on opioid-related issues in patients who require specialized attention. On activation of this EMR-based tool, the following patient data autopopulated in the consult: recent and active opioid prescription(s), UDS data from the previous 365 days, and PDMP review data from the previous 365 days. The consulting provider was then required to enter data on



Figure 3. Patients Who Received Concomitant Opioid and Benzodiazepine Derivative Prescription

concomitant mental health disorders that were deemed pertinent to opioid safety as well as obstructive sleep apnea (OSA) status (OSA diagnosis and continuous positive airway pressure machine receipt and adherence).

The consulting provider was required to indicate whether the patient had an active BZD prescription. If yes, a text field allowed the provider to enter the specific agent(s) prescribed and dose(s). Data were required in all fields for the e-consult to be considered ready for pain clinic review. Common pain clinic recommendations included orders for additional laboratory tests to assess adherence and potential toxicity, drug tapers, and consideration for complementary and alternative medicine (CAM). If a drug taper was recommended (either opioid or BZD), specific taper schedules would be provided by a pharmacist specializing in pain management.

Targeted Patient Intervention

In April 2014, the POC and Mental Health service began a targeted review of all outpatients receiving combination opioid and BZD therapy. First, the POC distributed to each mental health provider a list of patients who were receiving combination opioid and BZD therapy. An opioid/BZD combination risk assessment tool (Table 2) was developed by the POC and made available to assist with these patient reviews. This tool prompted a provider to assess a patient's stability on the current regimen as well as the presence of any absolute or relative contraindications to concomitant BZD and opioid use. Providers documented whether a discussion regarding the risks and benefits of opioids and BZDs had occurred with the patient. The tool encouraged providers to document a continued indication for combined BZD and opioid therapy use and whether the lowest effective BZD

dose was being prescribed. A standardized BZD taper protocol also was developed by the POC to assist providers if a BZD taper was indicated. A total of 222 patients were reviewed over 7 months from April 2014 to October 2015.

Following completion of this targeted review in October 2015, the POC required that starting any patients on opioid and BZD combination therapy would require a specialist consult. For existing COT patients, a mental health consult would be required to initiate BZD therapy. For stable patients on BZD therapy, a pain clinic consult was required before initiating an opioid prescription. The Pharmacy service acted as a gatekeeper for these agents and refused to dispense either new agent until the proper consults had been submitted unless clinical necessity of an agent was apparent (ie, opioid prescription following invasive surgery).

Variable	Baseline	6 Months Postconsult	Difference, %
Median morphine equivalent daily dose, mg	300	240	-20.0
Annual urine drug screen, n	41	54	31.7
Annual prescription drug monitoring program, n	11	49	345.0
Active benzodiazepine use	17	4	-76.5

Table 3. Impact of Pain Clinic e-Consult at 6-MonthFollow-up (n = 58)

The final targeted patient intervention occurred following deployment of the opioid safety review e-consult tool in September 2015. To review the highest risk COT patients, each PCP was given a list of their patients who were taking \geq 200 mg MEDD. With support from the primary care service chief, PCPs were required to submit an e-consult for every patient who did not meet the e-consult exclusion criteria. In the fourth quarter of fiscal year (FY) 2014, and first quarter of FY 2015, 116 RHJVAMC patients received \geq 200 mg MEDD with 49 meeting the exclusion criteria. Of the 67 patients eligible for pain clinic review, e-consults were placed for 58 patients over a 7-month period. The remaining 9 patients did not receive an e-consult because taper was initiated by the patient's PCP without pain clinic assistance (6), aberrant patient behavior was identified during data collection (2), and patient was transitioned to palliative care (1).

Provider Education

A primary goal of the POC was to educate PCPs on opioid safety, to ensure that each provider was able to use evidence-based medicine and identify potential high-risk situations during patient encounters. Provider education was delivered by physician and pharmacist pain specialists and took place from September 2013 to January 2015 at existing primary care meetings. Topics included UDS interpretation, opioid/BZD combination risks, the goals and requirements of the VA OSI, and legal requirements of the South Carolina Reporting and Identification Prescription Tracking System (SCRIPTS) PDMP.

Patient Education

Patient education was delivered through informational brochures either mailed or given out during clinic visits. The first brochure was mailed to patients and described the VA OSI goals and its potential impact on patients. A second handout described the risks associated with opioid/BZD combination therapy and encouraged patients to discuss these risks and alternate options with their providers. It was made available to primary care and mental health teams for distribution to patients.

RESULTS

Interventions spanned 19 months, with an average of 1 intervention per month. The highest number of POC interventions in a single month was observed in October 2014, with 3 individual interventions from 3 separate categories.

Impact of POC Interventions on COT Monitoring

During the study period, patients meeting COT criteria who received an annual UDS increased from 47.8% to 75.5%, a 56.7% increase from baseline (Figure 1). During the same period, patients with an annual PDMP review note in their medical record also increased from 4.1% to 19.6%, a 324% increase from baseline (Figure 2). Although the study period began in FY 2012 third quarter, FY 2014 first quarter was the baseline for PDMP review note data collection because VA providers were not legally allowed to access the SCRIPTS database prior to FY 2014.

Impact of Interventions on High-Risk Opioid Prescribing

Patients who received an opioid prescription and a BZD derivative in the same fiscal quarter decreased 41.7% during the study period (Figure 3). A significant improvement was observed in each clinical variable at 6 months postintervention among high-dose COT patients who received an opioid safety review e-consult (Table 3). The median opioid dose per patient decreased 20% from baseline, from 300 mg MEDD to 240 mg MEDD. The number of patients with an annual UDS increased 31.7% from 41 to 54 patients. The number of patients with an annual PDMP review also increased 345%, from 11 patients to 49 patients. Finally, the number of patients with an active BZD order decreased > 75% from 17 patients at baseline to 4 patients at 6-month follow-up.

In the FY 2014 third quarter, prior to activation of the opioid safety review e-consult tool, 100 patients received high-dose COT. Follow-up at the conclusion of fourth quarter FY 2015 revealed 64 such patients, which represented a 36% decrease from baseline.

DISCUSSION

During the study period, the POC used a variety of interventions from 4 distinct categories. Overall, these interventions successfully increased measures of appropriate COT monitoring (ie, UDS and PDMP utilization) and management of high-risk COT. Substantial improvements also were seen in the subgroup of patients receiving high-dose COT following creation and use of the opioid safety review e-consult tool.

Other VHA opioid management improvement initiatives were successful at reducing high-dose opioid prescribing through interventions similar to those described in this study. However, these initiatives did not address opioid monitoring practices or opioid/BZD combination therapy.^{25,26} To the authors' knowledge, no previous opioid management improvement initiatives have reported improvements in provider use of a state PDMP database.

There are a number of factors that also may have helped lead to the successful outcomes observed during the study period. First, the creation of an informatics tool allowed for sustained interventions and patient/provider education were certainly beneficial, the impact of these efforts wanes as time moves forward. Inevitably, a patient's and a provider's focus move to the next important issue, and new patients meet the criteria of the original targeted intervention.

Group Health Cooperative implemented an opioid risk reduction initiative that successfully increased UDS use over a 2-year postimplementation period.^{21,26} While this initiative used a number of similar interventions to those implemented in this study (patient and provider education, targeted patient intervention), an informatics tool was not used. The annual UDS rate at the conclusion of the Group Health initiative was 50%, which contrasts with a final rate of 75.5% in this study. Although it is difficult to draw comparisons between the studies given differences in populations studied, periods of evaluation, and varying baseline annual UDS rates, the current study results demonstrate the potential effectiveness of informatics tools to help drive enduring changes in practice.

An additional factor that had a positive impact on outcomes the continued support and advocacy from RHJVAMC clinical and administrative leadership. A targeted review of all patients receiving concomitant BZDs and opioids would not be possible without mental health department leaders who believed in the value of the time consuming undertaking. Furthermore, an e-consult tool is effective only if actually submitted for patients and if a specialist's recommendations are then followed by a PCP.

Finally, the interdisciplinary nature of the POC contributed to the success of each intervention described in this study. Patients receiving COT often have many complex physical, psychological, and social issues that must be considered in order to make a positive impact on patient care. To appropriately and effectively address these issues requires close collaboration between specialists from multiple disciplines.

Limitations

This study has several important limitations. First, its retrospective nature presents obvious documentation challenges. A second limitation is the brief period of evaluation following a number of POC interventions. For instance, 3 interventions took place in January 2015, leaving only 3 FY quarters of effectiveness data. Furthermore, increased awareness of the risks associated with opioid therapy in the VHA and the health care industry across the study period may have independently impacted the improvements observed in this study.

The lack of an assessment of both patient-centered and clinical outcomes is an additional limitation of this study. Rates of annual UDS and PDMP database reviews and the number of patients receiving highrisk COT are only surrogate metrics that may indicate appropriate prescribing and monitoring of these. Obtaining a UDS or PDMP review is meant to provide a practitioner with additional information to interpret when caring for a patient. These data are only meant to complement-not replace-skilled patient assessment by a provider. Although the authors observed no major patient or clinical adverse events during the study period, the possibility exists that a patient may have been negatively impacted by a population-level initiative to improve surrogate measures of appropriate drug use.

Future studies should assess changes in measures, such as pain scores, legitimate adverse events, and overdose occurrences in order to evaluate whether such opioid improvement initiatives truly benefit the patients who are ultimately affected by each intervention.

CONCLUSION

This study demonstrates the successful implementation of a VHA-based opioid management initiative to increase appropriate COT monitoring and appropriate management of high-risk patients. It is the authors' hope that the findings may add to the growing body of literature describing successful opioid improvement initiatives and serve as a tool for other health systems that are confronted with these same issues.

Author disclosures

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REFERENCES

- Manchikanti L, Fellows B, Ailinani H, Pampati V. Therapeutic use, abuse, and nonmedical use of opioids: a ten-year perspective. *Pain Physician*. 2010;13(5):401-435.
- Garcia MM, Angelini MC, Thomas T, Lenz K, Jeffrey P. Implementation of an opioid management initiative by a state Medicaid program. J Manag Care Spec Pharm. 2014;20(5):447-454.
- 3. Edlund MJ, Austen MA, Sullivan MD, et al. Patterns of opioid use for chronic noncancer pain in the Veterans Health Administration from 2009 to 2011. *Pain*. 2014;155(11):2337-2343.
- 4. Office of National Drug Control Policy. Prescription

drug abuse. https://obamawhitehouse.archives.gov /ondcp/prescription-drug-abuse1. Accessed April 18, 2017.

- Chou R, Ballantyne JC, Fanciullo GJ, Fine PG, Miaskowski C. Research gaps on use of opioids for chronic noncancer pain: findings from a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. J Pain. 2009;10(2):147-159.
- Chou R, Fanciullo GJ, Fine PG, et al; American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10(2):113-130.
- The American Pain Society, The American Academy of Pain Medicine. Guideline for the use of chronic opioid therapy in chronic non-cancer pain: evidence review. http://americanpainsociety.org /uploads/education/guidelines/chronic-opioid -therapy -cncp.pdf. Accessed April 18, 2017.
- Von Korff M, Deyo RA. Potent opioids for chronic musculoskeletal pain: flying blind? *Pain*. 2004;109(3):207-209.
- Angst MS, Clark JD. Opioid-induced hyperalgesia: a qualitative systematic review. *Anesthesiology*. 2006;104(3):570-587.
- Abs R, Verhelst J, Maeyaert J, et al. Endocrine consequences of long-term intrathecal administration of opioids. J Clin Endocrinol Metab. 2000;85(6):2215-2222.
- Younger JW, Chu LF, D'Arcy NT, Trott KE, Jastrzab LE, Mackey SC. Prescription opioid analgesics rapidly change the human brain. *Pain*. 2011;152(8):1803-1810.
- U.S Department of Health and Human Services, Substance Abuse and Mental Health Service Administration Office of Applied Studies. Results from the 2004 national survey on drug use and health: national findings. http://medicalmarijuana.procon .org/sourcefiles/2k4results.pdf. Updated September 8, 2005. Accessed April 18, 2017.
- Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. Ann Intern Med. 2010;152(2):85-92.
- Centers for Disease Control and Prevention (CDC). Emergency department visits involving nonmedical use of selected prescription drugs—United States, 2004-2008. MMWR Morb Mortal Wkly Rep. 2010;59(23):705-709.
- Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. JAMA. 2016;315(15):1624-1645.
- 16. U.S. Federal Drug Administration. FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. http://www.fda.gov/Drugs/DrugSafety /ucm518473.htm. Published August 31, 2016. Ac-

cessed April 18, 2017.

- U.S. Department of Veterans Affairs. Pain management, VHA directive 2009-053. https://www .va.gov/painmanagement/docs/vha09paindirective .pdf. Published October 28, 2009. Accessed April 18, 2017.
- U.S. Department of Veteran Affairs, U.S. Department of Defense. VA/DoD clinical practice guideline for management of opioid therapy for chronic pain. https://www.va.gov/painmanagement/docs/cpg _opioidtherapy_summary.pdf. Published May 2010. Accessed May 8, 2017.
- Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. JAMA. 2013;309(7):657-659.
- Gwira Baumblatt JA, Wiedeman C, Dunn JR, Schaffner W, Paulozzi LJ, Jones TF. High-risk use by patients prescribed opioids for pain and its role in overdose deaths. JAMA Intern Med. 2014;174(5):796-801.
- Zedler B, Xie L, Wang L, et al. Risk factors for serious prescription opioid-related toxicity or overdose among Veterans Health Administration patients. *Pain Med.* 2014;15(11):1911-1929.
- Centers for Disease Control and Prevention. CDC grand rounds: prescription drug overdoses a U.S. epidemic. MMWR Morb Mortal Wkly Rep. 2012;61(1):10-13.
- Jones CM, McAninch JK. Emergency department visits and overdose deaths from combined use of opioids and benzodiazepines. *Am J Prev Med.* 2015;49(4):493-501.
- Morden NE, Zerzan JT, Rue TC, et al. Medicaid prior authorization and controlled-release oxycodone. *Med Care*. 2008;46(6):573-580.
- Westanmo A, Marshall P, Jones E, Burns K, Krebs EE. Opioid dose reduction in a VA health care system—implementation of a primary care populationlevel initiative. *Pain Med.* 2015;16(5):1019-1026.
- Kryskalla J, Kern S, Gray D, Hauser P. Using dashboard technology to monitor overdose risk. *Fed Pract.* 2014;31(9):8-14.
- Centers for Disease Control and Prevention. CDC grand rounds: prescription drug overdoses a U.S. epidemic. MMWR Morb Mortal Wkly Rep. 2012;61(1):10-13.
- U.S. Department of Veterans Affairs. Patient aligned care team (PACT). https://www.patientcare.va.gov /primarycare/PACT.asp. Updated September 22, 2016. Accessed April 18, 2017.
- Liu Y, Logan JE, Paulozzi LJ, Zhang K, Jones CM. Potential misuse and inappropriate prescription practices involving opioid analgesics. *Am J Manag Care.* 2013;19(8):648-665.
- Reisfield GM, Webster LR. Benzodiazepines in long-term opioid therapy. Pain Med. 2013;14(10): 1441-1446.