Magnitude of the Problem

Prescription opioids are commonly used to treat acute and malignant pain, and, over the last decade, have increasingly been used in the management of chronic pain. Acute and chronic pain affect many Americans every year. Chronic pain alone is reported by more than 100 million Americans annually, with pain affecting more Americans than diabetes, heart disease, and cancer combined [1]. The annual costs of chronic pain, including medical costs of pain care and the economic costs related to disability days, lost wages, and lost productivity, range from $560 billion to $635 billion (in 2010 dollars) [1]. Although opioids are an essential tool for the treatment and management of acute, postoperative, and procedural pain, as well as for chronic pain related to cancer in the palliative care setting [1], use of opioids for chronic pain is more controversial because of the limited evidence surrounding the safety and efficacy of long-term opioid use for chronic pain [2]. Nevertheless, clinical practice guidelines recommend judicious use of opioids in appropriately selected and monitored patients [3].

The use of opioids has increased dramatically over the last decade. Between 1999 and 2010, the number of prescription opioids dispensed roughly doubled and the sales rate of prescription opioids (in kg/10,000 population) increased fourfold [4], with an estimated 201.5 million opioid prescriptions dispensed in 2009 [5]. In 2009, the prescription opioid hydrocodone was the single most commonly prescribed medication in the United States, and opioid analgesics were the third most commonly prescribed class of medications overall, leading the United States to spend approximately $8.4 billion on opioids in 2010 [6]. This increased use of opioids has come with unintended and serious health and social consequences. There is limited evidence on the effectiveness of long-term use of opioids and it is not clear that the dramatic increase in the use of opioids has led to improved treatment of pain overall, especially of chronic pain [7].

Opioids cause a number of ADEs that affect patients in both inpatient and outpatient settings. These ADEs are detrimental to the health and quality of life of patients [8]. Opioid ADEs include oversedation and respiratory depression; gastrointestinal adverse events, such as nausea, vomiting, and constipation; opioid-induced hyperalgesia; pruritus; and immunological and hormonal dysfunction [9]. All these ADEs were considered by the Federal Interagency Workgroup (FIW) for Opioid ADEs as important possible targets of the ADE Action Plan; however, the FIW determined that addressing ADEs related to unintentional opioid overdoses (i.e., oversedation, respiratory depression) were the highest priority because of the associated mortality and morbidity. Opioid overdoses constitute a tremendous public health burden that is potentially amenable to measurable prevention efforts, and a coordinated action plan could aid in prevention.

Prescription opioid–related deaths are considered to be one of the Nation's leading preventable public health problems.

Opioid overdose is a significant cause of drug-related injury and an important cause of adverse drug events. Opioids are central to the ADE Action Plan because they are a common cause of ADEs [10] and the leading cause of pharmaceutical overdose deaths [11]. By 2010, the number of prescription opioid overdose deaths had increased for the 11th straight year to 16,651 deaths [10], which exceeds the number of overdose deaths involving heroin and cocaine combined [10], and represents a quadrupling of the approximately 4,000 prescription opioid-related deaths reported in 1999 [10]. Moreover, the number of emergency department (ED) visits related to opioid misuse and abuse more than doubled from 2004 to more than 420,000 emergency department visits in 2011 [12]. Prescription opioid abuse is estimated to result in more than $72 billion in health care-related costs each year [13].

Access to safe and effective pain care remains an important problem in the United States; efforts to minimize the burden of harms from opioids should be implemented in parallel with efforts to ensure patients suffering from pain receive the most effective and safest treatment available.

The Institute of Medicine report *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research* outlines the challenges faced by Americans affected by pain [1]. The Opioids Section of the ADE Action Plan is informed, in part, by the findings and recommendations of this seminal report. All recommendations in the ADE Action Plan should be taken in the context of improving overall patient care through providing the safest and most effective, evidence-based pain care. In pain care, treatment decisions require that the potential benefits of opioid analgesia be

weighed against the potential safety risks of opioid treatment. Therefore, these recommendations recognize the importance of the clinician's judgment in the context of patient-centered care.

Because the dramatic increase in the use of opioids over the past decades is largely attributed to use for chronic pain, this section's recommendations for safer outpatient opioid treatment will focus on long-term opioids used for chronic pain. However, safe opioid prescribing is needed in all settings, including acute, postoperative, and periprocedural situations.

Distinguishing overdoses that occur during the normal course of care from misuse/abuse will be important in efforts to prevent opioid ADEs.

The ADE Action Plan's Opioids Section targets preventing opioid ADEs in patients prescribed opioids for pain, including patients who are injured through aberrant drug behavior. Discussion of patients who are prescribed opioids for addiction treatment, patients diverting opioids, and patients injured through suicide attempts is outside of the scope of the ADE Action Plan.

Although not specifically addressed in the ADE Action Plan, misuse and abuse of prescription opioids is an important public health problem and is the current target of several Federal and statewide initiatives by agencies such as the Centers for Disease Control and Prevention (CDC), Drug Enforcement Administration (DEA), Food and Drug Administration (FDA), National Institute on Drug Abuse (NIDA), Substance Abuse and Mental Health Services Administration (SAMHSA), and the White House Office of National Drug Control Policy (ONDCP). The FIW for Opioid ADEs acknowledges that there is a continuum of aberrant drug-related behaviors, and misuse and abuse are strong predictors for prescription opioid ADEs. The ADE Action Plan defers to the work of other Federal Agencies with regard to the specific issue of prescription opioid misuse and abuse.

The accurate categorization of opioid-related overdose deaths resulting from therapeutic use, versus misuse and abuse, is extremely challenging from a public health surveillance and epidemiologic perspective. Patients who are appropriately prescribed opioids can gradually drift into the spectrum of misuse/abuse through aberrant drug-related behaviors, such as increasing the dose or frequency of their opioids without consulting their prescriber [14]. This makes it difficult to target patients who are misusing/abusing opioids because it is challenging to identify patients who drift from therapeutic use to misuse/abuse. Aside from the practical difficulties in collecting data that can differentiate opioid ADEs from the normal course of care versus those arising from opioid misuse and abuse, the clinical definitions of addiction, dependence, misuse, and abuse are all still under debate within the pain

community [15]. The ambiguous definitions of misuse/abuse also make it difficult to draw conclusions from available data. As a result, the ADE Action Plan recommendations do not differentiate between patients who may misuse opioids. Instead, the Action Plan recommendations seek to reduce harm in all patients who are prescribed opioids for pain. The Action Plan supports developing a consensus on clinical and surveillance definitions of these terms but recognizes that this is outside of the scope of the plan. The ADE Action Plan does recognize the limitations of the data available and is cautious not to draw conclusions beyond those that the data can explain. For example, the CDC identified more than 16,651 opioid overdose deaths in 2010 [10], but it was not possible to distinguish deaths that occurred in the normal course of care when using medications as prescribed from deaths that resulted from intentional misuse and abuse. SAMHSA's Drug Abuse Warning Network (DAWN) estimated that more than 420,000 ED visits resulted from nonmedical use of prescription pain relievers in 2011 [12]. However, limited data are available about the number of ED visits for opioid ADEs during the normal course of care. Because of these limitations, much of the data cited throughout the opioid section of the ADE Action Plan may include patients who deliberately misuse/abuse opioids. These limitations are noted whenever applicable.

Surveillance

Understanding trends in opioid injuries and safe prescribing practices requires accurate, timely, and adequately representative information on key process and outcome measures—at national, regional, and facility levels.

A number of Federal- and State-based surveillance systems provide data on opioid ADEs. Broadly, these surveillance systems can be categorized as measuring three types of outcomes: (1) clinical (primary) outcomes (e.g., ED visits, deaths); (2) intermediate (surrogate) outcomes (e.g., clinical or laboratory values that precede or lead to clinical outcomes); and (3) process measures, indicators of actions aimed at mitigating the risk for clinical or intermediate outcomes (e.g., use of urine drug tests or State Prescription Drug Monitoring Program [PDMP] data). Clinical outcomes and process outcomes are most applicable to opioid ADEs because the prevention utility and role of intermediate outcomes is not clearly established. The identified Federal surveillance strategies have generally not been designed to assess intermediate outcomes related to opioid ADEs. A summary of Federal surveillance systems and selected State surveillance systems specific to opioid ADEs is presented in **Table 11**.

Currently available Federal surveillance systems outlined in the other sections are also capable of assessing the national opioid ADE burden. Federal systems involved in direct patient care (e.g., IHS, VHA) can capture regional- and facility-level information on the quality of opioid management. **Table 12** provides a summary of opioid ADE-related metrics from currently available Federal surveillance systems.

Table 11. Summary of Opioid ADE Metrics Collected by Federal and Relevant State Surveillance Systems

Source	Overview
National Vital Statistics System (NVSS), CDC	▪ Collects data from all death certificates filed by States and territories in the United States, including deaths involving drugs. ▪ Uses ICD codes to identify the underlying causes of death (e.g., drug overdose) and contributing causes (e.g., specific pharmaceutical or illicit drugs).
Drug Abuse Warning Network (DAWN), SAMHSA	▪ Collects data for drug-related ED visits from a nationally representative sample of U.S. non-Federal, short-stay, general medical and surgical hospitals with one or more EDs open 24 hours a day. ▪ Completed data collection in 2011; data are being incorporated into a larger National Center for Health Statistics (NCHS) survey.
Prescription Behavior Surveillance System (PBSS), CDC, FDA, BJA (under development)	▪ Will collect de-identified data from multiple State Prescription Drug Monitoring Programs (PDMPs). ▪ Number of participating PDMPs continues to increase, with the goal of collecting nationally representative data to develop surveillance reports for each participating State.
Prescription Drug Monitoring Programs (PDMPs)	▪ 49 States have legislative authority for PDMPs, and 47 States have active systems to collect State-level data related to the prescribing and dispensing of controlled substances. ▪ PDMPs collect patient, prescriber, dispensing pharmacy, and drug information.

Abbreviations: ADE = adverse drug event; BJA = Bureau of Justice Assistance; ED = emergency department; DAWN = Drug Abuse Warning Network; DEA = Drug Enforcement Administration; ICD = International Classification of Diseases; NCHS = National Center for Health Statistics; NVSS = National Vital Statistics System; PBSS = Prescription Behavior Surveillance System; PDMP = Prescription Drug Monitoring Program; SAMHSA = Substance Abuse and Mental Health Services Administration

Table 12. Summary of Metrics Related to Opioid ADEs Collected by Federal and Relevant State Surveillance Systems

Geographic Scope	Data Collection Method	Opioid ADEs or Management Metrics: Inpatient Settings	Opioid ADEs or Management Metrics: Outpatient Settings
National ADE Incidence/Rates	Administrative claims and/or EHR data	***AHRQ (NIS):*** ▪ Inpatient stays with ICD-9-CM codes indicative of opioid ADEs	***AHRQ (NEDS):*** ▪ ED visits with ICD-9-CM codes indicative of opioid ADEs ***CMS (Medicare Part D Claims):*** ▪ Outpatient prescribing to detect fraud and abuse
	Medical-record review	***AHRQ (MPSMS):**** ▪ Opioids are not currently captured by MPSMS system, but will be included after the conversion to QSRS.	***CDC (NEISS-CADES):*** ▪ ED visits for opioid overdoses and other ADEs, not related to misuse/abuse ***CDC (NVSS-Mortality):*** ▪ Deaths due to opioid overdose ***SAMHSA (DAWN):***** ▪ ED visits for opioid ADEs
Regional-/ Facility-level ADE Incidence/Rates (Quality Improvement)	Administrative claims and/or EHR data	▪ Not available	***DOD:*** ▪ Outpatient clinic visits, ED visits, hospitalizations with ICD-9-CM codes and/or CPT codes ***VA:*** ▪ VA/DOD guideline-based process measures ▪ Outpatient clinic visits, ED visits, hospitalizations for opioid overdoses & other relevant ADEs per ICD codes and/or CPT codes and prescription data (e.g., naloxone Rx) ***VA/DOD/State PDMP:*** ▪ Number of opioids prescribed linked with patient and prescriber ▪ Number of patients with multiple opioid prescribers ▪ Number of patients on high daily dose of opioids
Spontaneous Reports		***FDA:*** ▪ Clinician-diagnosed or patient-reported ADE	***FDA:*** ▪ Clinician-diagnosed or patient-reported ADE

Abbreviations: ADE = adverse drug event; ARCOS = Automation of Reports and Consolidation Order System; CPT = Current Procedural Terminology; DAWN = Drug Abuse Warning Network; DEA = Drug Enforcement Administration; ED = emergency department; EHR = electronic health record; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; PDMP = Prescription Drug Monitoring Program; QSRS = Quality and Safety Review System; SAMHSA = Substance Abuse and Mental Health Services Administration
* In 2015, MSPMS will be replaced by the Quality and Safety Review System (QSRS).
** Surveillance using DAWN is currently undergoing transition to CDC's National Hospital Care Survey.

Outcome and process measures related to opioid ADEs are lacking.

Currently, few validated metrics are available to assess national- or facility-level burden of opioid ADEs. Opportunities for improvement include the development and validation of clinical outcome and process measures, standardized definitions for opioid ADEs, requirements for reporting, and research into validated metrics that can reliably identify opioid ADEs.

PDMPs and PBSS represent important opportunities for advancing surveillance to reduce opioid ADEs.

One of the opportunities for advancing surveillance is continuing to develop PDMPs and the PBSS so as to optimally capture the data needed to identify high-risk prescribing patterns and to better understand risk factors for opioid ADEs. Ideally, PDMPs should be able to track patients across settings (including across different States), identify high-risk prescribing practices, and alert prescribers to aberrant drug-related behaviors in patients prescribed opioids.

Future surveillance efforts should capture opioid ADEs on the basis of validated process and outcome measures, differentiate opioid ADEs that occur in the normal course of care from those arising from opioid misuse/abuse, and identify ADEs occurring during transitions of care.

A number of potential process measures—such as number and doses of opioids prescribed, number of patients with multiple prescribers, number of patients on high daily doses of opioids, and number of patients co-prescribed opioids and sedatives—are available through data collection sources, such as EHRs and PDMPs. Federal Agencies should explore the best methods to collect and manage these data to allow for accurate, real-time evaluation of trends in validated process measures. **Figure 19** summarizes the recommendations to advance surveillance strategies for opioid ADEs.

Figure 19. Federal Interagency Workgroup Recommendations for Actions That Can Potentially Advance Surveillance Strategies for Opioid ADEs

Actions That Can Potentially Advance Surveillance Strategies for Opioid ADEs

- **Determine the adequacy of diagnostic and procedural coding for capturing opioid-related overdose events.**
  - Assess specificity, sensitivity, PPV, and NPV of ICD and CPT codes for capturing opioid-related overdose events.
  - Develop, assess, and validate novel measures for identifying and recording opioid ADEs (outlined in **Table 15**).
- **Address strengths and limitations of using process measures to identify opioid ADEs.**
- **Study associations between process measures and risk of opioid ADEs in inpatient and outpatient settings.**
- **Improve access to more integrated EHR data with linked pharmacy and outcomes data.**
- **Identify appropriate ADE surveillance metrics for opioid ADEs in inpatient and outpatient settings.**
- **Develop better surveillance definitions for opioid-related overdose events.**
  - Clarify criteria for identifying opioid ADEs that occur in the normal course of care versus those arising as a result of opioid misuse and abuse.
- **Identify appropriate ADE surveillance metrics for opioid ADEs.**
- **Improve the capabilities and use of PDMPs.**
  - Promote increased use of PDMP systems by providers.
  - Maintain funding for PDMP development at the State and Federal level.
  - Strive for real-time data reporting and cross-setting interoperability for PDMPs.

Abbreviations: ADE = adverse drug event; CPT = Current Procedural Terminology; EHR = electronic health record; ICD = International Classification of Diseases; NPV = negative predictive value; PDMP = Prescription Drug Monitoring Program; PPV = positive predictive value

Evidence-Based Prevention Tools

Many evidence-based guidelines for prescribing opioids for chronic pain address the issue of opioid safety [3, 16, 17, 18, 19]. Specifically, the guidelines make patient-centered care central to the decisionmaking process through assessing patients at risk for opioid ADEs and balancing the goals of pain management with the risk of opioid ADEs. Risk factors for inpatient and outpatient opioid ADEs differ in a number of ways. In inpatient settings, system-wide changes may be the most important target for ADE prevention because many opioid ADEs occur from medication and prescribing errors and inadequate monitoring of patient outcomes. In outpatient settings, safer prescribing and monitoring by providers and patient-centered interventions are critical because problems such as inappropriate

medication use (e.g., inappropriate dose, issues of adherence, aberrant medication-related behavior) are likely to play a far larger role in causing opioid ADEs in these settings than in inpatient settings [14]. Federal Agencies have a number of strategies to promote safe opioid prescribing and reduce opioid ADEs; these can serve as a model for private stakeholders. Federal Agencies should continue to develop, study, and validate opioid ADE prevention strategies and promote the adoption of validated ADE prevention strategies throughout the continuum of care. Current and future Federal assets related to the safe management of opioid therapy are summarized in **Figure 20**.

Figure 20. Federal Assets Related to Safe Management of Opioid Therapy, as Identified by the National Quality Strategy Priorities

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Resources for Safer Care—Health Care Provider Knowledge

- **DOD/VA:**
  - **Opioid Prescribing Protocol/ Guidelines**—Includes recommendations for assessing patients for appropriate pain therapy.
  - **Education opportunities**—Provider education Web portal (Talent Management System [TMS]) offers several continuing education courses on pain management, including a course on **"Opioid Therapy for Acute and Chronic Pain."**
  - **Opioid Safe Program** at Womack Army Medical Center (Fort Bragg, North Carolina)—Primary care clinicians provide high-risk patients prescribed opioids with kits containing naloxone, along with training in identifying and responding to overdose symptoms.
- **FDA:**
  - **Risk Evaluation and Mitigation Strategies (REMS)**—Required strategy for extended-release and long-acting opioids; FDA developed a *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics* and maintains a list of compliant continuing education (CE) programs for prescribers that include this curriculum.
  - **Opioid Dose Conversion Table**—Safe and reliable dose conversion table is based on updated evidence.
- **IHS:**
  - **TeleBehavioral Health Center of Excellence Pain and Addictions course**—15-series Webinar training program provides specialized training on how to treat pain and addictions.
  - **"Pain Champion" Training**—63-hour CE course trains local and regional experts, using the Project ECHO Model, which shares expertise by utilizing telehealth technology to connect an ECHO Team (primary care, specialists, and other providers integral to a patient-centered medical home team) to providers in rural and underserved locations.
- **NIH:**
  - **NIDAMED Physician Education Tools**—The National Institute on Drug Abuse (NIDA) created online tools and resources for medical professionals on safe pain management, including two classes entitled **"Safe Prescribing for Pain"** (2 CME/CE credits) and **"Managing Pain Patients Who Abuse Rx Drugs"**[i] (1.75 CME/CE credits). In addition to these two pain-focused educational resources, NIDA has developed an additional resource, **"Substance Use Disorders in Adolescents: Screening and Engagement in Primary Care Settings,"** which can be used by health care professionals to screen adolescents for aberrant prescription drug use and substance abuse disorders.
- **SAMHSA:**
  - **Opioid Overdose Prevention Toolkit**—Equips communities and local governments with materials to develop policies and practices to help prevent opioid-related overdoses and deaths, and addresses issues for first responders, treatment providers, and those recovering from opioid overdose.[ii]

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[i] Available at: http://www.drugabuse.gov/nidamed/etools

[ii] Available at: http://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit/SMA13-4742

Resources for Patients and Family Engagement

- **ACL:**
  - **Chronic Disease Self-Management Education Programs**—Provide education and tools to older adults and adults with disabilities to help them better manage chronic conditions including chronic pain.[i]
- **DEA:**
  - **National Take-Back Initiative**—Program gives patients a safe place to dispose of unused opioids.
- **FDA:**
  - **REMS**—Patient counseling document to guide education on risk and opioid management for patients on extended-release or on long-acting opioids.
- **VA:**
  - **"Taking Opioids Responsibly: For Your Safety and the Safety of Others"**—A patient education tool.

Resources To Promote Best Practices Within Communities

- **VA:**
  - **VHA National Pain Management Strategy**[ii]—Uses facility-level pain management committees to provide oversight and coordination of pain management activities to align care practices with the best practices.

Resources for Communication and Care Coordination[iii]

- **AHRQ:**
  - **Project RED**—Includes a number of medication-related strategies (i.e., active medication reconciliation, medication teaching for patients and caregivers, development of medication list for patients and their health care providers).
- **DOD:**
  - **Sole Provider Program (SPP**)—Instituted by the Army as a risk mitigation program for high-risk patients, the SPP identifies high-risk patients and assigns a single provider and one alternate who are authorized to prescribe opioids.
- **IHS:**
  - **Nationally Clinical Pharmacy Specialists (NCPS) Program**[iv]—Advanced pharmacy certification that allows for pharmacists to provide pain management at Gallup, NM; Anchorage, AK; and Claremore, OK.
  - Pharmacist-run pain management clinics with pharmacists prescribing medications, and ordering and interpreting labs per protocol.
- **VA:**
  - **Systems to track patient progress**—VA is piloting a mobile application for smartphones (VA Pain Coach) designed to provide tools to help patients set personal goals for pain management; track their symptoms, functioning, and self-care behaviors over time; and provide guidance on pain management strategies for patients and caregivers.
  - **Opioid Renewal Clinic at the Philadelphia VA Medical Center**—Primary care physicians refer at-risk patients to a pharmacist-run prescription management clinic, where an onsite pain nurse practitioner and a multispecialty pain team work together to stabilize the patient on an effective pain management plan before returning the patient to primary care management.

Abbreviations: CE = continuing education; DEA = Drug Enforcement Administration; REMS = Risk Evaluation and Mitigation Strategy; SPP = DOD Sole Provider Program; TMS = VA Talent Management System

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[i] Available at: http://www.aoa.gov/AoARoot/AoA_Programs/HPW/ARRA/PPHF.aspx

[ii] Available at: http://www.va.gov/PAINMANAGEMENT/VHA_Pain_Management_Strategy.asp

[iii] Available at: http://www.cdc.gov/homeandrecreationalsafety/overdose/research.html

[iv]Available at: http://www.usphs.gov/corpslinks/pharmacy/cpharm_creds.aspx

Inpatient Settings

In 2001, the Joint Commission developed standards for pain treatment to promote access to adequate pain management. In that context, The Joint Commission also identified opioids as an important cause of inpatient ADEs, with the most dangerous ADE being respiratory depression. The 2011 Joint Commission Sentinel Event Alert "Safe Use of Opioids in Hospitals" recommended improved assessment and management of pain to avoid accidental opioid overdose [20]. Accepted standards of care recommend a systematic approach to patient assessment and patient monitoring. Federal Agencies, including VA and DOD, have identified the following potential targets for reducing opioid ADEs: initiating patients on a high dose of opioids, converting between opioid formulations, and opioid dose titration. **Figure 21** outlines opportunities to advance ADE prevention strategies/tools in inpatient settings organized around the National Quality Strategy framework.

Figure 21. Opportunities for Advancing Opioid ADE Prevention Strategies/Tools, as Identified by the National Quality Strategy Priorities—Inpatient Settings

Safer Care	▪ Expand dissemination of evidence-based opioid guidelines/ protocols (e.g., dosing changes, management of high-risk individuals)
Patient and Family Engagement	▪ Promote patient education to improve the safety of care transition
Effective Communication and Coordination of Care	▪ Develop more optimal and integrated health IT opioid management tools ▪ Coordinate care through practices such as medication reconciliation and discharge counseling
Science-Driven Prevention and Treatment	▪ Promote systematic and coordinated care ▪ Promote safe practices at point of initiation of inpatient opioids ▪ Promote the use of evidence-based tools for morphine equivalent dose (MED) and transitions between formulations
Promotion of Best Practices Within Communities	▪ Use metrics to monitor the use of opioid safety "best practices" ▪ Promote the use of evidence-based guidelines for monitoring

Abbreviations: MED = morphine equivalent dose

Outpatient Settings

Opioid ADEs in outpatient settings are a multifaceted problem. Although the ADE Action Plan does not directly address the issue of misuse/abuse, it does advocate for steps to improve prescribing behaviors

to prevent patients who are prescribed opioids from abusing opioids. Although the factors driving opioid overdoses are not completely understood, a number of factors have been associated with increased risk for opioid overdose in the outpatient setting, based on varying degrees of evidence, and can serve as targets for outpatient opioid overdose prevention. These risk factors are: concomitant use of central nervous system (CNS) depressants (especially benzodiazepines) [14, 20, 21], high daily opioid dose [22, 23, 24, 25, 26], recent initiation of opioid therapy in treatment-naive patients [20, 27, 28], multiple opioid prescribers [14, 29], mental health disorder co-morbidities [14, 20, 21, 28, 30], medical co-morbidities (e.g., sleep apnea) [3], active or history of substance abuse [20, 21, 28, 29], aberrant medication-related behaviors [14, 28, 31, 32], and higher risk formulations (e.g., methadone) [33]. Federal Agencies can play an essential role in promoting evidence-based strategies to address opioid overdose risk factors and promote safe practices. **Figure 22** presents opportunities to advance ADE prevention strategies/tools in outpatient settings organized around the National Quality Strategy Priorities.

Figure 22. Opportunities for Advancing Opioid ADE Prevention Strategies/Tools, as Identified by the National Quality Strategy Priorities—Outpatient Settings

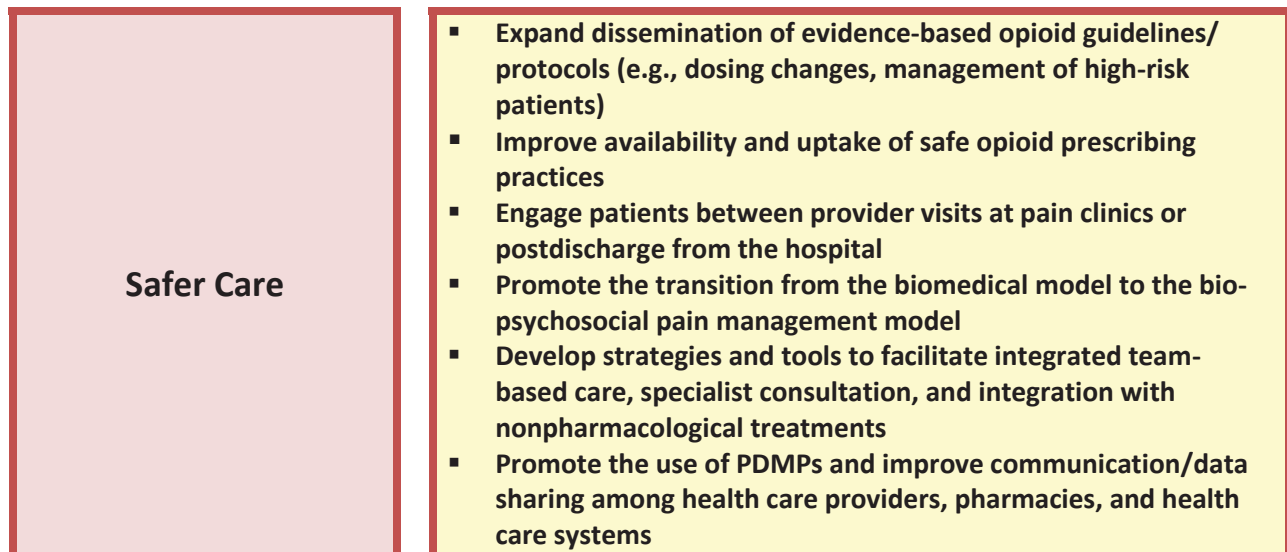| **Safer Care**	**Expand dissemination of evidence-based opioid guidelines/ protocols (e.g., dosing changes, management of high-risk patients)** **Improve availability and uptake of safe opioid prescribing practices** **Engage patients between provider visits at pain clinics or postdischarge from the hospital** **Promote the transition from the biomedical model to the bio-psychosocial pain management model** **Develop strategies and tools to facilitate integrated team-based care, specialist consultation, and integration with nonpharmacological treatments** **Promote the use of PDMPs and improve communication/data sharing among health care providers, pharmacies, and health care systems**

Figure 22. Opportunities for Advancing Opioid ADE Prevention Strategies/Tools, as Identified by the National Quality Strategy Priorities—Outpatient Settings (continued)

Patient and Family Engagement	▪ Develop and distribute patient education materials and strategies, using the principles of health literacy and theories of behavioral change ▪ Spread public health messages promoting safe opioid storage, use, and disposal, and not sharing opioids with friends or family ▪ Educate patients and their families to recognize early signs of dependence
Effective Communication and Coordination of Care	▪ Develop more optimal and integrated health IT opioid management tools ▪ Integrate opioid-specific targets into care transition models
Science-Driven Prevention and Treatment	▪ Promote systematic and coordinated care through strategies such as team-based care and medication reconciliation ▪ Promote the use of evidence-based strategies for managing risk factors associated with opioid overdoses ▪ Increase availability of mental health and substance use disorder treatment for patients on opioid therapy ▪ Promote the use of health IT tools to identify high-risk opioid prescribing practices
Promotion of Best Practices Within Communities	▪ Use metrics to monitor the use of opioid safety "best practices" ▪ Promote effective strategies identified by Federal Agencies that engage in patient care

Federal Agencies should explore ways to improve uptake of evidence-based strategies for safe opioid prescribing, including increased use of prescribing guidelines for chronic pain treatment and didactic provider training on opioid prescribing for both trainees and fully qualified clinicians (e.g., continuing education). More importantly, Federal Agencies should support training methods, interventions, and tools to encourage, model, and facilitate safe opioid prescribing.

Opioid prescribing guidelines for the treatment of chronic pain promote assessment of patient risk factors prior to initiating opioid therapy and recommend continued assessment of patient therapy goals and outcomes to determine the effectiveness and appropriateness of therapy. Prescribing guidelines also provide consensus-based strategies on how to reduce the risk for opioid ADEs. Knowledge of these strategies is necessary, although not sufficient for appropriate opioid prescribing; Federal Agencies should continue to work to educate clinicians on safe and appropriate opioid prescribing, and use available mechanisms to promote clinician education and effective behavior change. Federal Agencies

should work to develop, evaluate, and disseminate (1) training methods that include modeling, practice, expert collaboration, and/or feedback on real-patient cases (e.g., Project ECHO, Academic Detailing, expert consultation and mentoring); (2) interventions to identify and address high-risk cases (e.g., aberrant drug-related behavior or risk factor screening and intervention, high-risk patient treatment program, audit and feedback, or panel management systems); and (3) reminders and tools that guide clinicians in real time (e.g., computerized decision support systems, clinical reminders, dose determination tools).

Federal Agencies should promote patient-centered, multimodal, team-based care, from the health system level down to the clinician level, to personalize pain management, properly manage patients with high-risk medical and mental health co-morbidities, and intensively manage patients at high risk for opioid overdose.

Federal Agencies should promote evidence-based practices for pain management, including but not limited to opioid therapy. Federal Agencies should promote practices and services that identify and properly manage co-morbidities that increase the risk of opioid ADEs. This includes management of behavioral, mental health, and medical risk factors for unintentional and intentional opioid overdose and opioid abuse, as well as use of nonopioid pharmacological therapies and nonpharmacological therapies as part of an overall pain management plan. Currently, there is limited access to multimodal, evidence-based pain management and treatment of medical and psychiatric co-morbidities. Federal Agencies should promote access to evidence-based, multimodal, and interdisciplinary care for the management of chronic pain and co-morbidities. The Affordable Care Act provisions that support Mental Health parity may improve access to services that address mental health co-morbidities. Increased uptake of existing Health and Behavioral Assessment and Intervention CPT codes may also address this challenge.

Federal Agencies should develop and encourage the use of patient education materials and tools, in accordance with health literacy principles, to empower the patient to use opioids safely and encourage patient engagement.

Patients can play a major role in increasing the safe use of prescription opioids. To promote safe opioid use at home, patients should be educated about the safe and proper use of opioids for pain management, not sharing opioids, secure storage of opioids, and safe disposal of any opioids that are not used as part of therapy. Patient education materials, including materials the prescriber provides, should be developed using principles of health literacy to ensure that the patient understands the messages presented.

Patient education should also include ways to identify signs of misuse, abuse, dependence, and addiction, and to identify and treat an overdose. Federal Agencies should help develop, evaluate, and disseminate effective training, tools, and programs to provide patients with the skills and resources necessary to safely respond to moderate to severe pain and signs of misuse, abuse, and overdose, as well as to manage opioid therapy (e.g., medication take-back programs, overdose education and naloxone distribution programs, electronic tracking and reminder tools, suicide hotlines, and relaxation skills training).

Federal Agencies involved in patient care play an important role in assessing and promoting best practices for pain management and opioid safety.

BOP, DOD, IHS, and VA, all of which provide direct patient care, have taken steps to advance the practice of pain management and improve opioid safety. Because DOD and VA serve active-duty service members and military veterans who often have injuries requiring pain management, these agencies have been actively pursuing evidence-based pain management and systems to promote opioid safety. **Table 13** outlines the initiatives that are currently underway in VA and DOD systems and can be evaluated, modeled, and expanded to the private sector. DOD and VA have developed their own opioid prescribing guidelines for chronic pain [15] and have developed system-based methods to measure how the guidelines are followed and monitor trends associated with the use of opioid prescribing guidelines; however, prescriber adherence to the prescribing guidelines could be optimized with a system of continuous improvement. These agencies can serve as a model for the private sector as a system of continuous improvement and a system that promotes evidence-based pain management and evidence-based opioid ADE prevention strategies.

Table 13. Systematic Actions From VA and DOD Facilities for Safe and Effective Opioid Use for Pain Management

System	Action
Systematic Strategy	▪ **VA National Pain Management Strategy**—Outlines systematic strategies to improve pain management while maintaining opioid safety. ▪ **VA/DOD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain**—Provides evidence-based recommendations on when and how to effectively and safely use opioids for chronic pain.
Performance Measurement	▪ Structure measures—The VA Health Care Analysis and Information Group created and administered a survey assessing organization, policy, staffing, and availability of pain management services at health care facilities in 2010. ▪ Process measures—VA developed a set of administrative data-based metrics that assess facility-level adherence to key recommendations of the *VA/DOD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain*. ▪ Outcome measures—VA's electronic Mental Health Assistant makes validated assessments for patient outcomes available for use in the EHR, including the Pain Outcomes Questionnaire (POQ), West Haven Yale Multidimensional Pain Inventory (WHYMPI), and the Brief Pain Inventory (BPI).
Point-of-Care Clinical Management and Information Support	▪ **VA's ATHENA System**—Opioid system is a point-of-care decision support system to guide opioid management. ▪ VA inpatient tools for converting among different strengths/formulations of opioids. ▪ VA's Academic Detailing program uses clinical pharmacists and computerized panel management dashboards to work with primary care providers to address patient and clinical risk factors within their patient panel. ▪ VA's Opioid Safety Initiative uses performance metric-based reviews and feedback to identify and assist providers with elevated rates of clinical risk factors within their patient caseload. ▪ VA's SCAN-ECHO program links a community of primary care providers with pain specialists, using telehealth technology to provide co-management, consultation, and training on difficult patient cases.
Co-Morbidity Management/ Individualized Care	▪ Mental Health Assessment and Treatment—VA requires annual screening for depression, using the Patient Health Questionnaire (PHQ-2), and for posttraumatic stress disorder (PTSD) using the Primary Care—PTSD (PC-PTSD) screen with referral for additional assessment and treatment of positive cases.

Abbreviations: BPI = Brief Pain Inventory; EHR = electronic health record; PHQ-2 = Patient Health Questionnaire; POQ = Pain Outcomes Questionnaire; PC-PTSD = Primary Care Posttraumatic Stress Disorder Screen; PTSD = posttraumatic stress disorder; SCAN-ECHO = Specialty Care Access Network—Extension for Community Healthcare Outcomes; WHYMPI = West Haven Yale Multidimensional Pain Inventory

Incentives and Oversight

Current work of Federal partners is important for monitoring administrative prescription data to identify high-risk prescribing practices and eliminate fraud, waste, and abuse related to opioids.

Prevention of Opioid Adverse Drug Events in Medicare Part D

Effective January 1, 2013, CMS implemented a new policy in Medicare Part D, requiring plan sponsors to better address potential overutilization of opioids in their prescription drug benefit plans through improved drug utilization controls and case management. The goal of this policy is for Part D sponsors to reduce the overutilization of opioids among their enrollees. The policy, described in the Contract Year (CY) 2013 Final Call Letter on April 2, 2012, with supplemental guidance issued on September 6, 2012, includes a medication safety-focused approach, while maintaining beneficiary access to needed medications. Through implementation of the Part D opioid policy, overutilization of opioids can be identified and addressed, and related ADEs may be reduced.

As part of their opioid overutilization programs, for cases not addressed through improved prospective formulary management, Part D sponsors are expected to use retrospective drug utilization reviews (DURs) to identify at-risk beneficiaries and engage in case management with their prescribers. The policy permits appropriate claim controls on coverage of opioids for identified enrollees, including safety edits and quantity limits applied at point of sale (POS), with prescriber agreement or when prescribers are not responsive to case management. The suggested retrospective DUR methodology to identify beneficiaries who are at the highest risk for opioid ADEs is based on cumulative daily morphine equivalent dose (MED) across all opioids used by the beneficiary for chronic pain and accounts for the beneficiary's use of multiple prescribers and pharmacies. The guidance also addresses data sharing among Part D plan sponsors when a beneficiary for whom an individual claim control has been implemented to prevent Part D coverage of unsafe dispensing of opioids, moves from one Part D plan to another.

CMS will monitor the implementation of the new opioid policy by Part D sponsors and perform an interim evaluation of its impact in 2014. Although not a requirement in the Final Call Letter for Contract Year 2014, CMS strongly encouraged all sponsors to consider developing the ability to implement drug-level POS edits based on cumulative MED across the opioid class as soon as possible.

State Medicaid Drug Monitoring for ADEs in the Fee-for-Service Outpatient Pharmacy Program[i]

Pharmacy coverage is an optional benefit under Federal Medicaid law; however, all States currently provide coverage for outpatient prescription drugs to most enrollees within their Medicaid programs. The Medicaid prescription drug programs include the management, development, and administration of systems and data collection necessary to operate the Medicaid Drug Rebate program, the Federal Upper Limit calculation for generic drugs, and the DUR Program.

The Medicaid DUR Program promotes patient safety through State-administered utilization management tools and processes. The State Medicaid agency's electronic monitoring system screens prescription drug claims to identify problems, such as therapeutic duplication, drug–disease contraindications, incorrect dosage or duration of treatment, drug allergy, and clinical misuse or abuse, in order to minimize ADEs. DUR involves ongoing and periodic examination of claims data to identify patterns of medically unnecessary care and implements corrective action when needed.

Federal partners should expand monitoring of administrative prescription data to identify high-risk prescribing practices and eliminate fraud, waste, and abuse related to opioids.

Opportunities to advance the prevention of opioid ADEs through incentives and oversight-based strategies are summarized in **Figure 23**. Incentive and oversight levers that could advance opioid ADE prevention fall into three categories: (1) health care quality measures that are utilized in such programs as CMS value-based purchasing incentive programs (e.g., EHR Meaningful Use Incentive Program, Hospital Pay-for-Reporting, Inpatient Prospective Payment System); (2) reimbursement or coverage of services; and (3) identification of inappropriate opioid prescribing, fraud, and abuse through payor data. Although the FIW recommendations address the public payor perspective, the opportunities identified may also influence private sector advancements in this area, allowing for private payors to learn from successful public sector strategies.

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[i] Detailed information on the Medicaid DUR program, along with reports the States submit annually on the operation of their programs can be found at: http://medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Benefits/Prescription-Drugs/Drug-Utilization-Review.html

Figure 23. Federal Interagency Workgroup Recommendations for Actions That Can Potentially Advance Health Care Policy Strategies for Opioid ADE Prevention

Actions That Can Potentially Advance Health Care Policy Strategies for Preventing Opioid ADEs

Inpatient Settings

- Expand national health care quality reporting measures to include concepts related to multidisciplinary, systematic, and coordinated models of care.
- Develop and validate health care quality reporting measures that can be used to assess safe opioid prescribing and appropriate monitoring in the inpatient setting.

Outpatient Settings

- Address payment/coverage barriers to uptake of evidence-based, high-quality ADE prevention strategies and multimodal, team-based pain management.
- Expand national health care quality reporting measures to include ones *specific* to opioid ADE prevention through validated process measures that identify high-risk practices.
- Use administrative data from public and private payors and State PDMPs to identify high-risk patients and high-risk prescribers contributing to misuse/abuse and fraud.

Transitions of Care/Coordinated Care

- Address barriers to more integrated pain management.

Abbreviations: ADE = adverse drug event; PDMP= Prescription Drug Management Program

Health Information Technology (Health IT)

Federal Agencies that develop, promote, and incentivize EHR standards play an important role in advancing health IT–based strategies for inpatient opioid ADE prevention.

EHRs can serve an important role in providing patient-specific information that is necessary for making appropriate clinical decisions by providers. EHRs can also support the use of clinical decision support (CDS) to identify appropriate starting doses and MEDs between different opioid formulations to help clinicians safely transition between opioid formulations and identify appropriate doses. EHRs can also provide clinical reminders and templates to prompt and facilitate recommended clinical practices, and might improve assessment, documentation, and collaborative treatment planning for patient risk factors and aberrant behaviors.

The FIWs for ADEs proposed EHR (Stage 3) MU electronic clinical quality measures for EHRs that can potentially advance opioid ADE prevention.

Health care quality measures are important in helping to advance opioid ADE prevention efforts. In June 2013, the FIW for Opioid ADEs recommended a set of measure considerations to the Quality Measures Workgroup of the Health Information Technology Policy Committee. That committee, convened by the HHS ONC, makes recommendations for candidate measures for the Stage 3 EHR MU requirements. This will potentially support and advance opioid ADE prevention and monitoring for consideration in Stage 3 of the MU Incentive Program. These recommendations are summarized in **Table 14**. The recommendations are strictly for data collection purposes, to help clinicians and researchers gain a better understanding of the potential risk factors associated with opioid ADEs. There are currently no nationally endorsed metrics for opioid ADEs. As a result, the proposed recommendations were developed *de novo* or are based on VA-specific measures and require further development and validation as a tool for reducing opioid ADEs. After initial recommendation, measures under consideration are submitted to CMS for further review, development, and testing. Final measure acceptance is dependent on rigorous and complete internal and external public reviews.

The outpatient metrics detailed in **Table 14** targeted long-term opioid use for chronic pain and are modeled after measures that are currently in use by VA to measure adherence to the *VA/DOD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain*.

Table 14. Measure Considerations for EHR (Stage 3) MU Requirements That Can Potentially Advance Opioid ADE Prevention, as Proposed by the Federal Interagency Workgroup for Opioid ADEs

Metric	Description and Justification
Outpatient Clinical Quality Measure Concepts	
Patients on high daily dose of long-term opioid therapy	▪ There is an association between high daily dose of opioids and opioid ADEs, which requires further study to understand the impact on clinical practice.
Patients co-prescribed long-term opioid therapy and CNS depressants	▪ Co-prescribing of opioids with CNS depressants, especially benzodiazepines, is associated with opioid overdose deaths.
Patients on long-term opioid therapy given a toxicology screen prior to initiating therapy and at least once a year while on long-term opioid therapy	▪ All guidelines recommend assessment of risk related to substance abuse prior to initiating opioids and while patients are on therapy.
Patients on long-term opioid therapy who were checked in to the relevant Prescription Drug Monitoring Program prior to initiating therapy and at least every year if on chronic opioid therapy	▪ Guidelines recommend monitoring PDMPs when available. ▪ Early data show that PDMPs may be effective, although more research will be necessary as PDMPs continue to be developed and used.
Patients on long-term opioid therapy who have evidence of a written opioid care management plan	▪ All guidelines recommend that patients starting on long-term opioid therapy have an opioid care management plan that identifies the goals of therapy and the expectations for the patient.
Number of patients on long-term opioid therapy who have evidence of mental health assessment	▪ All guidelines recommend assessment for mental health disorders prior to initiating opioids, and treatment as appropriate.
Number of patients in facility or practice prescribed opioids	▪ Numbers are based on a VA measure that is used to compare prescribing rates across facilities.
Inpatient Clinical Quality Measure Concepts	Blank
Opioid-naive patients started on high-dose opioids in the inpatient setting	▪ Inappropriate prescribing is a significant problem that can lead to opioid overdose in the inpatient setting, especially in high-potency formulations.
Clinical Decision Support (CDS) Rule Concepts	
Clinical decision support rules to support all measure concepts	▪ There should be supporting clinical decision support to promote best practices and improve measured processes.

Abbreviations: ADE = adverse drug event; CNS = central nervous system; IV = intravenous; PCA = patient-controlled analgesia; PDMP = Prescription Drug Monitoring Program

Research (Unanswered Questions)

There remain a number of unanswered questions related to the prevention of opioid ADEs. As a result, there is a great opportunity for impact through research. Federal resources can play a pivotal role in

addressing research questions that can advance opioid safety and improve overall pain management. These are summarized in **Figure 24**.

Figure 24. Federal Interagency Workgroup Recommendations for Actions That Can Potentially Advance Research Strategies for Opioid ADE Prevention

Actions That Can Potentially Advance Research Areas for Opioid Safety

Clinical Science Domain

(CDC, AHRQ, FDA, NIH, public–private sector collaborations)

- Evaluate the effectiveness of prevention strategies (e.g., UDS, maximum doses, opioid agreements, single opioid prescriber) that are recommended in opioid prescribing guidelines.
- Improve standardization and coordination of surveillance systems addressing opioid ADEs.
- Promote standardized definitions/criteria for aberrant behavior, misuse, abuse, and adverse events to compare results across studies, settings, and health systems.
- Study real-world management of patients identified as high risk for opioid ADEs (e.g., promote the establishment and use of voluntary patient registries).
- Evaluate the clinical outcomes of using PDMPs and the effects on prescribers and patients.
- Develop strategies to better coordinate care and improve data sharing between settings.

Clinical/Laboratory/Bench-Top Science Domain

(CDC, NIH, public–private sector collaborations)

- Research biochemical and genetic mechanisms for the etiology of chronic pain.
- Fund and coordinate a comprehensive evaluation of the safety and efficacy of long-term opioid therapy for chronic pain through high-quality randomized controlled clinical trials supplemented by data collected from clinical care.
- Research risk factors associated with ADEs to define high-risk prescribing practices and identify patients at risk for opioid ADEs.
- Examine emerging pharmacogenomics related to hypermetabolizers of opioids.
- Pursue innovative drug development for abuse resistant opioid formulations and nonopioid drugs for refractory pain.
- Evaluate the effectiveness of and adopt adjunctive and behavioral modalities that augment pain therapy and reduce opioid use for chronic pain.

Abbreviations: ADE = adverse drug event; PDMP = Prescription Drug Monitoring Program; UDS = urine drug screen

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