Adverse Drug Event Prevention: Diabetes and Opioids
This *National Action Plan for Adverse Drug Event Prevention* (ADE Action Plan) seeks to engage all stakeholders in a coordinated, aligned, multisector, and health-literate effort to reduce the ADEs that are most common, clinically significant, preventable, and measurable. The ADE Action Plan identifies the Federal Government’s highest priority strategies and opportunities for advancement, which will have the greatest impact on reducing ADEs. Implementation of these strategies is expected to result in safer and higher quality health care services, reduced health care costs, informed and engaged consumers, and ultimately, improved health outcomes.

The Office of Disease Prevention and Health Promotion (ODPHP), in conjunction with the Federal Interagency Steering Committee and Workgroups for ADEs, led the development of the ADE Action Plan. Specifically, representatives of as many as 13 Federal Agencies and non-Federal subject matter expert consultants contributed to the ADE Action Plan, to draw attention to ADEs as a major patient safety and public health issue.

The ADE Action Plan provides Federal Agencies and external stakeholders with a framework to identify strategies and select specific actions to take. The intended end users of the Action Plan are policymakers, health care professionals, public and private sector organizations, and communities that can organize and take action toward preventing high-priority ADEs.

The ADE Action Plan is organized into seven sections. The first four sections outline the scope and development of the ADE Action Plan, identify Federal surveillance resources to measure and monitor the burden of ADEs, describe overall prevention approaches by identifying key determinants of ADEs, and review incentives and oversight opportunities to prevent ADEs. The next three sections of the ADE Action Plan address in detail the high-priority ADE targets (anticoagulants, diabetes agents, and opioids) that are the focus of the ADE Action Plan, highlighting the most pertinent actions to potentially advance each of the areas of surveillance, evidence-based prevention tools, incentives and oversight, and research (unanswered questions), as well as the role of health information technology (health IT) in advancing these efforts. Some of these sections provide recommendations or information that informs other areas. The final section presents conclusions and outlines next steps.
Adverse Drug Events: Magnitude of the Problem

ADE Prevention Is a Patient Safety Priority
An adverse drug event has been defined by the Institute of Medicine as “an injury resulting from medical intervention related to a drug” [1]. This broad term encompasses harms that occur during medical care that are directly caused by the drug including but are not limited to medication errors, adverse drug reactions, allergic reactions, and overdoses [1] [Figure 1]. A medication error is defined as “inappropriate use of a drug that may or may not result in harm;” such errors may occur during prescribing, transcribing, dispensing, administering, adherence, or monitoring of a drug [2,3]. In contrast, an adverse drug reaction (ADR) is “harms directly caused by a drug at normal doses” [3].

Figure 1. Terms Relevant to Drug-Related Harm [2]

A large majority of ADEs are preventable. In 2006, 82 percent of the United States population reported using at least one prescription medication, over-the-counter medication, or dietary supplement, and 29 percent reported using five or more prescription medications [4]. Among older adults (65 years of age or older), 57–59 percent reported taking five to nine medications and 17–19 percent reported taking 10 or more over the course of that year [4]. Given the U.S. population’s large and ever-increasing magnitude of medication exposure, the potential for harms from ADEs constitutes a critical patient safety and public health challenge.

ADEs can occur in any health care setting, including inpatient (e.g., acute care hospitals), outpatient, and institutional and noninstitutional long-term care (LTC) settings (e.g., nursing homes, group homes). The likelihood of ADEs occurring may also increase during transitions of care (e.g., discharge from a hospital to a nursing home or patients’ move from one health care provider or setting to another), when
information may not be adequately transferred between health care providers [5] or patients may not completely understand how to manage their medications [6, 7, 8].

In inpatient settings, research indicates that ADEs are among the largest contributors to hospital-related complications [9, 10]. It has been estimated that ADEs comprise one-third of hospital adverse events [9], affect approximately 2 million hospital stays annually [9, 11], and prolong hospital length of stay by approximately 1.7 to 4.6 days [11, 12, 13]. Data regarding how ADEs contribute to postdischarge complications or during other types of care transitions are lacking. One single-center study based in a tertiary care academic medical center identified ADEs as the most common cause of postdischarge complications occurring within 3 weeks of hospital discharge (accounting for two-thirds of postdischarge complications) [14]; in this study, 24 percent of postdischarge ADEs were judged to be preventable, and in another, similar study, 27 percent of postdischarge ADEs were judged to be preventable and 33 percent ameliorable [15]. In outpatient settings, nationally representative surveillance data indicate that ADEs account for more than 3.5 million physician office visits [16], an estimated 1 million emergency department (ED) visits [17], and approximately 125,000 hospital admissions each year [17]. An analysis of 2011 data indicated that ADEs were three times more likely to be present on admission than during the hospital stay [18].

The economic impact of ADEs has been inadequately studied. Older data indicate that ADEs impose a large financial burden on health care expenditures [12, 13]; one study estimated ADEs incurred $5.6 million (1993 USD) in excess hospital costs [12]. National estimates suggest that ADEs contribute an additional $3.5 billion (2006 USD) to U.S. health care costs [19]. Older adults experience the highest population rates of ADEs resulting in ED visits and are seven times more likely than younger persons to have an ADE that requires emergent hospital admission [16, 20]. Analysis of 2011 data indicated that Medicare beneficiaries are at the highest risk of acquiring an ADE during a hospital stay with Medicare reimbursing 75 percent of inpatient ADEs attributable to the most common medications [20]. These ED visits and hospital admissions from ADEs, a significant number of which are considered preventable, contribute to an enormously overburdened Medicare system [9].

**Focus on High-Impact Targets and Populations**

The *National Action Plan for Adverse Drug Event Prevention* focuses on common, clinically significant, preventable, and measurable ADEs. A key group of ADEs are particularly dangerous and largely preventable, and for these reasons, they are high-priority targets for national and local ADE prevention efforts.
Medication Classes Most Commonly Implicated in ADEs

In a nationally representative sample of hospitalized Medicare beneficiaries, the targets of the ADE Action Plan were identified as three of the most commonly implicated drug classes in ADEs: anticoagulants, opioids, and insulin [9]. Conservative estimates indicate that hospitalized patients experience 380,000 to 450,000 ADEs each year, with a large majority of these attributable to anticoagulants and opioids [17]. A large percentage of these ADEs were judged to be preventable.

In outpatient settings, national public health surveillance data indicate that a small group of key medication classes—those that are characterized by a narrow therapeutic index or require routine laboratory monitoring—cause the most outpatient medication-related harms [19, 21]. In a recent, nationally representative sample of hospital admissions for ADEs among older adults, an estimated two-thirds of admissions involved just four medication classes, three of which are preventable targets of the ADE Action Plan: anticoagulants (e.g., warfarin), insulin, and oral diabetes agents (e.g., sulfonylurea) [20]. A significant proportion of ADEs in this sample resulted from unintentional overdoses or supratherapeutic effects (e.g., bleeding due to excessive anticoagulation or hypoglycemia from excessive insulin administration) [20].

Most Vulnerable Populations

It is recognized that several patient populations may be especially vulnerable to ADEs, including the very young (pediatric patients), older adults, individuals with low socioeconomic status (SES) or low health literacy, those with limited access to health care services, and certain minority races or ethnic groups. To date, data commonly implicate age as a principle underlying risk factor for ADEs and suggest that older adults are particularly vulnerable to ADEs, likely owing to altered pharmacokinetics, polypharmacy, or cognitive decline [22, 23, 24]. For example, older adults comprise approximately 35 percent of all inpatient stays but contribute to approximately 53 percent of inpatient stays complicated by ADEs [Figure 2] [11]. Analyses of cost data indicate that Medicare-covered patients experience significantly higher rates of ADEs than both privately insured and Medicaid-covered patients. In the outpatient setting, national surveillance data indicate that older adults are two to three times more likely to have an ADE requiring a physician office or ED visit and seven times more likely to have an ADE requiring hospital admission [Figure 3] [19, 20]. The aging of the population and the vulnerability of older adults to ADEs will have significant implications for Medicare. In 2050, the number of Americans aged 65 and older is projected to be 88.5 million, more than double its population in 2010 of 40.2 million [25]. Spending in the United States for prescription drugs in 2010 was $259.1 billion and is expected to double
over the next decade [26]. Total expenditures on the Medicare Part D program alone in 2012 were $66.9 billion and are projected to reach $165.1 billion by 2022 [27].

**Figure 2. Hospital Stays Complicated by Adverse Drug Events, Distribution by Age [11]**

*2008 data analyzed from the Healthcare Cost and Utilization Project, AHRQ

**Figure 3. Rate of Ambulatory Visits for Adverse Drug Events, Distribution by Age [28]**

*2005–2007 data analyzed from the National Ambulatory Medical Care Survey and the National Hospital and Ambulatory Medical Care Survey, CDC
Underserved and Rural Communities

Any steps to reduce the incidence of ADEs should take into consideration the available resources of the health care provider, institution, and surrounding community. In underserved and rural communities, limited access to health care services, shortages of qualified health care personnel, slower adoption of electronic health records (EHRs), higher rates of older adults with chronic conditions, low health literacy, and reduced revenue may affect the successful implementation of approaches outlined in this document [29, 30].

Limited staff resources and slower adoption of EHRs affect current surveillance efforts, which rely on clinical chart abstractions. In a rural or underserved community, the health care provider may be forced to choose between dedicating time to patient care and investing time in reporting rates of ADEs. Even as the Nation moves toward a more seamless system for reporting these errors through the use of EHRs, underserved communities will be at a disadvantage, as EHR adoption rates continue to be higher within facilities with more financial resources, and rural communities continue to lag behind their urban counterparts [31, 32].

Implementing ADE prevention efforts requires extensive staff training, investment of financial resources, and coordination of providers—all of which may be challenging in communities where staffing is limited, providers are not located within the same geographic community, and financial resources are scarce [33]. In rural communities especially, coordination of medications across health care providers may be limited, as only generalists may be available in the community and prescribing specialists may be many miles away [34]. Rural and underserved communities may be less capable of taking advantage of advances in technology, such as the use of clinical decision support (CDS) in EHRs, and are less likely to have access to e-prescribing systems, which serve as a valuable tool to track inappropriate dosages, drug-drug interactions, and drug-allergy interactions.

The complexity of the care that pharmacists provide patients necessitates that patients should have access to the health care provider responsible for their care during all aspects of medication therapy. Although such local access is not always possible in low-volume, rural settings, leveraging technology to access remotely delivered care can result in both direct intervention and enhanced patient education. Provider involvement is crucial to supporting consumer engagement in shared decisionmaking regarding medication management. This may be more challenging within underserved and rural communities, as evidence suggests that individuals in rural communities and those with lower SES have lower health literacy [29].
Rural health care providers like critical access hospitals (CAHs) are not subject to some of the same reporting requirements and financial incentive programs as other providers. For example, although the majority of CAHs report quality measure information to the Centers for Medicare & Medicaid Services’ (CMS) Hospital Compare Web site, these hospitals are exempt from this requirement, which means that changes in CMS programs and policies may not have the same impact on some rural populations.

Finally, within underserved communities, there is a significant delay in the translation of research into practice [35]. Thus, even proven interventions or new findings related to reducing ADEs may take many years to benefit rural and underserved communities.

**Federal Interagency Steering Committee and Workgroups for ADEs**

***The Call for Action***

In 2010, the President signed the Patient Protection and Affordable Care Act (Affordable Care Act) into law, strengthening and modernizing health care [36]. One of the goals of the Affordable Care Act is to reduce the mounting health care costs that have put a strain on patients, employers, and our Federal budget. The U.S. Department of Health and Human Services (HHS) is responsible for implementing many of the health reform changes, including an objective aimed at improving health care quality and ensuring patient safety. In order to achieve this objective, HHS has developed several key strategies, two of which relate directly to ADEs:

- Reduce health care–associated infections, ADEs, and other complications of health care delivery through quality and safety promotion efforts.
- Establish the Partnership for Patients, a public–private partnership to help improve the quality, safety, and affordability of health care for all Americans.

In December 2011, the U.S. Senate sent a bipartisan letter to the Secretary of HHS requesting that the Department convene a Federal interagency task force to identify patients at risk for ADEs and opportunities to improve the care provided to patients at highest risk for ADEs. The letter specifically requested that the task force include in their considerations care transitions, the role of health IT, identification of existing and needed measures, and the impact of new Medicare reimbursement models. The ADE Action Plan specifically addresses each of these considerations.
In September 2012, in response to the heightened awareness of the contributions of ADEs to health care-related harms and costs, the Office of the Assistant Secretary for Health (OASH) marshaled the wide-ranging and diverse resources of Federal partners to form an extensive interagency partnership, the Federal Interagency Steering Committee [Appendix A], whose goal would be to develop a National Action Plan for ADE Prevention, to be modeled after the National Action Plan to Prevent Healthcare-Associated Infections [37].

**Structuring the ADE Action Plan**

Given the substantial breadth and depth of ADEs and the complexity in attempting to address the full scope of medication-related harms, the members of the Federal Interagency Steering Committee determined that the ADE Action Plan would focus on those ADEs that (1) account for the greatest number of measurable harms, (2) can be effectively measured, and (3) are considered largely preventable. Among the drug classes considered for the ADE Action Plan targets were: anti-infectives, antineoplastic agents, anticoagulants, insulin/oral diabetes agents, opioids, and benzodiazepines. Owing to the morbidity and mortality associated with their harms and their well-established amenability for prevention, the Steering Committee selected anticoagulants, diabetes agents (insulin and oral agents), and opioids as the three high-priority drug classes that would be initial targets for the ADE Action Plan.

Under the leadership of the Office of Disease Prevention and Health Promotion (ODPHP), the Federal Interagency Steering Committee established three separate Federal Interagency Workgroups (FIWs), each with a focus on one of the three high-priority drug classes. The FIWs initiated discussions to identify coordinated approaches to ADEs from these high-priority drug classes, specifically in the areas of surveillance, evidence-based prevention tools, incentives and oversight, and research (unanswered questions) [Figure 4]. In addition, each FIW considered health information technology (health IT) as a potential resource that could enhance the work in each of these areas.
The release of the ADE Action Plan should be viewed as only the beginning of a coordinated process that will result in stakeholders who are more engaged, aware, and knowledgeable of issues regarding the safe use of prescribed medications to prevent ADEs. Although the ADE Action Plan primarily reflects the efforts and resources of Federal Agencies, outlining ADE prevention goals and, more importantly, achieving ADE reductions and improving patient safety is neither complete nor feasible without further engagement of professional organizations. These include medical, nursing, pharmacy, and other allied health professionals; academia; consumer advocates; patients; and other private sector stakeholders. Consequently, the ODPHP, the Federal Interagency Steering Committee, and the FIWs for ADEs will continue to identify opportunities to engage these entities and gather their feedback. The goal is to use coordinated Federal partnerships, public and private sector collaborations, and aligned approaches to improve the quality and safety of health care, reduce health care costs, and improve the health and quality of life of millions of people in the United States. The Federal Interagency Steering Committee
anticipates that future iterations of the ADE Action Plan will provide both updates on progress in addressing the three high-priority ADE targets and expansion to other drug classes. Advances in surveillance systems will support the Federal Government’s ability to monitor the impact of Federal coordination, as well as nationwide progress in reducing ADEs.
Magnitude of the Problem

According to the CDC, diabetes mellitus affects 25.8 million people or 8.3 percent of the U.S. population [1]. In 2010, the national prevalence of diagnosed and undiagnosed diabetes mellitus among persons 20 years of age and older was estimated to be about 258 million persons, or 11 percent of all persons in this age range. For those 65 years of age or older, the prevalence of diagnosed and undiagnosed diabetes was estimated to be 10.9 million persons, or 27 percent of all persons in this age group. Among the 26 million individuals living with diabetes, it is estimated that 95 percent have type 2 diabetes. Patients with type 2 diabetes are at increased risk for serious long-term complications, such as cardiovascular disease and kidney disease [1]. Insulin and oral diabetes agents play an important role in controlling glycemic levels in patients with diabetes mellitus, thereby helping to prevent these complications. Among adults diagnosed with either type 1 or type 2 diabetes, 18 percent take insulin only, 13 percent take both insulin and oral medication, 50 percent take oral medication only, and 18 percent do not take either insulin or oral medication [1].

Recognizing that not all diabetes agents are associated with severe hypoglycemia (e.g., metformin monotherapy), this section of the ADE Action Plan will use the term “diabetes agents associated with serious hypoglycemia” to refer to insulin and secretagogue oral agents, predominantly sulfonylureas. Because of inconsistent definitions in the literature, the FIW for Diabetes Agents ADEs has chosen to use the term “serious hypoglycemia,” recognizing that this terminology does not represent Federal or agency perspectives. For the purpose of this Action Plan, “serious hypoglycemia” is defined as requiring third-party assistance (e.g., from a family member and/or medical personnel, or leading to an emergency department visit or hospital admissions) or blood glucose lower than 40 mg/dL, recognizing that there is a gradient of severity in these episodes (discussed further below).

The increasing burden of serious hypoglycemic events has been recognized as an important public health issue, potentially affecting millions of persons [2, 3, 4, 5, 6]. Historically, many but not all agencies
and organizations have emphasized “intensive” glycemic therapy (defined as attempting to achieve HbA1c values < 7 percent) as a goal for “most” persons with diabetes. However, an increase in rates of serious hypoglycemic events among patients in intensive control groups compared with those in generalized control groups has now been observed in several clinical trials, such as ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluations), ACCORD (Action To Control Cardiovascular Risk in Diabetes) and VADT (VA Diabetes Trial), which noted an increase in the rate of serious hypoglycemic events among patients in their intensive control groups compared with those assigned to the more generalized control group [7, 8, 9, 10, 11]. This occurred in the absence of significant health benefit. In a large health maintenance organization, the risk for hypoglycemia tended to be higher in patients with either near-normal or very poor glycemic control [12].

*Diabetes agents, including insulin and secretagogues, are common causes of hypoglycemic events across inpatient and outpatient health care settings.*

**Inpatient Settings**

In a nationally representative sample of Medicare beneficiaries hospitalized in 2008, hypoglycemia was identified as the third most common ADE [13]. Nearly all identified cases of hypoglycemia in this report were considered to be preventable. In other studies, clinically significant hypoglycemia (defined as <40 mg/dL) has been identified in 0.4 percent of non-ICU patient days, 1.9 percent of ICU patient days, and 2 percent to 5 percent of hospitalized patients with diabetes [14, 15, 16]. Hypoglycemia, defined as <50 mg/dL, was reported to account for 2.8 percent of patient days, 1.8 percent of hospitalized days, and 7.7 percent of admissions across three separate studies [17, 18, 19]. In addition, on the basis of 25,145 hospital visits in the 2004 Medicare Patient Safety Monitoring System (MPSMS) sample, an estimated 10.7 percent of patients exposed to insulin or oral diabetes agents experienced an ADE [20].

The Institute for Safe Medication Practice (ISMP) has identified insulin as an inpatient high-alert medication [21]. Data indicate that approximately one-quarter of all patient safety incidents involving insulin resulted in patient harm, and insulin may be implicated in 33 percent of medication error–related deaths [21, 22, 23, 24, 25, 26]. Insulin-related medication errors have been reported across all units of the hospital and can occur at multiple stages of the medication use process, with the majority of errors occurring at the time of prescribing and administration [21, 22, 23, 24, 25, 26].
Outpatient Settings

Diabetes agents (i.e., insulin and oral agents) are among the most common medication classes resulting in U.S. emergent hospitalizations for ADEs [27]. Between 2007 and 2009, among persons older than 65 years of age, insulin was implicated in an estimated 13.9 percent of emergent hospitalizations and oral agents were implicated in 10.7 percent of U.S. emergent hospitalizations annually [27]. From 1999 to 2010, preliminary data indicate that rates of hospital admissions for hypoglycemic events among Medicare beneficiaries increased by 22.3 percent while the rates of hospital admissions for hyperglycemia significantly decreased [27]. However, these data may underestimate the magnitude of the problem, as most hypoglycemic episodes are often treated outside of the emergency department or hospital setting [28]. In a survey of persons with diabetes from a large HMO, the self-reported rate of serious hypoglycemia (i.e., needing third-party assistance) in the year prior to the survey was 30 percent for insulin, 9 percent for secretagogues, and 6 percent for other non-hypoglycemic medications [29, 30]. In addition, studies have shown that higher frequencies of severe/serious hypoglycemic events were associated with lower socioeconomic status, duration of the disease, and depression [31, 32, 33].

Long-Term Care (LTC) Settings

CMS data indicate that approximately 33.4 percent of individuals receiving services in a certified nursing home have either type 1 or type 2 diabetes [34]. Recent data regarding the burden of hypoglycemic events among individuals residing in LTC facilities are not available. However, the primary risk factors for hypoglycemia (e.g., advanced age, recent hospitalization, and polypharmacy) are highly prevalent among nursing home residents [35, 36].

National surveillance data for hypoglycemia need to better distinguish between serious and minor hypoglycemic events.

The American Diabetes Association (ADA) defines serious hypoglycemia as a situation requiring help from a third party (e.g., by family member, paramedic, or emergency department personnel) [31]. The ADA has also defined documented symptomatic hypoglycemia as an event during which typical symptoms of hypoglycemia are accompanied by a measured plasma glucose concentration ≤70 mg/dL. In contrast, mild or minor episodes are classified as events that are self-treated [31]. In clinical care, hypoglycemic events in patients with diabetes may be defined as an abnormally low plasma glucose concentration that exposes the individual to potential or actual harm [32, 37]. However, these definitions have not been consistently utilized in published studies. Thus, the incidence of hypoglycemia reported in the literature is varied, and incidence in those at highest risk for these events is unknown [32, 37].
Surveillance

Federal partners should promote efforts to collect accurate and timely data to more effectively measure burden and trends of hypoglycemic events.

Currently, a limited number of Federal surveillance systems have the capacity to assess the national scope of hypoglycemic events associated with diabetes agents. Examples of these systems are summarized in Table 8. Despite availability of these systems, several challenges remain in identifying hypoglycemic events associated with diabetes agents. First, definitions for hypoglycemia are variable, making comparisons of results among surveillance systems and the literature difficult. Second, many existing Federal and private sector health systems do not have sufficiently integrated data systems that can provide the comprehensive information necessary to identify persons at risk for hypoglycemic events and enable precise categorization of numerators and denominators across the continuum of care. Third, existing surveillance metrics may need to be revisited to ensure accuracy, reliability, and clinical relevance consistent with current medical knowledge. Finally, the accuracy of diagnostic and procedural codes (International Classification of Disease [ICD] codes, including External Causes of Injury [E-codes]) for identifying hypoglycemic events need to be further evaluated; the limited data that are available, however, suggest an algorithmic approach to use of such codes is necessary to reliably capture hypoglycemic events associated with diabetes agents [38]. The development of more robust EHR systems can potentially support the creation of new clinical quality measures and decision support tools to facilitate improvements in the identification and management of patients with hypoglycemia.

Table 8. Summary of Metrics Related to Diabetes Agent ADEs (Hypoglycemia), Collected by Federal Surveillance Systems

<table>
<thead>
<tr>
<th>Geographic Scope</th>
<th>Data Collection Methods</th>
<th>Diabetes Agent ADE or Management Metrics: Inpatient Setting</th>
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<tr>
<td>National ADE Incidence</td>
<td>Administrative claims and/or EHR data</td>
<td>AHRQ (HCUP):*&lt;br&gt;- Inpatient stays with ICD-9-CM (962.3) codes and E-codes (E932.3)</td>
<td>FDA (Sentinel Initiative, Mini-Sentinel): **&lt;br&gt;- ED visits, hospitalizations for hypoglycemic events</td>
</tr>
<tr>
<td>National ADE Incidence (+/-Rates)</td>
<td>Medical record review</td>
<td>AHRQ (MPSMS): ***&lt;br&gt;- Inpatient stays with combination of laboratory triggers (e.g., glucose ≤50 mg/dL or glucose ≤70 mg/dL but &gt;50 mg/dL) and clinical triggers (e.g., administrations of D50)</td>
<td>CDC (NEISS-CADES):&lt;br&gt;- ED visits, emergent hospitalizations for laboratory abnormalities, hypoglycemic events as diagnosed by clinicians, and documented in medical record narrative</td>
</tr>
<tr>
<td>National ADE Incidence</td>
<td>Administrative data and survey data</td>
<td>Not available</td>
<td>AHRQ (NEDS):&lt;br&gt;- Derived from AHRQ’s State ED databases and from State inpatient database&lt;br&gt;- Used to estimate number of events (i.e., numerator data)</td>
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Table 8. Summary of Metrics Related to Diabetes Agent ADEs (Hypoglycemia) Collected by Federal Surveillance Systems (continued)

<table>
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<tr>
<td>National-, Regional-, Facility-level Spontaneous Reports</td>
<td>Voluntary reporting</td>
<td><strong>DOD (Patient Safety Reporting System)</strong>&lt;br&gt;- Any clinician-diagnosed or patient-reported ADEs&lt;br&gt;- <strong>FDA (FAERS):</strong>&lt;br&gt;- Any clinician-diagnosed or patient-reported ADEs&lt;br&gt;- <strong>VA (VA ADERS):</strong>&lt;br&gt;- Any clinician-diagnosed or patient-reported ADEs</td>
<td><strong>DOD (Patient Safety Reporting System)</strong>&lt;br&gt;- Any clinician-diagnosed or patient-reported ADEs&lt;br&gt;- <strong>FDA (FAERS):</strong>&lt;br&gt;- Any clinician-diagnosed or patient-reported ADEs&lt;br&gt;- <strong>VA (VA ADERS):</strong>&lt;br&gt;- Any clinician-diagnosed or patient-reported ADEs</td>
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<tr>
<td>Regional-/Facility-level ADE Incidence (+/- Rates)—Quality Improvement</td>
<td>Administrative claims and/or EHR data</td>
<td><strong>IHS (Resource and Patient Management System [RPMS-EHR]):</strong>&lt;br&gt;- Adverse Reaction Tracking (ART) System entry related to a diabetes agent&lt;br&gt;- EHR entry in the Problem List of “hypoglycemia”&lt;br&gt;- <strong>VA (Integrated Databases):</strong>&lt;br&gt;- ADE identified by ICD-9-CM codes, primary hospitalizations, emergency department or clinic visits, and laboratory values (blood glucose, HbA1c). An algorithm has been developed and validated to identify hypoglycemia in VA patients.</td>
<td><strong>DOD (Pharmacovigilance Defense Application System):</strong>&lt;br&gt;- Outpatient clinic visits, ED visits, hospitalizations using relevant ICD-9-CM codes and/or CPT codes&lt;br&gt;- <strong>VA (Integrated Databases):</strong>&lt;br&gt;- ADE identified by ICD-9-CM codes, primary hospitalizations, emergency department or clinic visits, and laboratory values (blood glucose, HbA1c). An algorithm has been developed and validated to identify hypoglycemia in VA patients.&lt;br&gt;- <strong>IHS Resource and Patient Management System (RPMS-EHR):</strong>&lt;br&gt;- ART System entry related to a diabetes agent&lt;br&gt;- EHR entry in the Problem List or purpose of visit of “hypoglycemia”</td>
</tr>
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</table>

*ICD-9-CM 962.3 refers to “Poisoning by insulins and antidiabetes agents,” and E932.3 refers to “insulins and antidiabetic agents causing adverse effects in therapeutic use.”

**Currently, FDA Sentinel initiative covers more than 125 million lives; however, these do not constitute a nationally representative sample.

***In 2015, MSPMS will be replaced by the Quality and Safety Review System (QSRS).

**Abbreviations:** ADE = adverse drug event; ART = adverse reaction tracking; CPT = Current Procedural Terminology; D50 = 50 percent dextrose; ED = emergency department; EHR = electronic health record; HbA1c = hemoglobin A1c; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; mg/dL = milligrams per deciliter; NHIS = National Health Interview Survey
Federal partners should support use of standardized definitions of hypoglycemia and reporting of hypoglycemia in national surveys to advance surveillance efforts. Actions that can potentially advance surveillance strategies for ADEs from diabetes agents are summarized in Figure 13. National surveillance using population-based sampling or administrative claims data may be efficient ways of collecting nationally representative data on serious hypoglycemic events. These studies can provide estimates of the national burden. For example, CDC’s National Health Interview Survey (NHIS), a cross-sectional household survey of noninstitutionalized civilians in the United States, contains questions about diabetes status and treatment. NHIS may provide an opportunity for increased surveillance of hypoglycemic events on a population health basis. Questions related to the presence and frequency of hypoglycemic events could potentially be considered for incorporation into such national health surveys.

However, reducing ADEs requires individual providers and patients to act at the point of care. Federal Agencies that provide direct care to patients can go beyond retrospective approaches to implement proactive clinical approaches that utilize electronic health records (EHRs) and telehealth for identification and surveillance of patients who are at risk for hypoglycemia.
Figure 13. Actions That Can Potentially Advance Surveillance Strategies for Diabetes Agent ADEs

**Actions That Can Potentially Advance Surveillance Strategies for Diabetes Agent ADEs**

- **Address gaps in standard surveillance definitions for hypoglycemic events.**
  - Clearly define both severe/serious and mild hypoglycemic events.
  - When possible, confirm findings of surveillance data with medical record review to minimize opportunities for bias or misclassification.

- **Assess the adequacy of diagnostic and procedural coding for identifying hypoglycemic events.**
  - Assess specificity, sensitivity, PPV, and NPV of ICD and CPT codes for capturing hypoglycemic events.

- **Coordinate efforts across the Federal Government and the private sector to enhance inpatient monitoring of hypoglycemic events.**
  - Refine AHRQ Common Formats utilized by Patient Safety Organizations to include data on hypoglycemic events.
  - Identify whether existing national patient safety reporting systems (e.g., CDC’s National Healthcare Safety Network) could be used to facilitate inpatient tracking and monitoring of hypoglycemic events.

- **Improve availability and access to integrated EHR data with linked pharmacy, laboratory, and outcomes (e.g., admission–discharge) data at national and local levels.**

- **Improve efforts to collect additional information on hypoglycemic events within the ambulatory setting (e.g., events resulting in emergency department visits or hospitalizations).**
  - Consider utilizing surveys such as the Medicare Current Beneficiary Survey (MCBS), the National Health and Nutrition Survey (NHANES), and the National Health Interview Survey (NHIS) to collect population-based estimates of hypoglycemic events.

**Abbreviations:** ADE = adverse drug event; CPT = Current Procedural Terminology; EHR = electronic health record; ICD = International Classification of Diseases; MCBS = Medicare Current Beneficiary Survey; NHANES = National Health and Nutrition Survey; NHIS = National Health Interview Survey; NPV = negative predictive value; PPV = positive predictive value

**Evidence-Based Prevention Tools**

The American Diabetes Association (ADA) Standards of Medical Care in Diabetes and the ADA/American Geriatric Society (AGS) guidelines, as well as the Department of Veterans Affairs and Department of Defense (VA/DOD) guidelines, all interpret the scientific evidence as supporting individualization of
target glycemic goals based on life expectancy, co-morbid conditions, social support, and personal preference [39, 40, 41, 42]. The AGS, in the context of the American Board of Internal Medicine Foundation’s Choosing Wisely Campaign, has indicated that the use of medications other than metformin to lower HbA1c to <7.5 percent in most persons with type 2 diabetes aged 65 or older is not warranted [43]. This recommendation is based on the potential of harms (relative to that of benefit) noted when patients have major co-morbid conditions or limited life expectancy [43, 44]. Figure 14 identifies currently existing Federal resources that address diabetes management and that can potentially be leveraged to advance hypoglycemia prevention.

Figure 14. Federal Assets Related to Management of Diabetes Agents, as Identified by the National Quality Strategy Priorities

<table>
<thead>
<tr>
<th>Resources for Safer Care—Health Care Provider Knowledge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AHRQ:</strong></td>
</tr>
<tr>
<td>– Oral Diabetes Medications for Adults With Type 2 Diabetes: An Update—Provides a systematic review of all oral diabetes medications, including evidence about the risk of hypoglycemia</td>
</tr>
<tr>
<td><strong>BOP:</strong></td>
</tr>
<tr>
<td>– Management of Diabetes Clinical Practice Guidelines—Provides recommendations for the medical management of Federal inmates with diabetes</td>
</tr>
<tr>
<td><strong>DOD/VA:</strong></td>
</tr>
<tr>
<td>– Clinical Practice Guidelines for the Management of Diabetes—Provides structured framework to help improve patient outcomes, along with evidence-based guidelines and identification of outcome measures</td>
</tr>
<tr>
<td><strong>FDA:</strong></td>
</tr>
<tr>
<td>– Risk Evaluation and Mitigation Strategy—Mandatory risk management plans that use risk minimization strategies beyond professional labeling to ensure that benefits of medications outweigh their risks</td>
</tr>
<tr>
<td><strong>IHS:</strong></td>
</tr>
<tr>
<td>– Standards of Care and Clinical Practice Recommendations: Type 2 Diabetes—Provides guidance to clinicians and educators with regularly updated recommendations, useful clinical tools and resources, patient education material and a bibliography</td>
</tr>
<tr>
<td>– Diabetes Treatment Algorithms—Developed to provide clinicians with a quick reference based on national guidelines, these algorithms reflect a collaborative effort between Indian health system professionals. Cards can be accessed by mobile devices and/or printed for use in the clinical setting.</td>
</tr>
<tr>
<td>– Quick Guide Cards—Summarize important elements of care, including the importance of individualized target setting for HgA1c</td>
</tr>
<tr>
<td>– Advancements in Diabetes Seminars—Hour-long live virtual seminars that provide CME/CE credit and feature updates on appropriate treatment for patients with diabetes including practical tools</td>
</tr>
<tr>
<td><strong>NIH:</strong></td>
</tr>
<tr>
<td>– National Diabetes Information Clearinghouse—Information on diabetes blood tests</td>
</tr>
</tbody>
</table>
**Figure 14. Federal Assets Related to Management of Diabetes Agents, as Identified by the National Quality Strategy Priorities (continued)**

<table>
<thead>
<tr>
<th>Resources for Patients and Family Engagement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACL:</strong> Community organizations offer various programs that have been or are currently supported in part by Federal funds, such as</td>
</tr>
<tr>
<td>- <strong>Stanford Diabetes Self-Management Program</strong>—6-week program to help participants better manage their diabetes, including information about methods to deal with symptoms of hypoglycemia</td>
</tr>
<tr>
<td>- <strong>National Council on Aging Better Choices, Better Health-Diabetes</strong>—6-week online workshop to learn self-management techniques, including curriculum on hypoglycemia</td>
</tr>
<tr>
<td>- <strong>HomeMeds℠ Medication Management System</strong>—Multidisciplinary collaborative providing patient counseling, reassessment, and adjustment of medication regimens for older adults in various nonacute health care settings (e.g., home care)</td>
</tr>
<tr>
<td><strong>AHRQ:</strong></td>
</tr>
<tr>
<td>- <strong>Medicines for Type 2 Diabetes: A Review of the Research for Adults</strong>—Summary of research on benefits and possible side effects of diabetes agents to guide patients in discussions with their health care provider</td>
</tr>
<tr>
<td>- <strong>Premixed Insulin for Type 2 Diabetes: A Guide for Adults</strong>—Guide compares benefits, side effects, and costs of a newer type of premixed insulin with other kinds of insulin and pills for diabetes</td>
</tr>
<tr>
<td>- <strong>Methods for Delivering Insulin and Monitoring Blood Sugar: A Review of the Research for Children, Teens, and Adults With Diabetes</strong>—Discusses what research says about different ways to measure blood sugar and take insulin</td>
</tr>
<tr>
<td><strong>FDA:</strong></td>
</tr>
<tr>
<td>- <strong>Medication Guides</strong> (available for a variety of diabetes agents, including sulfonylurea-thiazolidinedione combination product)</td>
</tr>
<tr>
<td><strong>NIH:</strong></td>
</tr>
<tr>
<td>- <strong>What I Need to Know About Diabetes Medicines</strong>—Online resource which includes guidance on hypoglycemia</td>
</tr>
<tr>
<td>- <strong>Hypoglycemia</strong>—Resource defining hypoglycemia, potential causes, treatment, and prevention (available in National Diabetes Information Clearinghouse)</td>
</tr>
<tr>
<td>- <strong>National Diabetes Information Clearinghouse</strong>—Information on diabetes blood tests</td>
</tr>
<tr>
<td><strong>NIH/CDC:</strong></td>
</tr>
<tr>
<td>- <strong>Know Your Blood Sugar Numbers</strong>—Resource on how to test blood glucose level (produced by National Diabetes Education Program)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resources for Communication and Coordination of Care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AHRQ:</strong></td>
</tr>
<tr>
<td>- <strong>Project RED</strong>—Includes a number of medication-related strategies (e.g., active medication reconciliation, medication teaching for patients and caregivers, development of medication list for patients and their health care providers)</td>
</tr>
<tr>
<td><strong>NIH/CDC:</strong></td>
</tr>
<tr>
<td>- <strong>Helping the Child with Diabetes Succeed: A Guide for School Personnel</strong>—Resources for school personnel with guidance on preventing and treating hypoglycemia at school (produced by National Diabetes Education Program)</td>
</tr>
</tbody>
</table>

**Inpatient settings**

Appropriate glycemic control in inpatient settings requires a careful balance in managing the risks associated with both hyperglycemia and hypoglycemia. Target values for glycemic control recommended by the Federal sector and multiple private and public stakeholder agencies should be
individualized. Each patient would thus need an individual approach toward mitigating the risk of hypoglycemia. Uncontrolled hyperglycemia has been associated with poor outcomes in a dose/response relationship, and use of intensive insulin therapy has been associated with reductions in mortality in epidemiological studies and high visibility single-site randomized trials in ventilated ICU (mixed surgical and nonsurgical) patients [45]. However, these results were not replicated in a large, multicenter trial (the NICE-SUGAR study), in which serious hypoglycemia was increased in the intensive insulin therapy arm and associated with increased mortality [46]. Professional society-recommended upper-level glycemic targets in the ICU setting range from 150 mg/dL (Society of Critical Care Medicine) to 200 mg/dL (American College of Physicians). The strength of evidence for glycemic control in non-ICU settings is of low quality [47].

**Federal partners should facilitate the use of systems that enhance recognition and documentation of risk factors that contribute to inpatient hypoglycemic events.**

The risk for hypoglycemic events may be increased due to numerous hospital-, provider-, and patient-related risk factors and actual events can result from iatrogenic factors, especially related to administration of medications. There are a number of individual patient characteristics that may increase an individual’s likelihood of experiencing a hypoglycemic event, including low body mass index (BMI), cachexia, age, and congestive heart failure. Iatrogenic factors include using insulin and/or oral hypoglycemic agents too aggressively, inappropriately, or without sufficient followup in the hospital setting. Hypoglycemic events also can result if there are additional changes in a patient’s drug regimen that alter insulin resistance (e.g., treatment with corticosteroids) or the metabolism of hypoglycemic agents [48, 49, 50].

The use of insulin and oral diabetes agents, failure to adjust diabetes regimens in response to decreases in oral intake, and unexpected deviation from normal hospital routines have been identified as common risk factors in iatrogenic hypoglycemia [50]. Unexpected interruption of tube feedings or other sources of nutrition and failure to respond appropriately to an initial hypoglycemic event are also among the most common, and potentially most preventable, sources of iatrogenic hypoglycemic events. Studies have shown that more than 40 percent of patients who experience one iatrogenic episode go on to suffer at least one additional distinct hypoglycemic event that is largely preventable [50]. It is critical that clinical judgment, not metrics, guide medication administration and glycemic targets for individual patients.
Effective prevention of inpatient diabetes agent adverse events requires multidisciplinary coordination.

A systematic approach is essential to promoting the safe and appropriate use of insulin in inpatient settings. Medication errors can occur at multiple stages in the medication process. Therefore, information should be shared across all health care providers and shifts. This includes documentation of all nutritional intake, coordination of meal time/blood glucose testing, as well as any changes in normal routine (e.g., reduced dietary intake or use of parenteral nutrition). The use of an EHR, as well as the use of order sets and medication protocols, can support templates for tracking this information. Clear documentation of any initial event is important to support coordination across all inpatient health care providers, as is the sharing of template order sets such as those in use by the VA [51]. For ICU patients in the VA, this dashboard reports quarterly the proportion of patient days on a hypoglycemic agent with any hypoglycemic event (glucose ≤45 mg/dL and/or ≤60 mg/dL) and the proportion of patients on hypoglycemic agents with a mean glucose >180 mg/dL, as well as risk-adjusted outcomes [52, 53]. These efforts are supported by shared resources, including the VA/DOD guidelines, template order sets to manage hyperglycemia and hypoglycemic events, references, a special section on reducing hypoglycemic events, and other educational materials. Similarly, efforts to reduce inadvertent interchanges between medications that are commonly mistaken for one another (e.g., U-500 and U-100 insulin) can enhance prevention efforts by ensuring that medications that may look alike or sound alike are clearly labeled and stored separately [21, 22, 23, 24, 25, 26, 45, 46, 48, 49, 50, 54, 55].

Efforts are underway to evaluate effectiveness of implementing specific strategies to reduce the prevalence of hypoglycemic events in inpatient settings.

One CMS-funded effort, the Partnership for Patients (PfP) Initiative, is currently testing the scaling of prevention strategies for hypoglycemic event prevention in inpatient settings. A multiphase approach with the following elements was used with the aim of decreasing hypoglycemic events:

- Adopting a basal/bolus insulin protocol
- Instituting a nurse-driven protocol for hypoglycemia
- Ensuring the coordination of mealtime blood glucose testing, insulin administration, and meals

Other opportunities for advancing diabetes agent ADE prevention strategies/tools in inpatient settings are summarized in Figure 15.
### Figure 15. Opportunities for Advancing Diabetes Agent ADE Prevention Strategies/Tools, as Identified by the National Quality Strategy Priorities—Inpatient Settings

#### Patient and Family Engagement
- **Individualized target setting**
  - Acknowledgment of patient risk factors (e.g., BMI, cachexia, age, CHF, advanced malignancy, renal or liver disease)
  - Understand iatrogenic factors (e.g., nutritional intake, patient compliance, regimen change)
- **Educate patients on any self-management implications of changes to insulin regimen using teach back method**
- **Educate patients on use of products for treating low blood glucose, including over-the-counter products [56]**
- **Provide hypoglycemia diabetes patient education materials**
- **Understand patient adherence with medication and diet regimen and daily barriers that patients encounter**
- **Consider the use of a standardized process to assess individual patient need for devices for self-administration in the event of an urgent or emergent hypoglycemic event [57]**

#### Effective Communication and Coordination of Care
- **Multidisciplinary coordination and collaborative health care professional partnerships (including hospitalists, endocrinologists, nurses, pharmacists, and dietitians) throughout the medication process [58, 59, 60, 61, 62]**
- **Education of health care professionals on the importance of effective communication and coordination of care**
- **Engagement with pharmacists, nurses, dietitians, and other health care professionals at the time of discharge**
- **Minimize fragmentation of medical care**
- **Support development of tools that facilitate**
  - Improved prescribing of diabetes agents to minimize the potential for medication errors
  - Improved identification of root causes of hypoglycemic events
  - Improved patient compliance to/adherence with medication/diet and daily barriers that patients encounter
Figure 15. Opportunities for Advancing Diabetes Agent ADE Prevention Strategies/Tools, as Identified by the National Quality Strategy Priorities—Inpatient Settings (continued)

**Science-Driven Prevention and Treatment**

- Consider individual patient characteristics in selecting diabetes agents and glycemic targets
- Use protocols to
  - Assess risk during initial evaluation
  - Reassess risk periodically
- Assess cause of prior events
- Support development of standardized tools for insulin administration (e.g., insulin infusion protocols)
- Ensure consistency in order sets
- Use standardized, evidence-based order sets (avoid free text)
- Conduct root cause analysis of hypoglycemic events when appropriate
- Capture critical information associated with hypoglycemic events at admission or discharge:
  - Prior history of hypoglycemic episodes
  - Past diabetes medication management
  - Level of glycemic control
  - Assessment of patient’s cognitive abilities, literacy level, visual acuity, dexterity, cultural context, and financial resources for acquiring outpatient diabetic medications and supplies

**Promotion of Best Practices Within Communities**

- Encourage multidisciplinary care coordination [31, 44]
- Consider individual patient circumstances (e.g., cognition, life expectancy, sedation) [31]
- Ensure professional supervision during any medication changes

Abbreviations: BMI = body mass index; CHF = congestive heart failure

**Outpatient Settings**

Because of the complexity of the patient population comprising those at highest risk of experiencing hypoglycemic events (e.g., older persons), the FIW reviewed several conceptual models to help guide the development of the strategic framework. Of the models reviewed, the most influential and comprehensive is the Chronic Care Model, which uses a systematic approach to restructuring medical care to create partnerships between health systems and communities [63, 64, 65]. To improve chronic care, the model includes system requirements for health care organizations, community resources, self-management support, delivery design, decision support, and clinical information.
Shared decisionmaking, which engages the patient, families, and other designated individuals in disease management, is an essential element of ongoing care. In order to participate in decisions related to the patient’s illness in the context of his or her belief systems and culture, he or she must have sufficient information and must clearly understand it. Patients need to be both informed and engaged. As such, health care provider education should emphasize cultural competency, health literacy/numeracy, shared decisionmaking practices, and motivational interviewing [39, 63, 64, 66].

A key element of any strategy to reduce the risk of hypoglycemic events is recognizing the importance of existing co-morbid conditions that may affect adherence and risk of medication side effects, as well as physical function and quality of life. Type 1 diabetes and type 2 diabetes are chronic diseases. Management for the broad categories of diabetes will not be the same for everyone because of the differences in underlying etiology and the demographics of the affected populations, as well as the length of time from when the patient was diagnosed with diabetes. Co-morbid conditions are more common in patients with type 2 diabetes, particularly as they age [65, 67, 68, 69]. According to the Medical Expenditure Panel Survey (MEPS), most adults with diabetes have at least one co-morbid chronic disease and as many as 40 percent have at least three [69, 70, 71, 72]. Finally, throughout the aging process, individuals are at increased risk for co-morbid disease independent of diabetes [65, 67, 68, 69], which may complicate diabetes management and increase morbidity and mortality.

Self-management of hypoglycemia occurs almost exclusively in the ambulatory care setting. Management of hypoglycemic events in the home, school, workplace, and long-term care settings may reduce subsequent events that require emergency department visits or hospitalizations. Patient self-management may be affected by co-morbidities. Impaired renal function can prolong the half-life of insulin and alter sulfonylurea degradation, resulting in increased incidence of hypoglycemic events. Cognitive impairment adversely affects patients’ ability to self-manage their diabetes and is associated with cardiovascular morbidity and mortality. Depression may also pose significant barriers to appropriate diabetes control by affecting the ability to maintain a healthy lifestyle, including exercise, good dietary habits, and adherence to a prescribed regimen [73, 74].

Federal partners should facilitate prevention efforts that are based on a patient-centered approach.

To date, outpatient prevention tools for hypoglycemic events have not explicitly recommended a comprehensive assessment of chronic co-morbid conditions as major contributing risk factors for hypoglycemia, in addition to social and educational factors. Use of a framework that identifies
contributing social determinants, as well as medical and mental health risk factors, can permit the
development of individualized approaches to glycemic targets, medication side effects (including but not
limited to hypoglycemia), and social and educational support.

Federal and private sector professional guidelines recommend educating patients, families, and
caregivers regarding the parameters for diabetes medications, including timing with meals and activities,
identifying blood glucose levels that require immediate provider notification, as well as blood glucose-
level patterns that require notification on a more routine basis [31, 39, 40, 66]. National and
international organizations such as The Joint Commission and the World Health Organization have
developed guidelines to prevent ADEs associated with the use of look-alike, sound-alike medications
[70, 71, 72]. Look-alike, sound-alike medications were identified as a National Patient Safety Goal
(NPSG) by The Joint Commission and the Institute for Safe Medication Practices (ISMP) in 2005. For
example, the NPSG identified that HumaLOG has been confused with HumaLIN. Organizations such as
the ADA, The Joint Commission, and the ISMP have identified a number of recommendations for the
care of older adults with diabetes to prevent hypoglycemic events [31, 44]. The National Diabetes
Educational Program, jointly led by the National Institutes of Health and the Centers for Disease Control
and Prevention, has also developed resources specifically for children and teens with diabetes [75, 76].

The most recent private sector and Federal guidelines recommend individualized targets based on life
expectancy and the presence of chronic co-morbid conditions.

**Federal partners should support strategies that incorporate shared decisionmaking in
diabetes agent medication management, where appropriate.**

In clinical settings in which there is no single or ideal diagnostic treatment regimen, shared
decisionmaking is an important tool in guiding prescribing decisions. Several medical associations
endorse shared decisionmaking [39, 40]. For example, the VA/DOD Clinical Practice Guidelines for the
Management of Diabetes Mellitus in Primary Care (2010) as well as the American Diabetes Association
and European Association for the Study of Diabetes (EASD) June 2012 joint position statement on
hyperglycemia treatment all specifically note the importance of shared decisionmaking with the patient
when choosing goals of therapy [39, 42]. Promoting shared decisionmaking is one of several
opportunities for advancing diabetes agent ADE prevention strategies/tools in outpatient settings; these
are summarized in Figure 16.
### Safer Care

- Medication adjustments in response to changes in oral intake
- Coordination of meal time and blood glucose testing
- Care coordination across all health care professionals
- Medication reconciliation of diabetes medications
- Caution against use of sliding scale insulin in patients that may be at higher risk for hypoglycemia (e.g., older adults, those with dementia)
- Encourage a multidisciplinary care approach, including pharmacists, nurses, diabetes educators, dietitians
- Incorporate data from patient glucometers into the electronic health record to identify patients at risk

### Patient and Family Engagement

- Tools to establish individual patient goals
- Shared decisionmaking, including patient preferences
- Teach-back method in which patient is asked to explain the clinician’s instructions in his/her own words
- Train health care professionals on how to address cultural competency (literacy, language, cultural acceptability)
- Train health care professionals on how to address health literacy [58, 77, 78, 79, 80, 81, 82, 83]
- Awareness and education of patients/families on how to treat low blood glucose, including availability of products such as glucose tablets for home use [56]
- Understand patient compliance/adherence to medication and diet regimen and daily barriers patient encounters
- Explain risks of nocturnal hypoglycemia with patient and caregivers

### Effective Communication and Coordination of Care

- Provider training on effective use of decision aids
- Education of health care professionals on the importance of effective communication and coordination of care
- Health care professionals should be encouraged to ask their patients if they experience any challenges with diet and encourage dietitians to be part of this process
- Enhanced medication reconciliation at the time of hospital discharge [84]
### Patient education
- Checking medication expiration date
- Identification of home blood glucose goals
- Detection and treatment of adverse events
- Importance of consistent eating patterns
- Guidance on sick day management
- Information on accuracy of self-monitoring equipment

### Science-Driven Prevention and Treatment
- Development and enhancement of decision aids [85]
- Provider coordination of any changes in medication
- Addressing inaccuracy of self-monitoring of blood glucose with patients and caregivers [86, 87, 88, 89]**

### Promotion of Best Practices Within Communities
- Multidisciplinary care coordination [39, 40, 41, 51]
- Consideration of individual patient circumstances (e.g., cognition, life expectancy, sedation) [39, 40, 41, 51]
- Professional supervision during any medication changes

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*Section 3506 of the Affordable Care Act encourages greater use of shared decisionmaking in health care and funds an autonomous program that would develop standards for and certify patient decision aids.*

**The acceptable accuracy of these devices permitted by FDA is ±15 mg/dL of the results of the reference measurement at glucose concentrations <75 mg/dL or ± 20 percent at glucose concentrations >75 mg/dL [89]. International Standards Organization guideline permits ±15 mg/dL for values <75 mg/dL. Accuracy varies among meters [86, 87, 88], and additional error can be introduced by user parameters. These issues have recently been reviewed by the Food and Drug Administration [89].

**Federal partners should advance efforts to identify the role care transitions play in contributing to hypoglycemic events.**

Medication errors and ADEs have been linked to poor communication of instructions to the patient at the time of discharge [58, 59, 60, 61, 62]. This is particularly true for insulin regimens, which are inherently more complex to manage and administer than other types of chronic disease medications [90]. Because the day of discharge is not always conducive to retention of verbal instructions [58, 59, 60, 61, 62], clear written instructions can provide a reference for patients and their outpatient providers, and a format for medication reconciliation between inpatient and outpatient settings. In one study, an insulin-specific discharge instruction form provided greater clarity and more consistent directions for insulin dosing and self-testing of blood glucose (BG), in comparison with a generic hospital discharge form [58, 59, 60, 61, 62].
To assist with medication reconciliation during the transfer from inpatient to outpatient settings and to avoid postdischarge adverse events/complications that can result in readmission, AHRQ’s *Medications At Transitions and Clinical Handoffs (MATCH)* toolkit for medication reconciliation is a tool that can potentially be used to help facilitate medication reconciliation during transitions of care [84].

The ADA recommends a team approach to transitions to outpatient care that includes physicians, nurses, pharmacists, medical assistants, dietitians, case managers, and social workers. ADA recommends that the transition to outpatient care begin with a hospital admission assessment that obtains

- Prior history of diabetes or hyperglycemia, its management, and the level of glycemic control
- Early assessment of a patient’s cognitive abilities, literacy level, visual acuity, dexterity, cultural context, and financial resources for acquiring outpatient diabetic supplies, which allows sufficient time to prepare the patient for discharge [31, 44]

Other recommendations suggest that the following areas be reviewed and addressed before the patient is discharged from the hospital [40, 58, 59, 60, 61, 62]:

- Level of understanding related to his/her diagnosis of diabetes
- Self-monitoring of BG and explanation of home BG goals
- Definition, recognition, treatment, and prevention of hyperglycemia and hypoglycemia
- Identification of health care provider who will be responsible for diabetes care after discharge
- Information on consistent eating patterns
- Instructions on when and how to take BG-lowering medications, including administration of insulin
- Sick day management
- Proper use and disposal of needles and syringes

**Incentives and Oversight**

The Incentives and Oversight Opportunities section (Section 4) of the ADE Action Plan provides an overview of the existing Federal incentives and oversight resources that may be leveraged to help ADE
incidence overall. Figure 17, and the discussion that follows, outline incentives and oversight opportunities specific to the safe management of diabetes agents.

**Figure 17. Federal Interagency Workgroup Recommendations for Actions That Can Potentially Advance Health Care Policy Strategies for Diabetes Agent ADE Prevention**

*Actions That Can Potentially Advance Health Care Policy Strategies for Preventing Diabetes Agent ADEs*

- Update national health care quality reporting measures to better reflect more recent clinical guidelines regarding the need to individualize hypoglycemic risk targets.
- Expand nationally recognized health care quality reporting measures to include concepts related to multidisciplinary, systematic, and coordinated models of care for managing inpatient glycemic targets.
- Adopt health care quality reporting measures that reflect the latest advances in measurement science.
- Address payment/coverage barriers to uptake of evidence-based, high-quality ADE prevention strategies, such as use of patient engagement and health literacy principles.
- Expand Federal and industry health care quality reporting measures that reflect the need for individualization of glycemic targets that incorporate co-morbid conditions.
- Explore utility, feasibility, and validity of developing nationally recognized health care quality measures related to hypoglycemic events resulting in emergency department visits or hospitalizations from ambulatory care or community living settings.
- Improve EHR standards and tools to better identify patients at high risk for hypoglycemia.

**Transitions of Care/Coordinated Care**

- Address barriers to integrated communication and coordination across health care settings and providers.

**Abbreviations:** ADE = adverse drug event; EHR = electronic health record

The nationally endorsed quality measures that relate to the management of diabetes should be revisited to reflect changes in medical science and expanded to include measures of hypoglycemic events.

The National Quality Forum has endorsed a number of measures related to the management of diabetes. However, not all these measures reflect the latest evidence base related to hypoglycemia risks, and they have not yet been revisited to reflect the newest guidelines relevant to glycemic control from the ADA, VA/DOD, and AGS. Specifically, they do not exclude patients for whom HbA1c <8 percent would be inappropriate according to new guidelines, or stratify by medications (such as insulin). Neither do they address potential overtreatment in high-risk groups. Rates of hospital admissions for
hypoglycemia are not addressed as a preventable hospitalization. Table 9 below outlines the measures related to diabetes care that are currently nationally recognized and in use by a number of Federal programs, including the Centers for Medicare & Medicaid Services’ Physician Quality Reporting System.

Table 9. National Quality Forum (NQF)—Endorsed Health Care Quality Measures Specific to Diabetes Medication Management and Hospital Admissions*

<table>
<thead>
<tr>
<th>Measure ID</th>
<th>Measure</th>
<th>Measure Description</th>
<th>Steward</th>
</tr>
</thead>
</table>
| NQF 0731   | Comprehensive Diabetes Care** | This measure assesses the number of patients (18–75 years) who had each of the following:  
- Hemoglobin A1c (HbA1c) testing  
- HbA1c poor control (>9%)  
- HbA1c control (< 8%)  
- HbA1c control (<7%) for subset of patients <65 years of age with exclusions for certain co-morbid conditions  
- Eye exam performed  
- LDL-C screening  
- LDL-C control (<100 mg/dL)  
- Medical attention for nephropathy  
- BP control (<140/90 mmHg)  
- Smoking status & cessation advice | NCQA |
| NQF 0272   | Diabetes Short-Term Complications Admission Rate | The number of discharges for diabetes short-term complications per 100,000 population over the past year | AHRQ*** |
| NQF 0060   | Hemoglobin A1c (HbA1c) testing for pediatrics | The percentage of pediatric patients with diabetes who received an HbA1c test | NCQA |
| NQF 1789   | Hospital-Wide All-Cause Unplanned Readmission Measure | The measure estimates the hospital-level, risk-standardized rate of unplanned, all-cause readmission after admission for any eligible condition (including diabetes) within 30 days of hospital discharge | CMS |

*Note: Measures summarized in this table are specific to diabetes medication management and diabetes-related hospital admissions or readmissions. Measures related to ensuring proper disease state management of diabetes that are not associated with risk of hypoglycemia are not shown here.

** NQF 0731 assesses comprehensive diabetes care that includes elements not specific to monitoring the risk of hypoglycemia.

*** Does not include admissions for hypoglycemia.

Abbreviations: HbA1c= hemoglobin A1c
Health Information Technology (Health IT)

The FIWs for Diabetes Agent ADEs proposed EHR (Stage 3) Meaningful Use electronic clinical quality measures for EHRs, which can potentially advance diabetes agent ADE prevention.

The FIW for Diabetes Agent ADEs discussed and identified various health care quality measures specific to hypoglycemic agent safety that were amenable for incorporation into EHR-based quality measure strategies. One measure concept that is being considered is a measure based on administrative claims data (measure related to emergency department visits or hospitalizations due to hypoglycemia). The FIW recommended these measures (Table 10) to the Quality Measures Workgroup of the Health Information Technology Policy Committee, which is convened by the HHS Office of the National Coordinator (ONC) for consideration as possible candidate measures for Stage 3 EHR MU requirements [91]. After initial recommendation, measures under consideration are submitted to CMS for further reviews, development, and testing. Final measure acceptance is dependent on rigorous and complete internal and external public reviews.

Table 10. Measure Considerations for EHR (Stage 3) Meaningful Use Requirements That Can Potentially Advance Diabetes Agent ADE Prevention, as Proposed by the Federal Interagency Workgroup for ADEs

<table>
<thead>
<tr>
<th>Metric</th>
<th>Description and Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Quality Measure Concepts—Eligible Providers (Outpatient Settings)</strong></td>
<td></td>
</tr>
</tbody>
</table>
| 1. Percentage of patients on sulfonylurea/insulin therapy with out-of-range HbA1c | Assesses patients aged 65 and older with HbA1c <7% on sulfonylurea or insulin therapy with one of the following chronic co-morbidities:  
- Cognitive impairment/dementia  
- Advanced microvascular complications  
- Limited life expectancy  
- Current substance use |
<p>| Rationale | Providers should be alerted when patients are at high risk for hypoglycemia. |
| <strong>Clinical Decision Support (CDS) Rule Concepts—Eligible Providers (Outpatient Settings)</strong> | |
| 2. Alert to potential risk for hypoglycemic events | Clinical reminder to identify patients at high risk for hypoglycemic event |
| Rationale | Provider should be notified when a patient is high risk and either take action or comment on why no action was taken. |
| 3. Shared decisionmaking on HbA1c glycemic goals | Clinical guidance that glycemic target should be discussed and set through dialogue between patient and provider and mutually agreed-on target range incorporated into medical record |
| Rationale | HbA1c glycemic goal should be entered in a field that can record use of shared decisionmaking to identify target. |</p>
<table>
<thead>
<tr>
<th>Metric</th>
<th>Description and Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Patient-Centered Action Plan</td>
<td>Clinical documentation of steps to be taken once patient is identified as high risk for hypoglycemic event</td>
</tr>
<tr>
<td>Rationale</td>
<td>Captures activities undertaken to acknowledge and reduce risk.</td>
</tr>
<tr>
<td>5. Flowsheet</td>
<td>Flowsheet with certain elements should be presented on a single page to the physician.</td>
</tr>
<tr>
<td>Rationale</td>
<td>Clinician can view appropriate considerations and recommended next steps for patients at high risk for hypoglycemia.</td>
</tr>
</tbody>
</table>

Patient List Recommendation—Eligible Providers (Outpatient Settings)

<table>
<thead>
<tr>
<th>Metric</th>
<th>Description and Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Stratified patient list</td>
<td>Electronically generate patient list stratified by HbA1c and co-morbidities.</td>
</tr>
<tr>
<td>Rationale</td>
<td>Allow clinician to stratify individuals currently receiving hypoglycemic events agents therapy by their HbA1c value and certain co-morbidities that increase their risk for hypoglycemia.</td>
</tr>
</tbody>
</table>

### Table 10. Measure Considerations for EHR (Stage 3) Meaningful Use Requirements that Can Potentially Advance Diabetes Agent ADE Prevention, as Proposed by the Federal Interagency Workgroup for ADEs (continued)

<table>
<thead>
<tr>
<th>Metric</th>
<th>Description and Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Quality Measure Concepts—Eligible Hospitals (Inpatient Settings)</td>
<td></td>
</tr>
<tr>
<td>7. Hypoglycemic events, serious</td>
<td>Total number of hypoglycemic events, divided by the number of patients administered a diabetes agent</td>
</tr>
<tr>
<td>Rationale</td>
<td>Calculates percent of hypoglycemic events for all inpatients receiving diabetes agents.</td>
</tr>
<tr>
<td>8. Hyperglycemia</td>
<td>Total number of hyperglycemic hospital days (defined as elevated glucose level), divided by all individuals with a diagnosis of diabetes mellitus who were administered antidiabetic agents (except metformin)</td>
</tr>
<tr>
<td>Rationale</td>
<td>▪ Calculates percent of hyperglycemic events for all inpatients receiving diabetes agents.</td>
</tr>
<tr>
<td></td>
<td>▪ Serves as balancing measure to hypoglycemia measure.</td>
</tr>
<tr>
<td>9. Hypoglycemia, mild</td>
<td>Total number of days in which any hypoglycemic event (&lt;70 mg/dL) reported, divided by total number of hospital days for patients receiving a diabetes agent</td>
</tr>
<tr>
<td>Rationale</td>
<td>Currently no system to effectively track and monitor episodes of hypoglycemia that do not result in need for third-party assistance.</td>
</tr>
<tr>
<td>10. Recurrent Hypoglycemia</td>
<td>Patients suffering at least one recurrent hypoglycemic event on a subsequent hospital day during the same hospital stay</td>
</tr>
<tr>
<td>Rationale</td>
<td>Patients suffering at least one recurrent hypoglycemic event on a subsequent hospital day during the same hospital stay.</td>
</tr>
</tbody>
</table>

EHR Functionality/Usability Recommendation—Eligible Hospitals (Inpatient Settings)

<table>
<thead>
<tr>
<th>Metric</th>
<th>Description and Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. Documentation of etiology of hypoglycemic event</td>
<td>Total number of hypoglycemic events, divided by all patients administered a diabetes agent</td>
</tr>
<tr>
<td>Rationale</td>
<td>Captures etiology and actions to take (checklist) to prevent future events</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>12. Alert to potential risk for hypoglycemic events</strong></td>
<td>Clinical reminder and documentation of risk mitigation steps taken (checklist) when patient has experienced two or more blood glucose values of &lt;70 mg/dL</td>
</tr>
</tbody>
</table>
| **Rationale** | • When there is a patient with repeated blood glucose values of <70 mg/dL, provider should be alerted for potential risk.  
• Provider should be provided list of options to prevent future episodes or document why no action taken. |
Table 10. Measure Considerations for EHR (Stage 3) Meaningful Use Requirements that Can Potentially Advance Diabetes Agent ADE Prevention as Proposed by the Federal Interagency Workgroup for ADEs (continued)

<table>
<thead>
<tr>
<th>Metric</th>
<th>Description and Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>EHR Functionality/Usability Recommendation—Diabetes Agents Health Literacy/Numeracy (Inpatient &amp; Outpatient Settings)</td>
<td></td>
</tr>
<tr>
<td>13. Health literacy</td>
<td>Provision of patient education materials on diabetes medications that follow health literacy principles</td>
</tr>
<tr>
<td><strong>Rationale</strong></td>
<td>▪ Patients need educational materials that are easy to comprehend when prescribed a diabetes agent.  ▪ Materials should follow health literacy principles.  ▪ Materials should be available in patients’ native language.  ▪ Provider should ensure that the patient can understand and follow the materials.</td>
</tr>
<tr>
<td>14. Health numeracy</td>
<td>Test patient’s ability to calculate numeric values to ensure proper HbA1c levels.</td>
</tr>
<tr>
<td><strong>Rationale</strong></td>
<td>▪ Critical to persons with diabetes self-management to avert potential harms  ▪ Important when patient experiences changes in diet, exercise, or improper calculation of medication dose</td>
</tr>
</tbody>
</table>

**Abbreviations:** HbA1c = hemoglobin A1c; mg/dL = milligrams per deciliter

**Research (Unanswered Questions)**

As ADE prevention efforts evolve, key research opportunities have the potential to further advance the field of diabetes agent safety. These opportunities lie in areas such as health care provider education, patient education, surveillance, and incentives and oversight, and are summarized below, in Figure 18.
**Actions That Can Potentially Advance Research Areas for Diabetes Agent Safety**

**Provider Education (AHRQ, CDC, FDA, public–private partnerships)**
- Research on clinician decisionmaking and behavior related to prescribing and managing of diabetes agents (e.g., risk-benefit considerations, patient-centered prescribing, acceptance of principles of individualized care)
- Research on provider knowledge of HbA1c and point-of-care HbA1c testing, glucometer accuracy

**Patient/Caregiver/Family Education (AHRQ, CDC, FDA, NIH, public–private partnerships)**
- Research on the quality and impact of educational material for prevention of hypoglycemic events and other diabetes-related patient outcomes, and impact of individualizing glycemic targets
- Research on the quality and impact of health literacy and numeracy on the prevention of hypoglycemic events and other diabetes-related clinical outcomes
- Research the role of telephonic management of diabetes for certain patient populations for whom this modality may be appropriate

**Surveillance and Prevention (AHRQ, CDC, FDA, public–private sector collaborations)**
- Identify rates of serious hypoglycemic events in ambulatory care settings stratified by risk factors such as education level, health literacy, age, and co-morbid conditions.
- Identify how currently existing ADE prevention tools utilized during care transitions affect hypoglycemic events.
- Research the impact of co-morbid conditions (e.g., cognitive function) on hypoglycemic risks.
- Identify how EHRs and related tools (e.g., clinical decision support) could be leveraged to facilitate improved monitoring and prevention of hypoglycemic events.
- Improve integration of EHR data with pharmacy data to facilitate better identification of patients with diabetes and hypoglycemic events.
- Enhance data on rates of hypoglycemia and risk factors in long-term care settings.
- Evaluate how EHR-based medication management interventions affect patient outcomes.
- Evaluate impact of new methods of glucose monitoring (e.g., continuous glucose monitors).
- Further evaluate impact of hypoglycemic events on quality of life-related metrics.
- Identify potential opportunities for improvements in insulin packaging and evaluate impact of changes in insulin packaging on the incidence of insulin medication errors and ADEs.
**SECTION 7**

Opioids

**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**

<table>
<thead>
<tr>
<th>Source</th>
<th>Overview</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>National Vital Statistics System (NVSS), CDC</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 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

<table>
<thead>
<tr>
<th>Geographic Scope</th>
<th>Data Collection Method</th>
<th>Opioid ADEs or Management Metrics: Inpatient Settings</th>
<th>Opioid ADEs or Management Metrics: Outpatient Settings</th>
</tr>
</thead>
<tbody>
<tr>
<td>National ADE Incidence/Rates</td>
<td>Administrative claims and/or EHR data</td>
<td>AHRQ (NIS): ▪ Inpatient stays with ICD-9-CM codes indicative of opioid ADEs</td>
<td>AHRQ (NEDS): ▪ ED visits with ICD-9-CM codes indicative of opioid ADEs</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>CMS (Medicare Part D Claims):</strong> ▪ Outpatient prescribing to detect fraud and abuse</td>
<td></td>
</tr>
<tr>
<td>Regional-/Facility-level ADE Incidence/Rates (Quality Improvement)</td>
<td>Medical-record review</td>
<td>AHRQ (MPSMS): ▪ Opioids are not currently captured by MPSMS system, but will be included after the conversion to QSRS.</td>
<td>CDC (NEISS-CADES): ▪ ED visits for opioid overdoses and other ADEs, not related to misuse/abuse</td>
</tr>
<tr>
<td></td>
<td>Administrative claims and/or EHR data</td>
<td>▪ Not available</td>
<td><strong>CDC (NVSS-Mortality):</strong> ▪ Deaths due to opioid overdose</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>SAMHSA (DAWN):</strong> ▪ ▪ ED visits for opioid ADEs</td>
<td></td>
</tr>
<tr>
<td>Spontaneous Reports</td>
<td>FDA: ▪ Clinician-diagnosed or patient-reported ADE</td>
<td><strong>FDA:</strong> ▪ Clinician-diagnosed or patient-reported ADE</td>
<td></td>
</tr>
</tbody>
</table>

**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.
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

<table>
<thead>
<tr>
<th>Resources for Safer Care—Health Care Provider Knowledge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DOD/VA:</strong></td>
</tr>
<tr>
<td>- <strong>Opioid Prescribing Protocol/ Guidelines</strong>—Includes recommendations for assessing patients for appropriate pain therapy.</td>
</tr>
<tr>
<td>- <strong>Education opportunities</strong>—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.”</td>
</tr>
<tr>
<td>- <strong>Opioid Safe Program</strong> 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.</td>
</tr>
<tr>
<td><strong>FDA:</strong></td>
</tr>
<tr>
<td>- <strong>Risk Evaluation and Mitigation Strategies (REMS)</strong>—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.</td>
</tr>
<tr>
<td>- <strong>Opioid Dose Conversion Table</strong>—Safe and reliable dose conversion table is based on updated evidence.</td>
</tr>
<tr>
<td><strong>IHS:</strong></td>
</tr>
<tr>
<td>- <strong>TeleBehavioral Health Center of Excellence Pain and Addictions course</strong>—15-series Webinar training program provides specialized training on how to treat pain and addictions.</td>
</tr>
<tr>
<td>- <strong>“Pain Champion” Training</strong>—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.</td>
</tr>
<tr>
<td><strong>NIH:</strong></td>
</tr>
<tr>
<td>- <strong>NIDAMED Physician Education Tools</strong>—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” (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.</td>
</tr>
<tr>
<td><strong>SAMHSA:</strong></td>
</tr>
<tr>
<td>- <strong>Opioid Overdose Prevention Toolkit</strong>—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.</td>
</tr>
</tbody>
</table>

\[i\] For more information, visit [http://www.drugabuse.gov/nidamed/etools](http://www.drugabuse.gov/nidamed/etools)

### 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.

- **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:**

### Resources To Promote Best Practices Within Communities

- **VA:**
  - **VHA National Pain Management Strategy**—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

- **AHQRQ:**
  - **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**—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.

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

- **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 biopsychosocial 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
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

<table>
<thead>
<tr>
<th>System</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systematic Strategy</strong></td>
<td>▪ VA National Pain Management Strategy—Outlines systematic strategies to improve pain management while maintaining opioid safety.</td>
</tr>
<tr>
<td></td>
<td>▪ 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.</td>
</tr>
<tr>
<td><strong>Performance Measurement</strong></td>
<td>▪ 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.</td>
</tr>
<tr>
<td></td>
<td>▪ 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.</td>
</tr>
<tr>
<td></td>
<td>▪ 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).</td>
</tr>
<tr>
<td><strong>Point-of-Care Clinical Management and Information Support</strong></td>
<td>▪ VA’s ATHENA System—Opioid system is a point-of-care decision support system to guide opioid management.</td>
</tr>
<tr>
<td></td>
<td>▪ VA inpatient tools for converting among different strengths/formulations of opioids.</td>
</tr>
<tr>
<td></td>
<td>▪ 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.</td>
</tr>
<tr>
<td></td>
<td>▪ 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.</td>
</tr>
<tr>
<td></td>
<td>▪ 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.</td>
</tr>
<tr>
<td><strong>Co-Morbidity Management/Individualized Care</strong></td>
<td>▪ 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.</td>
</tr>
</tbody>
</table>

**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.
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.
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

<table>
<thead>
<tr>
<th>Metric</th>
<th>Description and Justification</th>
</tr>
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<tbody>
<tr>
<td><strong>Outpatient Clinical Quality Measure Concepts</strong></td>
<td></td>
</tr>
<tr>
<td>Patients on high daily dose of long-term opioid therapy</td>
<td>- There is an association between high daily dose of opioids and opioid ADEs, which requires further study to understand the impact on clinical practice.</td>
</tr>
<tr>
<td>Patients co-prescribed long-term opioid therapy and CNS depressants</td>
<td>- Co-prescribing of opioids with CNS depressants, especially benzodiazepines, is associated with opioid overdose deaths.</td>
</tr>
<tr>
<td>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</td>
<td>- All guidelines recommend assessment of risk related to substance abuse prior to initiating opioids and while patients are on therapy.</td>
</tr>
</tbody>
</table>
| 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