Introduction

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.

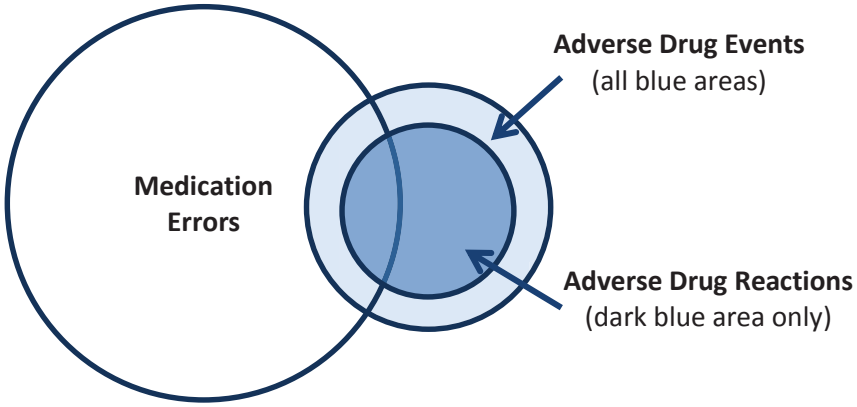
The ADE Action Plan is organized into seven sections. The first four sections outline the scope and development of the ADE Action Plan, identify Federal surveillance resources to measure and monitor the burden of ADEs, describe overall prevention approaches by identifying key determinants of ADEs, and 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.

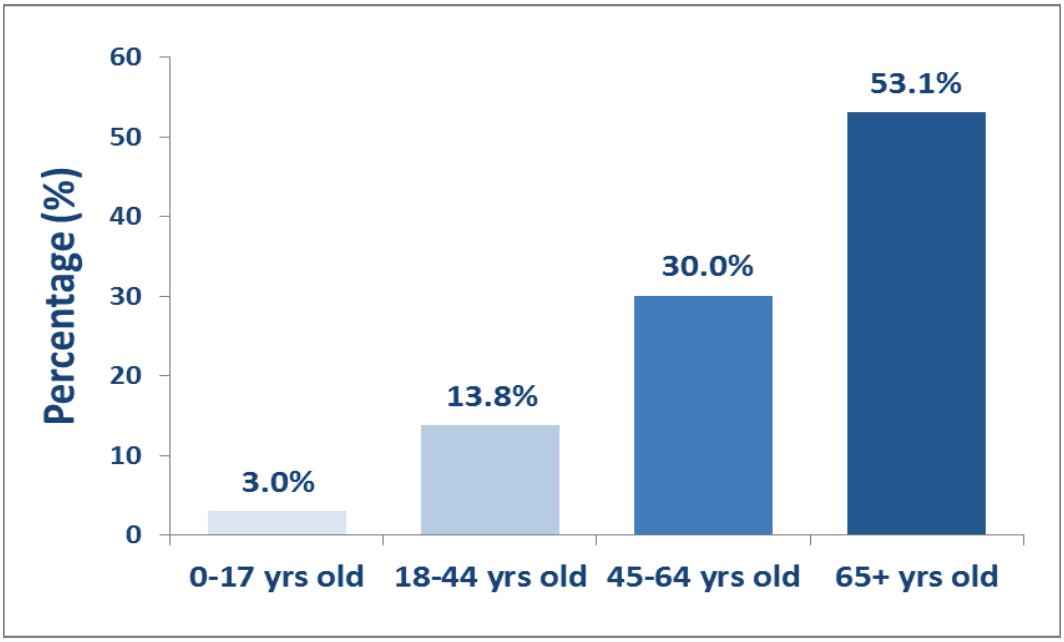
In outpatient settings, national public health surveillance data indicate that a small group of key medication classes—those that are characterized by a narrow therapeutic index or require routine laboratory monitoring—cause the most outpatient medication-related harms [19, 21]. In a recent, nationally 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

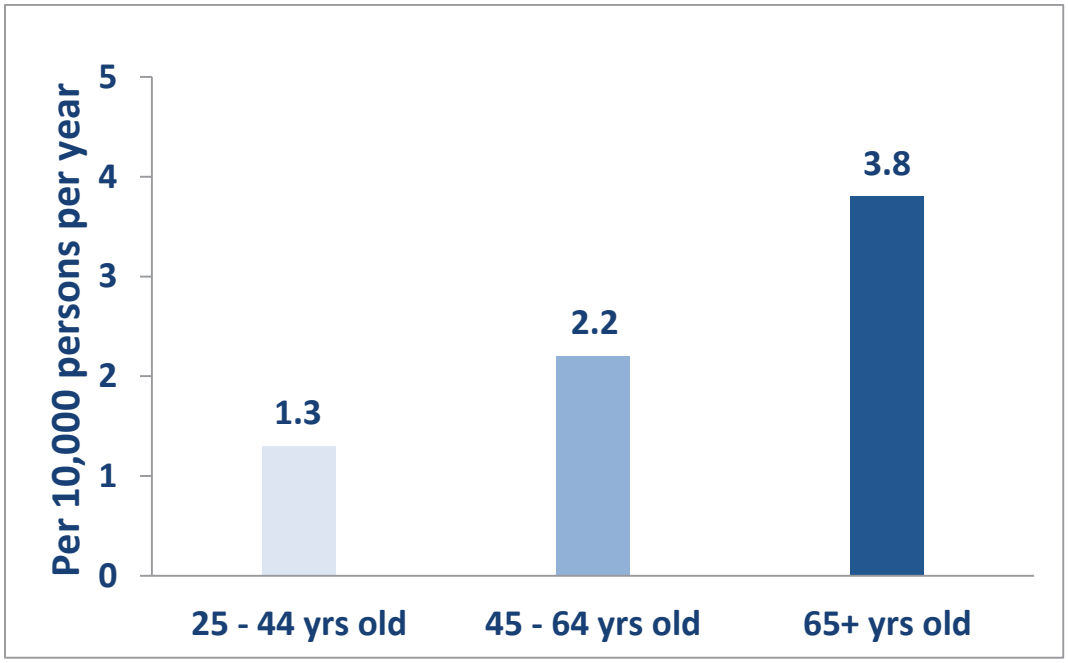
over the next decade [26]. Total expenditures on the Medicare Part D program alone in 2012 were $66.9 billion and are projected to reach $165.1 billion by 2022 [27].

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.

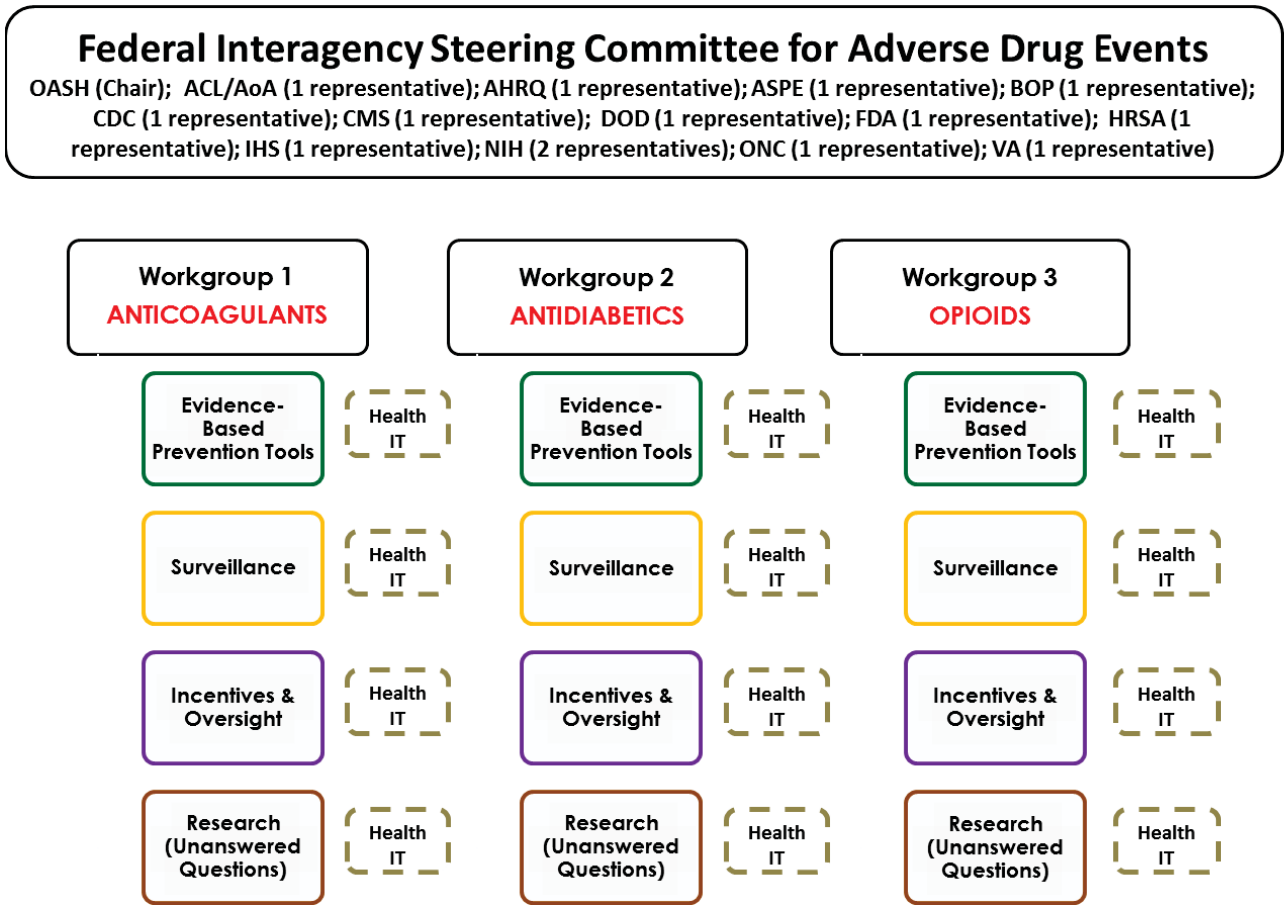
In September 2012, in response to the heightened awareness of the contributions of ADEs to health care-related harms and costs, the Office of the Assistant Secretary for Health (OASH) marshaled the wide-ranging and diverse resources of Federal partners to form an extensive interagency partnership, the 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, antineoplastics, 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.

Figure 4. Organizational Structure of the Federal Interagency Steering Committee and Workgroups for Adverse Drug Events



Abbreviations: Health IT = health information technology

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.

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