SECTION 2

Surveillance Resources

This section of the *National Action Plan for Adverse Drug Event Prevention* (ADE Action Plan) reviews the ways the burden and rates of ADEs can be measured to monitor the progress in prevention at a population-based level.

Specifically, this section

1) Describes considerations for choosing surveillance data sources and metrics
2) Briefly identifies existing Federal ADE surveillance systems and reviews their operating characteristics
3) Addresses future considerations for optimizing Federal ADE surveillance efforts

Opportunities for advancing surveillance to drive improvement are then outlined within each of these sections.

Considerations for Choosing Surveillance Data Sources and Metrics

Public health surveillance is defined as the "ongoing, systematic collection, analysis, and interpretation of health data, essential to the planning, implementation and evaluation of public health practice, closely integrated with the dissemination of these data to those who need to know and linked to prevention and control" [1]. Indeed, public health surveillance metrics and systems may address a wide variety of issues, use a wide variety of methodologies, and be conducted in numerous settings.

To identify surveillance data sources and metrics that would be most useful for assessing the public health impact of ADEs, a number of issues should be considered.

General Surveillance System Considerations

Quantification Versus Signal Detection

Public health surveillance can be used to quantify the scope and magnitude of known public health issues (e.g., disease tracking/quantification). Public health surveillance can also be conducted to identify new or previously unrecognized health issues (e.g., outbreak/signal detection). In choosing surveillance metrics for the ADE Action Plan, emphasis should first be placed on quantifying clinically recognized ADEs already identified as having significant public health impact (i.e., ADEs from anticoagulants, diabetes agents, and opioids). Once metrics are established to quantify these clinically recognized ADEs, identifying ADEs from medication classes that may not be as readily amenable to recognition and documentation (i.e., signal detection) can then be addressed.

Active Surveillance Versus Passive Surveillance (Voluntary Reporting)

Active surveillance involves proactively collecting information on a health condition. Active surveillance traditionally involves collecting primary data from health records or patients but can also involve targeted queries of databases containing previously collected health information (e.g., administrative claims data, EHR data). In contrast, passive surveillance typically relies on clinicians or patients to voluntarily report information to a surveillance system. Although voluntary (i.e., spontaneous) reporting can be crucial for identifying outbreaks (e.g., clusters of ADEs of unusually high magnitude) or previously unidentified or underappreciated adverse effects, active surveillance is the method that is typically required to reliably quantify scope and magnitude of a health problem and to assess trends.

Actual Harms/Injuries Versus Potential Problems/Medication Errors

Health surveillance can be carried out to identify potential problems or risk factors that may lead to patient injury (e.g., medication errors that can potentially lead to ADEs, potential medication-related problems brought about by polypharmacy); however, potential problems and risk factors do not necessarily lead to actual patient harm. Identifying potential problems may be useful for screening patients and targeting prevention efforts, but surveillance of actual patient injuries (e.g., hemorrhage, hypoglycemia, and loss of consciousness) should be prioritized whenever possible to evaluate the national health impact of large-scale or population-based ADE prevention efforts.

Although efforts to reduce medication errors are important, surveillance for medication errors is complicated by a number of factors. Determination of error is often subjective, dependent on voluntary reporting, and assigns or at least implies fault or blame. In addition, the large majority of medication

errors do not cause patient harm [2, 3]. Error reporting may be critical for monitoring safety within individual facilities, but using error reporting for national ADE surveillance poses substantial challenges in evaluating the impact of large-scale or population-based ADE prevention efforts on actual harms.

Considerations Specific to ADE Surveillance

Adverse "Drug" Events

ADE surveillance requires identification of an injury (e.g., hemorrhage, hypoglycemia, loss of consciousness, and/or associated laboratory abnormalities) *and* attribution of that injury to drug exposure. This complicates the interpretation of surveillance based on administrative claims data (i.e., International Classification of Diseases ICD-9-CM or ICD-10-CM coding) because administrative coding was not designed with the intent of conducting ADE surveillance, is variably used, and lacks the necessary linkage of outcomes of interest (harms) to the drugs. Even if administrative data can be used to identify which individuals received a drug and experienced an event, it may not be possible to determine if the event was an ADE or an independent event. Diagnostic codes that incorporate attribution of an adverse event to a drug (i.e., External Causes of Injury Codes [E-codes]) are underutilized and have been found to lack sensitivity for capturing ADEs [4]. Laboratory data may aid in identifying some ADEs, but not all ADEs are amenable to capture by way of laboratory triggers, and laboratory data are not uniformly available across all Federal surveillance data sources.

One way to address the limitations of administrative claims data is reviewing clinical documentation, which can provide detailed data for determining drug-induced injuries. Because surveillance based on reviewing clinical documentation can be resource-intensive and may be more prone to subjectivity, ADE surveillance based on clinical documentation has utilized sampling techniques and algorithmic detection methods [5, 6]. In research studies, detailed clinical review has been used to identify the absence of a medication (because of patient nonadherence, undertreatment, or omission) as a medication-related problem [7]. Although important for optimizing medication management, conducting national surveillance for adverse events attributable to such issues as undertreatment or medication omission is beyond the initial scope of this particular ADE Action Plan.

Medication Use/Drug Denominators

Although assessing the number of ADEs is a primary goal of surveillance, the number of patients being exposed to those drugs is also a very important consideration. If drug use varies over time, metrics that include drug use may aid in the interpretation of ADE incidence or burden by placing these estimates in the context of rates. Although reductions in the absolute number of ADEs may be observed over time,

absolute reductions may not be evident if medication use increases. Therefore, examining evolving trends over time in such factors as prescribing, medication use, and chronic disease burden will be important in assessing the impact of large-scale or population-based ADE prevention interventions.

Severity

Like most health conditions, adverse drug events can vary in severity. A common approach to surveillance is to start conducting surveillance on more serious outcomes (e.g., deaths, hospitalizations, ED visits), followed by surveillance of less serious events (e.g., visits for nonemergent care, such as physician offices, and self-treated incidents).

Setting

Surveillance commonly focuses on a specific setting (e.g., hospital or clinic) and may then expand to other settings (e.g., ambulatory care, long-term care facilities). The setting where the ADE is treated often differs from the setting where the exposure occurs. Using the admitting diagnosis or the first diagnosis can assist in determining where the event occurred.

Scope

For an ADE Action Plan that is national in scope, nationally representative data are most applicable. Due to cost constraints, most surveillance systems that are national in scope utilize statistical sampling to project national estimates, using data from selected sites.

Timeliness

Timeliness of surveillance data is important to link data to prevention and control actions.

Prevention Patterns

Finally, not all events under surveillance must be patient harms. If the effectiveness of a prevention strategy has been established, surveillance, including by pharmacist review, could be used to measure penetration of that strategy and provide further context to changes in trends.

Federal Systems That Conduct ADE Surveillance

Federal surveillance systems vary in the populations surveyed, focus, geographic scope, data sources, and collection methods, as well as the definitions and approaches utilized to capture anticoagulant, diabetes agent, and opioid ADEs. Collectively, these systems point to opportunities and challenges for Federal partners to optimize ADE surveillance efforts that are addressed in further detail under each of

the high-priority drug sections that appear later in the ADE Action Plan. Currently available Federal surveillance systems for conducting ADE surveillance and their operational characteristics are summarized in **Appendix B**. Only Federally supported surveillance systems that are currently utilized to conduct ongoing ADE surveillance are included. These surveillance systems use three general methods: active identification of adverse events from clinical records, passive reporting of adverse events, or searches of administrative and/or clinical databases for codes or values indicating adverse events.

1) Active nationally representative adverse event-monitoring systems based on structured medical record review include
    - Agency for Healthcare Research and Quality (AHRQ) Medicare Patient Safety Monitoring System (MPSMS)
    - Centers for Disease Control and Prevention (CDC) National Electronic Injury Surveillance System—Cooperative Adverse Drug Events Surveillance System (NEISS-CADES)
2) Passive national adverse event-reporting systems include
    - Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS)
3) Systems that identify adverse events from administrative claims databases include
    - AHRQ Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample (NIS), State Inpatient Databases (SID), and Nationwide Emergency Department Sample (NEDS)
    - FDA Sentinel Initiative, Mini-Sentinel Pilot

Although they may not be nationally representative, the following Federal integrated health networks also conduct adverse event surveillance and may incorporate all three general methods:

- Bureau of Prisons (BOP) quality improvement programs
- Department of Defense (DOD) Patient Safety Reporting System
- Indian Health Service (IHS) Resource and Patient Management System (RPMS-EHR)
- Veterans Health Administration (VHA) Integrated Databases/Adverse Drug Event Reporting System (VA ADERS)

The Federal passive (voluntary) reporting systems, such as FDA's FAERS, NIH's Drug-Induced Liver Injury Network (DILIN), and VHA's VA ADERS, were constructed to identify (and have identified many) signals of previously unrecognized, underappreciated, or rare ADEs. To do so, they were designed to include

reports in which the adverse event may or may not be related to the identified drug. They are not designed for complete accounting of ADEs or calculating population-based estimates. Patient Safety Organizations (PSOs) are independent, non-Federal voluntary reporting systems authorized under the Patient Safety and Quality Improvement Act of 2005 that may also be useful for signal detection and local reporting, but these organizations are not national in scope and may not focus on ADEs.

Federal active surveillance systems can provide estimates and rates of ADEs based on data compiled from millions of administrative claims. AHRQ's HCUP and FDA's Sentinel Initiative utilize administrative claims and ICD-9-CM codes to enumerate the risks of medication-related harms. However, claims data have limited ability to control for certain variables (e.g., co-morbidities) that may confound the link between drugs and certain outcomes and to assess medication adherence. Currently, Sentinel covers more than 125 million lives, which does not constitute a nationally representative sample, but for specific studies, FDA's Sentinel Initiative has the potential to access health records to confirm coded data or provide additional data. HCUP data can be extrapolated to provide national estimates, as well as regional- and State-level estimates for specific common ADEs.

By using structured clinical record review, AHRQ's MPSMS is able to provide population-based national estimates and rates for specific ADEs (ADEs due to anticoagulants and diabetes agents) in hospitalized patients and to examine correlations with other types of adverse events among the same patients (e.g., pressure ulcers, infections). CDC's National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance (NEISS-CADES) project can provide annual national estimates of emergency department visits and emergent hospitalizations attributed to harms from outpatient therapeutic drug use (excluding abuse or self-harm). Strengths of the system include its case identification method of reviewing free-text narratives of each case, which may provide additional contextual information on medication-related overdoses that are related to therapeutic use and errors. However, because both MPSMS and NEISS-CADES utilize statistical sampling from a national frame, regional or State-based estimates cannot be calculated or tied to local quality improvement efforts.

CDC's National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) provide annual national estimates on the utilization of ambulatory medical care in the United States. [8]. These sample surveys of visits can capture outpatient ADEs, as reported by E-codes found in the ICD-9-CM. Although these surveys are useful for calculating overall estimates of outpatient ADEs [9, 10], they are limited in the information they can provide on ADEs because of the small sample size of such visits in NAMCS and NHAMCS. CDC plans to integrate NHAMCS National

Hospital Discharge Survey and the Drug Abuse Warning Network into the National Hospital Care Survey, which will provide the ability to link patients within the same sampled hospital to outside data sources [11].

VHA's active surveillance system focuses on quality improvement for a selected population, utilizing the VHA's inpatient and outpatient care settings. The system comprises a comprehensive Drug Use Evaluation (DUE) program and a Medication Use Evaluation Tool (MUET), which identify patients at high risk for ADEs on the basis of pharmacy, laboratory, and diagnostic triggers. The system is an example of using facility-level surveillance data to assist health care providers in real-time decisionmaking to mitigate risks of ADEs in patients.

The BOP, DOD, VHA, and IHS also have systems that leverage both passive and active surveillance strategies, with a focus on quality improvement for the populations under their care (**Appendix B**).

Figure 5 highlights the strengths, weaknesses, opportunities, and threats of the Federal systems that can be used to conduct ADE surveillance.

Figure 5. Strengths and Limitations of Federal Systems That Conduct ADE Surveillance [12]

S: Strengths • Inpatient and outpatient settings addressed • Majority capture ADEs from high-priority drug targets (i.e., anticoagulants, diabetes agents, opioids) • Flexibility	**W: Weaknesses** • Some critical settings unaddressed (e.g., long-term care facilities, transitions of care) • Highly variable sensitivity, specificity, PPV, and NPV of diagnostic and procedural coding (i.e., ICD-9-CM and CPT) in capturing ADEs (i.e., not designed or intended for ADE surveillance) • Variable in their ability to link outcomes (harms) of interest to drugs • Timeliness
O: Opportunities • Harnessing of large datasets through public–private collaborations (e.g., FDA Sentinel Initiative) • Leveraging of linked EHRs and new communication technologies	**T: Threats** • Funding to support ongoing analyses of surveillance data

Abbreviations: ADE = adverse drug event; CPT = Current Procedural Terminology; EHRs = electronic health records; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; PPV = positive predictive value; NPV = negative predictive value

Future Considerations for Optimizing Federal ADE Surveillance Efforts

Existing Federal systems provide a starting point for national surveillance of adverse events from anticoagulants, diabetes agents, and opioids. Future considerations to optimize Federal ADE surveillance efforts are outlined in the following sections.

Refine and improve existing national systems

National surveillance using population-based sampling or administrative data is an efficient way of collecting nationally representative data on ADEs. Because administrative data collection and coding systems were not designed for the primary intent of ADE surveillance, mapping existing codes (e.g., ICD) and data collection (e.g., present on admission) to ADEs should be validated. However, it may be necessary to revise coding systems with ADE quantification in mind or consider alternative approaches to support better documentation of ADEs similar to the current approach used to document drug allergies. NEISS-CADES data are currently used to chart progress of the Healthy People 2020 objectives to reduce emergency visits for overdoses of oral anticoagulants and injectable diabetes agents (i.e., insulin). AHRQ is currently developing measures for specific (drug-type) ADEs that build on the current MPSMS ADE definitions, for use in the new Quality and Safety Review System (QSRS). There are ongoing opportunities to refine and validate the identification of specific ADEs from administrative and clinical databases. In addition, data on medication use that can be used to calculate ADE rates are needed to interpret whether changes in the number of ADEs may be caused by safety changes or changing patterns of medication use.

Opportunities for Clinical Setting Surveillance

Although national monitoring is useful for identifying burden and monitoring progress, actually preventing ADEs requires action by individual providers and patients at the health system level and, thus, an understanding of facility-level burden and trends in ADEs. The National Healthcare Safety Network (NHSN) is one example of how individual facility-level reporting of health care-associated infections (HAIs) has facilitated improved understanding of HAI burden, enabled facility-level prevention efforts, and driven national-level improvements in HAI burden [13]. Refining the next version of AHRQ Common Formats for reporting specific ADEs could provide another opportunity to facilitate reporting, analysis, and reduction of ADEs in individual facilities across the Nation. Quality and safety initiatives in anticoagulation management, hypoglycemic event monitoring, and opioid optimization that incorporate surveillance may also provide the opportunity for innovations. Surveillance innovations may be found in non-Federal collaboratives [14, 15] as well as in Federal integrated health networks.

Role of Federal Agencies That Provide Direct Patient Care

Federal Agencies that provide care for specific populations (e.g., BOP, DOD, HRSA, IHS, VHA) play an important role in facilitating the infrastructure necessary for monitoring ADEs at regional or facility levels, in rural settings, and in low-resourced settings. Collaborating on monitoring methods across Federal Agencies that directly care for patients at risk for ADEs, as well as collaborating with non-Federal partners such as PSOs, could aid the efficacy and efficiency of efforts. This would require an administrative structure to foster such ongoing collaborations and communication in this area.

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