

REPORTS OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

The following three reports were presented by Michael M. Miller, MD, Chair:

1. MANDATORY REPORTING OF DISEASES AND CONDITIONS (RESOLUTION 915-I-18)

Reference committee hearing: see report of Reference Committee K.

**HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
IN LIEU OF RESOLUTION 915-I-18
REMAINDER OF REPORT FILED
*See Policy H-440.813***

Resolution 915-I-18, introduced by the American College of Emergency Physicians and referred by the House of Delegates asks:

That our American Medical Association oppose mandated reporting of entire classes of patients and specific diagnoses unless compelling evidence exists to demonstrate that a serious public health and/or safety risk will be mitigated as a result of such reporting.

METHODS

English language reports were selected from searches of the PubMed, Google Scholar, and Cochrane Library databases from January 2009 to August 2019 using the search terms: “mandatory reporting,” “nationally notifiable condition,” “electronic case reporting,” “public health surveillance,” “chronic disease registry,” “mandatory reporting” and “noncommunicable disease.” Additional articles were identified by manual review of the reference lists of pertinent publications. Web sites managed by federal agencies, applicable professional organizations, and foundations were also reviewed for relevant information.

CURRENT AMA POLICY

The AMA has numerous policies calling for improved public health surveillance (e.g., antibiotic use and resistance, cannabis, Creutzfeldt-Jakob disease, firearm-related injuries and deaths, human immunodeficiency virus, infant mortality, lead poisoning, maternal mortality, new psychoactive substances, radon exposure, tobacco consumption, tuberculosis, vector-borne diseases, zoonotic diseases, etc). These policies do not address mandatory reporting or the burden of reporting on physicians. AMA policy also does not address the work underway to modernize public health surveillance and implement electronic case reporting (eCR) thereby removing the burden on physicians, labs, hospitals, and others required to report for the purposes of public health surveillance.

This report will define public health surveillance, explain the difference between mandatory reporting and nationally notifiable conditions, discuss the history of public health surveillance and its expansion beyond infectious diseases, and explain work underway to implement electronic case reporting (eCR) to both improve surveillance and alleviate the burden of reporting on those required to report. The Council on Science and Public Health recognizes public health surveillance is not without risks for individual participants and can pose ethical dilemmas. However, when conducted ethically, public health surveillance is justified for the common good to promote population health and reduce inequalities.¹ The ethical framework for conducting public health surveillance is outside the scope of this report.

BACKGROUND

Public health surveillance is the ongoing systematic collection, analysis, interpretation and dissemination of health data for the planning, implementation and evaluation of public health action.”² Public health surveillance is an essential public health function.³ Surveillance data can be used to estimate the magnitude of health problems, determine the distribution of illness in a population, depict the natural history of a disease, generate hypotheses, stimulate research, evaluate control measures, monitor changes, and facilitate planning.⁴

Disease surveillance usually begins in the health care setting as public health agencies collect disease information from health care providers, facilities, and clinical laboratories required to report diseases and conditions to public health agencies.⁵ In the United States, the authority to require notification of cases of diseases resides with the jurisdiction's state legislature.⁶ As a result, the list of diseases and conditions that are reported varies by state.⁶ In addition, the time frames for reporting, agencies receiving reports, persons required to report, and conditions under which reports are required also differ.⁶ Traditionally, disease reports were made manually or by telephone, mail, or fax.⁵ Reporters have indicated that manual submission of disease reports is time-consuming and disruptive to workflow.⁵

The Nationally Notifiable Disease List differs from mandatory reporting in that notifiable diseases are reported to the Centers for Disease Control and Prevention (CDC) on a voluntary basis by each jurisdiction. The Council of State and Territorial Epidemiologists works with the CDC to determine which conditions reported to local, state, and territorial public health departments are nationally notifiable.⁸

This Council on Science and Public Health report stems from the enactment of legislation in California in 2017 that requires the State Department of Public Health to collect data on the incidence of Parkinson's disease in California.⁸ The legislation also requires a hospital, facility, physician and surgeon, or other health care provider diagnosing or providing treatment to Parkinson's disease patients to report each case of Parkinson's disease to the department, beginning July 1, 2018.⁸

DISCUSSION

Historically, surveillance focused on infectious diseases, it then broadened to other topics, including chronic diseases (e.g., cancer and diabetes), occupational health, environmental health, hazard surveillance (toxic chemicals and physical and biological agents), and injury control (e.g., firearm-related injury).⁹ It is expected that additional diseases and conditions will be explored in the future.⁹ As state legislatures consider adding to their jurisdiction's list of diseases and conditions that are required to be reported to public health agencies, they should consult with state and national medical societies and public health agencies to ensure the requirements are based on scientific evidence and will meet the needs of population health.

Chronic Disease Surveillance

Chronic diseases are conditions that last 1 year or more and require ongoing medical attention or limit activities of daily living or both. Chronic diseases such as heart disease, cancer, and diabetes are the leading causes of death and disability in the United States and the leading drivers of health care costs.¹⁰ The rise in chronic disease burden led to the development of chronic disease surveillance systems. In the 1970s, morbidity from select chronic diseases came under surveillance through disease registries.¹¹ In the 1980s and 1990s, CDC and state health agencies collaboratively developed additional surveillance systems to monitor behavioral risk factors for chronic disease.¹¹ This led to the use of the Behavioral Risk Factor Surveillance System and the Youth Risk Behavioral Surveillance System to monitor health risk behaviors.¹¹ In 1992, Congress authorized the National Program of Cancer Registries at CDC to monitor local trends in cancer incidence and mortality with statewide, population-based cancer registries.¹¹ The benefits of public health surveillance on these conditions include determining incidence and survival rates, evaluating treatment efficacy, targeting educational and screening programs, and conducting research on etiology, diagnosis and treatment.

Neurological Conditions Surveillance

In 2016, as part of the 21st Century Cures Act, Congress authorized CDC to initiate development of a National Neurological Conditions Surveillance System to begin collecting and analyzing data on neurological disorders.²⁰ The CDC will begin by exploring and synthesizing data from existing sources to gain an increased understanding of multiple sclerosis and Parkinson's disease.²⁰ Once model approaches for surveillance are identified, the NCSS will be extended to other neurological conditions as resources allow.²⁰

On the state level, Nebraska was the first jurisdiction to implement a Parkinson's disease registry. The law requires that physicians and pharmacists report individuals diagnosed with Parkinson's and patients taking anti-Parkinson's medications to the Nebraska Department of Health and Human Services Regulation and Licensure.¹² In 2015, Utah launched its Parkinson's Disease Registry to understand the apparent rise in the disease in the state and uncover causes of the disease. Effective March 12, 2015, the Utah State Board of Health began requiring health care providers to

report cases of Parkinson's Disease and related movement disorders.¹³ California was the third state to require reporting of Parkinson's Disease. Since July of 2018, 122,727 records have been submitted to the California Parkinson's Disease Registry.¹⁴ These data will be used to: (1) determine the incidence and prevalence of Parkinson's disease in California; (2) examine disparities in Parkinson's disease risk; and (3) conduct demographic and epidemiological research and other studies of Parkinson's disease.¹⁵ These provisions under the California law are set to expire in 2020, but legislation is currently being considered to extend the registry and reporting requirements beyond 2020.

DIGITAL BRIDGE

The Digital Bridge, funded by the Robert Wood Johnson Foundation and the de Beaumont Foundation, provides a forum for key decision-makers in health care, public health and health information technology (IT) committed to promoting bidirectional, or two-way, information exchange between the health care and public health sectors.¹⁶ The Digital Bridge promotes the use of national health IT infrastructure to alleviate the administrative burden and costs of outdated, siloed data exchange practices.¹⁶ Goals for the Digital Bridge include: (1) easing the burden and costs for all stakeholder groups through a unified approach to information exchange; (2) advancing greater standards-based information exchange across public health and health care; and (3) laying the foundation for greater bidirectional exchange of data so that clinicians can be more informed about population health, environmental risks and outbreaks.¹⁶ The AMA is currently a member of the Governance Body for the Digital Bridge. Electronic case reporting (eCR) was the first use case for the Digital Bridge.

Electronic Case Reporting (eCR)

With more than 80 percent of office-based physicians having adopted electronic health record (EHR) systems, it is not surprising the future of public health surveillance is eCR, a process by which reportable conditions are automatically generated from EHR systems to public health agencies for review and action, in accordance with applicable health care privacy and public health reporting laws¹⁷ (see Figure). The advancement of eCR could lead to more accurate and timely case data for public health action resulting in improved detection of outbreaks, earlier identification of disease risk factors, and a decreased burden on mandatory reporters, including physicians.¹⁷

The electronic initial case report (eICR) would be identified in the EHR through a standard set of trigger codes that flag when a provider diagnoses a reportable condition based on International Classification of Diseases, Tenth Revision codes for diagnoses, LOINC (Logical Observation Identifiers Names and Codes) for laboratory testing orders, or SNOMED CT (Systematized Nomenclature of Medicine–Clinical Terms) for clinical information and laboratory results.¹⁶ The Association of Public Health Laboratories, Council of State and Territorial Epidemiologists, and CDC have already vetted the reportable trigger codes for 5 conditions (e.g., gonorrhea, chlamydia, salmonella, pertussis, and Zika virus infections) and are in the process of identifying codes for all reportable conditions.¹⁷

After potential cases are identified through trigger codes, the eICR will automatically be generated with case information.¹⁷ The eICR will contain a minimum set of data elements that have been established to be used for all conditions in all jurisdictions. The eICR will be transmitted from the EHR to an intermediary platform via secure, broadly used data transport mechanisms.¹⁶ On these platforms, a software application will assess the reportability of the disease or condition via a logic model based on the jurisdiction's mandated reporting requirements and then will route adjudicated cases to the appropriate agencies.¹⁷

The Reportable Conditions Knowledge Management System (RCKMS) is a software application that will unpack, transform, and adjudicate the eICR automatically in a secure environment to determine whether the potential case meets minimal criteria consistent with mandated reporting based on a standard logic specific to jurisdictional requirements. RCKMS will transmit reportable cases to jurisdictions for final classification and action.¹⁷ Health care providers will be informed when cases have been reported.¹⁶ CDC has supported the Health Level 7 Consolidated Clinical Document Architecture as the initial structure for transmitting the eICR, based on standards that are already in use.

Houston was the first pilot site under the Digital Bridge initiative to successfully launch eCR. Partners involved in the Houston demonstration include Houston Health Department, Houston Methodist, and Epic Systems.¹⁸ California, Kansas, Massachusetts, Michigan, New York, and Utah have also been selected as pilot sites.¹⁹ The CDC recently identified Parkinson's disease for inclusion as a test case for the Digital Bridge. The Digital Bridge and CDC have

committed to working with the California Department of Public Health to implement eCR across California health systems to collect data on Parkinson's disease cases seen by health care providers in a burden-free manner.

CONCLUSION

Public health surveillance is an essential public health function and coordination between health care and public health agencies is essential for the monitoring, control, and prevention of disease. The AMA has numerous policies calling for improved public health surveillance on a wide range of topics. A policy opposing mandatory reporting for specific conditions due the burden it places on physicians could jeopardize our understanding of disease occurrence and severity (e.g., cancer), as well as new causes, risk factors, and early identification of disease clusters. In addition to increases in disease incidence, reporting can also demonstrate the decline in disease among the population and help with the evaluation of prevention programs (e.g., vaccines).

To ensure that new diseases reporting requirements are based on the scientific evidence and will meet the needs of population health, the AMA encourages state legislatures to engage state and national medical specialty societies and public health agencies when proposing mandatory disease reporting requirements. The AMA should also support the modernization of public health surveillance systems and recognize the benefits of eCR in both improving public health surveillance through more accurate and timely data and alleviating the reporting burden on physicians.

RECOMMENDATIONS

The Council recommends that the following recommendation for new policy be adopted in lieu of Resolution 915-I-18, and the remainder of the report be filed.

Public Health Surveillance

That our AMA: (1) recognizes public health surveillance as a core public health function that is essential to inform decision making, identify underlying causes and etiologies, and respond to acute, chronic, and emerging health threats; (2) recognizes the important role that physicians play in public health surveillance through reporting diseases and conditions to public health authorities; (3) encourages state legislatures to engage relevant state and national medical specialty societies as well as public health agencies when proposing mandatory reporting requirements to ensure they are based on scientific evidence and meet the needs of population health; (4) recognizes the need for increased federal, state and local funding to modernize our nation's public health data systems to improve the quality and timeliness of data; (5) supports electronic case reporting, which alleviates the burden of case reporting on physicians through the automatic generation and transmission of case reports from electronic health records to public health agencies for review and action in accordance with applicable health care privacy and public health reporting laws; (6) will share updates with physicians and medical societies on public health surveillance and the progress made toward implementing electronic case reporting.

Figure



Source: The Digital Bridge

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2. REAL-WORLD DATA AND REAL-WORLD EVIDENCE IN MEDICAL PRODUCT DECISION MAKING

Reference committee hearing: see report of Reference Committee K.

HOUSE ACTION: RECOMMENDATIONS ADOPTED

REMAINDER OF REPORT FILED

See Policies H-100.992, H-110.986, H-406.987, H-410.948, H-450.933, H-480.938, D-100.982 and D-460.970

INTRODUCTION

Physicians are trained to implement the 5 steps of evidence-based practice (EBP) and rely on appropriate evidence to guide the clinical care they provide to their patients. The evidence relied upon in EBP has typically been generated from traditional randomized controlled trials (RCTs). Today, real-world data (RWD) and real-world evidence (RWE) are increasingly being used in health care decision making to augment evidence from RCTs.

The Council on Science and Public Health offers this overview of RWD and RWE to practicing physicians because it is important for all physicians to understand the genesis of data and derivation of evidence from sources other than traditional RCTs that is increasingly being used by the FDA in its approval of new products, new indications for products, or new labeling on products that are used in patient care. Although RWD and RWE have many applications in health care, this report remains narrow in scope and will focus only on the use of RWD and RWE that is fit for purpose to be used in medical product (that is, drug, biologic, and device) decision-making (Figure 1), such as the FDA's consideration of a new drug indication, labeling revision, or safety revision. The use of RWD and RWE as it applies to other topics, including augmented intelligence (AI), will be addressed at a later time.

RWD are the data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. RWE is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD.¹⁻³ RWD and RWE are playing an increasing role in health care decisions. Additionally, the use of RWD and RWE to answer scientific questions and guide more effective and cost-efficient medical product decision making is an active area of engagement for regulatory agencies. Stakeholder groups are actively working on ways to improve the development and use of RWD and RWE across a range of clinical and regulatory activities.

The 21st Century Cures Act (Cures Act), signed into law in December 2016, is designed to accelerate medical product development and bring new innovations and advances faster and more efficiently to patients.⁴ Among the provisions in the Cures Act is an added section to the Federal Food, Drug, and Cosmetic Act (FD&C Act) related to RWE which requires that the U.S. Food and Drug Administration (FDA) increase its use of evidence from clinical practice settings. Pursuant to this provision and the sixth Prescription Drug User Fee Act (PDUFA VI),⁵ FDA created a framework for evaluating the potential use of RWE to support the approval of a new indication for a drug or biological product already approved or to support or satisfy drug post-approval study requirements.¹ The FDA under the fourth Medical Device User Fee Act (MDUFA IV)⁶ is required to, among other things, evaluate the published guidance in 2017, *Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices*.⁷

In addition to the FDA's activities related to RWD, the National Institutes of Health (NIH) has developed its first Strategic Plan for Data Science providing a roadmap for modernizing the NIH-funded biomedical data science ecosystem;⁸ The National Academies of Sciences, Engineering, and Medicine (NASEM) remain engaged in RWD conversations with diverse stakeholders;⁹⁻¹² part of the Patient Centered Outcomes Research Institute (PCORI) mandate is to improve the quality and relevance of evidence to advance health care;¹³ and several thought leaders, including former FDA Commissioners, are commenting on the use of RWD for the advancement of health care.¹⁴⁻¹⁷

Many different types and sources of RWD exist, there is increasing availability of RWD, and new potential data sources are emerging. Both challenges and benefits to the use of these data exist. The Council on Science and Public Health initiated this report to inform physicians of the evolving use of RWD and RWE in medical product decision making. This report will define and clarify the current working definition and types/sources of RWD and RWE, evaluate challenges and benefits in using RWD, provide examples of RWD platforms and use of RWE, and explore considerations for generating RWE that is fit for regulatory purposes.

METHODS

English-language articles were selected from a search of the PubMed database through August 2018 using the search terms “real-world data” and “real-world evidence.” Due to the volume of results, the date range was limited to 2017 to present. Additional articles were identified from a review of the references cited in relevant, retrieved publications. Searches of websites of international and national government agencies and outcomes research organizations and associations were conducted to identify guidelines, position statements, and reports.

OVERVIEW OF RWD AND RWE

RWD are collected from a variety of sources with varied quality, reliability, and applicability including electronic health records (EHRs) from hospitals, physician offices, and clinics (diagnoses and medical history); medical and billing claims; product and disease registries; administrative data; pharmacies (including dose, dose regimen, and route of administration of medications); laboratory, radiology, and diagnostic test results; cost studies; prospective observational data; vital records databases; primary and secondary care data; and patient-generated data, including from in-home-use settings, wearables, biosensors, remote monitoring devices, mobile devices and applications, consumer surveys, and social media (Figure 2).^{1,9,17} Post-marketing data is the type of RWD currently used most often. RWD are typically more proximate to the patient and the patient experience; thus, they include primary source data, but they have a high potential for unstructured/inconsistent data collection and for missing data elements as compared to data collected for research or during clinical trials.¹⁸

The FDA is advancing a total product life cycle (TPLC) approach, a holistic approach that takes into account all of the steps and processes in the evolution of a medical product from conception to obsolescence, integrating information and knowledge across pre-market and post-market activities, to increase information-sharing and enhance decision-making. RWD and RWE are not a replacement for clinical trial data, but instead support the TPLC approach to medical product approval and surveillance; they will augment existing mechanisms which are known to have gaps, delays, and deficiencies that are inherent in any system that depends on active reporting by users.

RWE has the potential to inform therapeutic development, outcomes research, patient care, health care systems research, quality improvement, safety surveillance, and well-controlled effectiveness studies. RWE can provide answers to questions relevant to broad populations of patients that may not be possible or intended in the course of a traditional clinical trial and may reduce the number of individuals exposed to a faulty medical product and shorten the period of time before valid performance issues are identified and acted upon. Use of RWD and RWE may also save time and money throughout the TPLC. Additionally, RWE can be used to complement traditional clinical trials, generating more generalizable knowledge from larger, more inclusive populations of patients, providers, and health care delivery systems or settings that reflect actual use in practice.¹⁶

However, it is important to note that the RWE generated from RWD has limitations and challenges including confidentiality and proprietary concerns, the cost and work required to convert data for use in analyses, and sharing and collaboration considerations.¹⁹

FDA RWE Program Framework

Former FDA Commissioner Scott Gottlieb, MD, recently noted that RWD and RWE are a top strategic priority for the FDA and the Agency is “committed to realizing the full potential of these tools in advancing the development of novel therapeutic products and strengthening our regulatory oversight of medical products across the life-cycle continuum.”²⁰ The recently published *Framework for FDA’s RWE Program* (framework), issued by the FDA’s Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) is intended to develop a path for ensuring that RWE solutions are an integral part of the drug development and regulatory life cycle.²⁰

The CDER/CBER framework notes that the FDA’s work will be multifaceted and involve demonstration projects, stakeholder engagement, internal processes to promote shared learning and consistency in applying the framework, and the development of guidance documents to assist those using RWD to develop RWE to support FDA regulatory decisions.¹ The framework includes consideration of whether RWD are fit for use; whether the trial or study design used to generate RWE can provide adequate scientific evidence to answer or help answer the regulatory question; and whether the study conduct meets FDA regulatory requirements.¹

FDA currently uses RWE in safety surveillance and development of drugs for rare diseases, but there are other potential applications.¹⁸ The FDA program will focus on exploring the potential of RWD/RWE to support regulatory decisions about product effectiveness. Specifically, FDA's RWE Program will evaluate the potential use of RWE to support revisions to drug labeling such as changes in doses, dosing regimen or route of administration, and population or adding comparative effectiveness or safety information.¹ The framework also includes exploring the use of observational designs to generate RWE.

The FDA's Center on Devices and Radiological Health (CDRH) recently published guidance on the potential use of RWE for supporting initial decisions to approve or clear devices for use and includes the use a TPLC approach in their current strategic priorities.²¹ The guidance also addresses the use of RWE for post-marketing assurance of medical device safety and performance.⁷ Investigators have noted the high value of post-market evidence in evaluating the performance of modern medical devices outside of the context of a controlled clinical trial and have also noted that RWE can supplement or replace currently required post-approval studies, saving money and time.²²

CDER and CBER routinely use RWE to support post-marketing safety evaluation and, to a limited extent, to evaluate the effectiveness of medical products in certain rare diseases. CDER's and CBER's experience with Sentinel, a program described in more detail in Appendix A, is informing policy, guidance, frameworks, methods and platforms going forward. Sentinel is leading the way for CDRH to use RWE, from the National Evaluation System for Health Technology (NEST), in its product evaluations in pre- and post-market decisions; NEST is another program described in Appendix A.

Fit for Regulatory Purpose

The FDA states that any RWD/RWE used for regulatory purposes, including drug development and regulatory review, must be fit for purpose – it must be high-quality data that can support regulatory decision making and improve public health. Fit for purpose RWD requires data relevancy and data quality. The process of producing a fit for purpose RWD set begins with selection of one or more data sources, then cleaning, transforming, and linking data. Obtaining curated, high quality, unbiased data is a rate limiting step to obtaining RWE, which is labor intensive and costly.³

The Duke-Margolis Center for Health Policy and FDA published a framework in which they propose that developing RWE fit for regulatory purposes should be guided by the interplay of the regulatory question a sponsor seeks to address, the clinical context within which RWE is being generated, the availability of RWD that is both relevant and of acceptable quality; and the application of trusted methods for turning RWD into actionable evidence.²³

When RWE is identified and intended to be used in regulatory contexts, for example in the FDA's consideration of a new drug indication, labeling revision, safety revision, or risk-benefit profile, there are unique challenges that require careful consideration to characterize it as robust and representative of the population of interest.³ Not all research questions may be suitable for answering with RWE, traditional inferential statistics may be unable to identify clear treatment effects given variations in treatment effect definitions, clinical practice, and partial adherence to treatment, and it remains unclear how regulatory standards and compliance requirements designed for traditional clinical trials apply to RWE.²³ Additional work needs to be done to clarify the types of RWD and RWE that are robust enough to provide information to support regulatory guidance and decisions.²⁴

RWE vs. Traditional Clinical Trials

RCTs have traditionally served as the gold standard for generating evidence about medical products. RCTs are optimized to control variability and maximize data quality to produce data essential for regulatory approval by answering regulators' questions related to efficacy and safety.^{16,25} RCTs are often conducted with a narrowly defined group of patients and many investigators express concern that RCTs may not reflect the broad patient populations that will be exposed to an approved treatment in the real-world,²³ and that specific therapeutic interventions may perform differently in different patient cohorts based on age, gender, race, ethnicity, disease severity, comorbidities, or polypharmacy.^{17,25} RCTs are also complex, expensive, time consuming, and cannot answer all questions about a product or intervention.¹⁰ Some estimates state that clinical trials can take as long as seven years and cost more than \$2 billion.¹⁷ The FDA also recognizes that overly complex RCTs and unnecessary data collection can deter patient enrollment and discourage the development of second and third-to-market innovations and reducing competition and lowering prices.

According to the FDA framework, evidence from traditional clinical trials will not be considered RWE, but various hybrid or pragmatic trial designs and observational studies could generate RWE.^{1,14} Traditional RCTs, often referred to as explanatory trials generally measure efficacy – the benefit of a treatment under ideal conditions. Pragmatic trials measure effectiveness – the benefit of treatment in clinical practice. Pragmatic trials can test the same intervention as a traditional RCT, but they are conducted in real-world clinical practice settings, with typical patients and by qualified clinicians who may not have a research background, as detailed in the Salford Lung Study below.²⁶ Augmenting traditional RCTs with data from a broader, more diverse group of patients in different practice settings can increase the generalizability of trials, answer questions about subpopulations for treatments, or demonstrate proof of value to payers and patients, as has been done in some trials conducted within clinical registry populations.^{2,11,17} Many opportunities exist for leveraging RWE during the life cycle of product development (Figure 3).

Benefits of using RWD/RWE to support RCTs includes more efficient and targeted recruitment of patients for RCTs; expediting hypotheses generation to inform RCT design; identification of subpopulations with higher risk-benefit ratios; supporting the identification of drug development tools, such as biomarkers; trial feasibility assessment; supporting geographically distributed research cohorts; and improving the efficiency of studies for drugs approved under the FDA's expedited programs.^{1,17}

PRIVACY, SECURITY, AND ACCESSIBILITY

While many opportunities to leverage RWD and RWE to support regulatory efforts related to medical products exist, there are also barriers to their use.¹⁷ Among the biggest barriers to the use of RWD and RWE are data accessibility, privacy, and security concerns. While increasing the use of patient data is a priority for FDA and national thought leaders, also increasing is public, and AMA, concern about the secondary use of personal information. Noteworthy is a study evaluating RCT participant concerns about the risks of data sharing which found that most participants most were willing to share their data for a wide range of uses provided that adequate security safeguards were in place.²⁷

The Health Insurance Portability and Accountability Act of 1996 (HIPAA), safeguards the collection, storage, and disclosure of protected health information for covered entities, which includes health care entities and practitioners that electronically transmit health information, health plans, and clearinghouses.²⁸ HIPAA rules do not apply to deidentified health data, even as methods to reidentify individuals from other sources proliferate.²⁹ Privacy conversations related to RWD and RWE focus on ways to decrease risk of reidentifying deidentified data, data minimization, identifiers to remove from data sets, and expanding penalties and civil remedies available for data breaches and misuse, including reidentification attempts.³⁰

Access to RWD requires aggregation of the health data, which are usually stored in multiple silos and can suffer from incompatibility and data quality issues. Increasing the use of these data is challenging for several reasons including confidentiality and proprietary issues, costs and labor associated with raw data transformation, and incentives for data holders to share information that outweigh the disadvantages (for example, unauthorized use and competition).¹⁹

Data enclaves, secure networks through which confidential data can be stored and disseminated, are becoming popular.^{19,31} Data enclaves address two major barriers related to data sharing: data owners can maintain operational control of their data (granting permissions for analysis requests) and they eliminate the need to construct new, secure systems for each query or study.¹⁹ Multiple enclaves from different data owners can be linked to create data networks in which the systems format their data identically and execute identical analytic programs on the data. Typically, data enclaves in a network share aggregate results. Some data enclave networks, such as the FDA's Sentinel System, include the records of more than 100 million individuals.¹⁹

Networks can be centralized (for example, registries), decentralized (for example PCORnet and NEST), or distributed (for example, Sentinel). In a centralized system, all users are connected to a central network owner that stores data for others to access. Decentralized systems do not have one central owner, and instead use multiple central owners, each of which usually stores a copy of the resources users can access. In these models, data owners retain patient-level data behind the firewall of their institution, and issues related to the use and reuse of data resolved by the participants in the network.³² Distributed systems are similar to decentralized and do not have a single, central owner; users have equal access to data and share ownership of the data.

Additionally, patients are taking more control of their own data and creating shareable health records by authorizing data sharing from mobile applications, physician visits, pharmacy records, and more. Patients can share their

aggregated data upon request using an application such as Apple's new Health app. Using the Health app, patients and providers can share data and interact on Apple devices.³³ Over 350 health care institutions currently support this type of shareable health information.³⁴ However, substantial concerns remain about the potential for data misuse by third parties, especially when HIPAA does not apply.

DATA NETWORKS

Many stakeholders, including federal agencies, health systems, payers, and clinicians have made significant progress through investments in the curation, linkage, and analysis of electronic health-related data generated during the course of patient care. Much of these data are housed in clinical data warehouses or enclaves, organized into common data models, refreshed periodically, and subjected to quality assurance checks. Many of the networks are based on voluntary, nonexclusive collaborations in which institutions elect to participate in multi-center studies.

Several independent networks established and active for post-market medical product surveillance are now being leveraged to contribute to public-private collaboration for improved population-based evidence generation related to medical products on a much larger scale. Please see Appendix A for more details about several data networks.

RWE USE CASES

Although currently the most common use of RWE is retrospective analysis of existing data, increasingly, clinical trials are being conducted in real-world settings to improve the generalizability of results and to reduce inefficiencies related to establishing separate research infrastructures. These pragmatic clinical trials are conducted using existing clinical infrastructure to prospectively test interventions in every-day situations. Please see Appendix B for examples of RWE use cases.

CURRENT AMA POLICY

While no AMA policy currently addresses RWD or RWE specifically, AMA has extensive policy on related topics that were developed prior to the propagation of RWD and RWE. The relevant topics include data, registries, post-market surveillance, effectiveness evaluation, and clinical trials/drug approval. Because of the volume of related AMA policies referenced, please see Appendix C for the full text of policies.

Globally, AMA Policy H-100.992, "FDA," supports the principles that an FDA decision to approve a new drug, to withdraw the approval of a drug, or to change the indications for use of a drug must be based on sound scientific and medical evidence derived from controlled trials and/or post-market incident reports.

Data-related Policy

AMA Task Force to Address the Release of Physician Information. In 2007, AMA convened a task force to address the release of physician information. This task force was formed in response to physician profiling programs and "efficiency ratings." The task force assisted the AMA in the creation of Principles for the Public Release and Accurate Use of Physician Data, which provides a framework for the AMA to address the appropriate release and use of physical data in evaluating physician performance ("physician-specific data"). The task force also thought it was important for the AMA to specifically craft policy regarding the release and use of physician data by the federal government for all purposes ("physician data"). Board of Trustees (BOT) Report 18-A-09 details this task force and resulting recommendations that address safeguards for the release of physician data and physician profiles. The resulting AMA policy is guided by seven main principles: patient privacy safeguards; data accuracy and security safeguards; transparency requirements; review and appeal requirements; physician profiling requirements; quality measurement requirements; and patient satisfaction measurement requirements (Policies H-406.990, "Work of the Task Force on the Release of Physician Data," H-406.989, "Work of the Task Force on the Release of Physician Data," H-406.991, "Work of the Task Force on the Release of Physician Data," and H-406.996, "Use and Release of Physician-Specific Health Care Data").⁵⁷

Council on Legislation Workgroup on Health Care Data Transparency. In 2014, AMA's Council on Legislation (COL) established a workgroup to focus on health care data transparency. The intent of the workgroup was to develop guiding principles on the data and transparency efforts that should be pursued in order to improve care quality, reduce costs, prioritize the right set of regulatory reforms, and highlight innovative uses of health care data that benefit physicians. BOT Report 6-A-15 provides background on the health care data transparency and details the work of the COL.⁵⁸

The workgroup noted that our AMA has extensive policy on physician data transparency; however, it was created at a time when most of this information was not widely available and accordingly, focused on safeguards against releasing this information. The workgroup recognized the work of the 2007 task force, built on their policy recommendations (seven outlined principles) to reflect the new opportunities and potential uses of this information, and identified three components of a data transparency framework: transparency objectives and goals; data transparency resources; and challenges to transparency (Policy H-406.987, “Medical Information and Its Uses”).

The framework principles are intended to guide and develop AMA advocacy and policy as more data are sought by stakeholders and new uses of this information emerge. The framework principles recognize the new data environment and the need for physicians to engage in this area. Noteworthy statements in this policy include facilitation of more proactive use of health care data; support of the removal of barriers to accessing additional information from other payers and care settings, focusing on data that is valid, reliable, and complete; supporting definitions of quality based on evidence-based guidelines; promotion of efforts by clinical data registries, regional collaborations, Qualified Entities, and specialty societies to develop reliable and valid performance measures, increase data utility, and reduce barriers that currently limit access to and use of the health care data; and support of improvements in EHRs and other technology to capture and access data in uniform formats.

Data Ownership. Informational BOT Report 21-A-18 provided an overview of the current laws and regulations at the state and federal levels that address ownership, access, and use of patient data.⁵⁹ The report notes the importance of patients having appropriate access to their data and physicians having the tools and controls they need to be good stewards of their patients’ information while at the same time having the ability to share information to seamlessly coordinate the best care. Additionally, Policy D-315.984, “Ownership of Claims Data,” notes that our AMA will continue to monitor federal and state activities impacting the exchange of physician-generated health information, including claims data.

Additional Data-related Policy. Policy H-406.999, “Goal of Health Care Data Collection,” notes the AMA’s support for collection of health care data that can be used for education of both consumers and providers and made available to physicians and medical societies. AMA policy supports compliance with HIPAA Privacy and Security Rules and data accessibility to authorized users for purposes of treatment, public health, patient safety, quality improvement, medical liability defense, and research (Policy H-315.973, “Guiding Principles for the Collection, Use and Warehousing of Electronic Medical Records and Claims Data”).

Data Registries Policy

AMA policy encourages multi-stakeholder efforts to develop and fund clinical data registries for the purpose of facilitating quality improvements and research that result in better health care, improved population health, and lower costs. Additionally, policy encourages physicians and physician groups to participate in efforts to advance the development and use of clinical data registries and provides guidelines to help maximize opportunities for clinical data registries to enhance the quality of care provided to patients. AMA policy also notes that clinical registry data may be used to meet third-party quality reporting requirements with suggested guidelines and encourages a national clinical trial registry to promote subject safety, research quality, and to document previous trial participation (Policies H-450.933, “Clinical Data Registries” and D-460.972, “Creation of a National Registry for Healthy Subjects in Phase I Clinical Trials”).

Post-Market Surveillance/Adverse Event Reporting Policy

Several policies note our AMA’s support of post-market surveillance and adverse event reporting, including Ethical Opinion 8.8, “Required Reporting of Adverse Events,” which notes physicians’ responsibility to report suspected adverse events resulting from the use of a drug or medical device and Policy H-120.958, “Supporting Safe Medical Products as a Priority Public Health Initiative,” which encourages proper reporting of adverse events. Additional policies comment on the utility of manufacturer-conducted post-market surveillance to document long-term safety, effectiveness, and acceptance, encourages manufacturers to better study medication effects in pre- and post-marketing clinical trials, encourages mechanisms for data collection, monitoring, and analysis of medication-related problems by age group, and encourages the sharing of post-market surveillance information with the FDA (Policies H-75.990, “Development and Approval of New Contraceptives,” and H-100.968, “Improving the Quality of Geriatric Pharmacotherapy”).

Policy D-100.982, “Enhanced Physician Access to Food and Drug Administration Data,” urges the FDA to apply new tools to gather data after drugs are approved for marketing, including a broader use of targeted post-approval studies, institution of active and sentinel event surveillance, and data mining of available drug utilization databases.

Effectiveness Evaluation Policy

Policy H-110.986, “Incorporating Value into Pharmaceutical Pricing,” supports value-based pricing of pharmaceuticals that is evidence-based and the result of valid and reliable inputs and data that incorporate rigorous scientific methods, including clinical trials, clinical data registries, comparative effectiveness research, and robust outcome measures that capture short- and long-term clinical outcomes.

Clinical Trials/Drug Approval Policy

AMA has long-standing policy supporting clinical trials. Our AMA supports the development of transparent, collaboratively constructed clinical pathways that are implemented in ways that promote administrative efficiencies for both providers and payers; promote access to evidence-based care for patients; recognize medical variability among patients and individual patient autonomy; promote access to clinical trials; and are continuously updated to reflect the rapid development of new scientific knowledge (Policy H-410.948, “Clinical Pathways”). Additional policies include urging access to original source safety data from industry-sponsored trials upon request; support for ample federal funding of medical research, including basic biomedical research, translational research, clinical research and clinical trials, health services research, outcomes research, and prevention research; and support for accounting for the possible role of sex as a biological variable in vertebrate animal and human studies (Policies D-460.970, “Access to Clinical Trial Data,” H-460.926, “Funding of Biomedical, Translational, and Clinical Research,” and H-525.991, “Inclusion of Women in Clinical Trials”).

SUMMARY

Data are more widely collected, available, and accessible than in the past. Evidence and opportunities are mounting on ways to leverage new data sources as RWD and RWE to support regulatory efforts and value-based payment arrangements for medical products, yet privacy accessibility and privacy concerns remain. The FDA is actively engaged in understanding the potential of RWE to meet the established standards for adequate and well-controlled clinical investigations and pursuing its integration into drug development and regulatory review, the support of new indications for an approved drug, and its ability to satisfy post-approval study requirements. Advocates note that the use of RWD and RWE is crucial for incorporating patient experiences, currently often a gap in knowledge, into decision-making by drug companies, insurers, providers, and regulators.

In a 2017 Real-World Evidence Benchmark Survey, Deloitte noted that many health care stakeholders, including life sciences companies and others (payers, providers, regulators, and patients) are increasingly making high-impact decisions and attempting to demonstrate value using RWD.⁶⁰ The results of this survey illustrate that with its increasing availability and recognized worth, RWE has the potential to support, improve, and potentially accelerate the delivery of safe and cost-effective medical products.

If RWD and RWE are to be effectively leveraged for public health purposes, then shared learning and collaboration across clinicians, patients, health care systems, pharmaceutical companies, and regulators are necessary. An understanding of the limitations and barriers associated with the use of RWD must also be acknowledged and addressed. Recently, a group of former FDA commissioners offered recommendations and suggested requirements for advancing the generation and use of RWE to evaluate effectiveness and safety of drugs, biologics, and devices including adequate funding, regulatory clarity, access to data, improved data reliability and relevance, assured privacy and confidentiality, innovative, new models of drug development, and cooperation and collaboration.¹⁷

A component of the AMA’s strategic work starting in 2018 and beyond is to provide the physician perspective across health care technology sectors by promoting improved usability of and ready access to data for use in medical decision making and respect for the patient-physician relationship. Although extensive existing policies support the ideas and aims of RWD collection and the development of RWE, no policies specifically address the practice. As a leader in American medicine, our AMA has a unique opportunity to be a part of the evolving conversation related to the use of RWD and RWE for regulatory purposes.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following be adopted and the remainder of the report be filed:

1. Our AMA supports the generation and use of real-world data (RWD) and real-world evidence (RWE) fit for regulatory purpose to: (a) evaluate effectiveness and safety of medical products, while assuring patient privacy and confidentiality; (b) improve regulatory decision-making; (c) decrease medical product costs; (d) increase research efficiency; (e) advance innovative and new models of drug development; and (f) improve clinical care and patient outcomes.
2. Our AMA supports the aim of the U.S. Food and Drug Administration (FDA) to expand and clarify the use RWD and RWE in regulatory decision-making including in:
 - a. understanding the potential of RWE to meet the established standards for adequate and well-controlled clinical investigations;
 - b. pursuing the integration of RWE into medical product development and regulatory review; and
 - c. utilizing RWE to support new indications for approved medical products, and its ability to satisfy post-approval study requirements.
3. Our AMA supports that there be adequate funding of data infrastructure to allow for transparent data management capabilities, improved access to data by clinicians, especially physicians, as well as researchers and other stakeholders, and improved reliability and relevance of data.
4. Our AMA supports cooperation and collaboration of stakeholders to facilitate the collection and use of RWD and RWE that is deemed fit for regulatory purpose.
5. Our AMA will evaluate and develop a response to the educational needs of physicians seeking to understand the use of fit for purpose RWD and RWE in clinical practice.
6. That Policy H-100.992, “FDA,” be amended by addition to read as follows:

H-100.992, “FDA”

- (1) Our AMA reaffirms its support for the principles that: (a) an FDA decision to approve a new drug, to withdraw a drug's approval, or to change the indications for use of a drug must be based on sound scientific and medical evidence derived from controlled trials, real-world data (RWD) fit for regulatory purpose, and/or postmarket incident reports as provided by statute; (b) this evidence should be evaluated by the FDA, in consultation with its Advisory Committees and expert extramural advisory bodies; and (c) any risk/benefit analysis or relative safety or efficacy judgments should not be grounds for limiting access to or indications for use of a drug unless the weight of the evidence from clinical trials, RWD fit for regulatory purpose, and postmarket reports shows that the drug is unsafe and/or ineffective for its labeled indications.
 - (2) The AMA believes that social and economic concerns and disputes per se should not be permitted to play a significant part in the FDA's decision-making process in the course of FDA devising either general or product specific drug regulation.
 - (3) It is the position of our AMA that the Food and Drug Administration should not permit political considerations or conflicts of interest to overrule scientific evidence in making policy decisions; and our AMA urges the current administration and all future administrations to consider our best and brightest scientists for positions on advisory committees and councils regardless of their political affiliation and voting history.
7. That Policy D-100.982, “Enhanced Physician Access to Food and Drug Administration Data,” urging the FDA to apply new tools to gather data after drugs are approved for marketing, including a broader use of targeted post-approval studies, institution of active and sentinel event surveillance, and data mining of available drug utilization databases, be reaffirmed.
 8. That Policy H-110.986, “Incorporating Value into Pharmaceutical Pricing” supporting value-based pricing of pharmaceuticals that is evidence-based and the result of valid and reliable inputs and data that incorporate rigorous

scientific methods, including clinical trials, clinical data registries, comparative effectiveness research, and robust outcome measures that capture short- and long-term clinical outcomes, be reaffirmed.

9. That Policy H-406.987, “Medical Information and Its Uses,” identifying three components of a data transparency framework, be reaffirmed.
10. That Policy H-410.948, “Clinical Pathways,” supporting the development of transparent, collaboratively constructed clinical pathways that are implemented in ways that promote administrative efficiencies for both providers and payers; promote access to evidence-based care for patients; recognize medical variability among patients and individual patient autonomy; promote access to clinical trials; and are continuously updated to reflect the rapid development of new scientific knowledge, be reaffirmed.
11. That Policy H-450.933, “Clinical Data Registries,” encouraging multi-stakeholder efforts to develop and fund clinical data registries to facilitate quality improvements and research that results in better health care, improved population health, and lower costs be reaffirmed.
12. That Policy D-460.970, “Access to Clinical Trial Data,” urging the FDA to investigate and develop means by which scientific investigators can access original source safety data from industry-sponsored trials upon request; be reaffirmed.

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Figure 1. Scope of this report: Where does RWE fit into evidence-based practice?

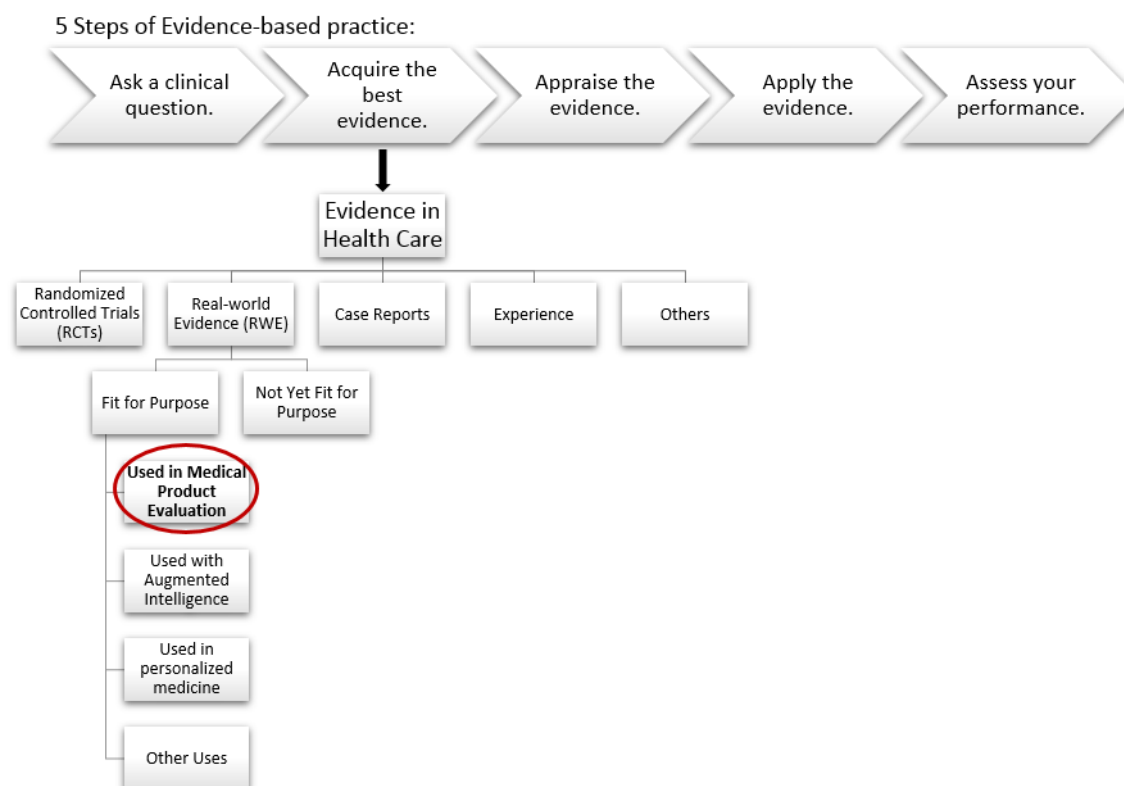


Figure 2.

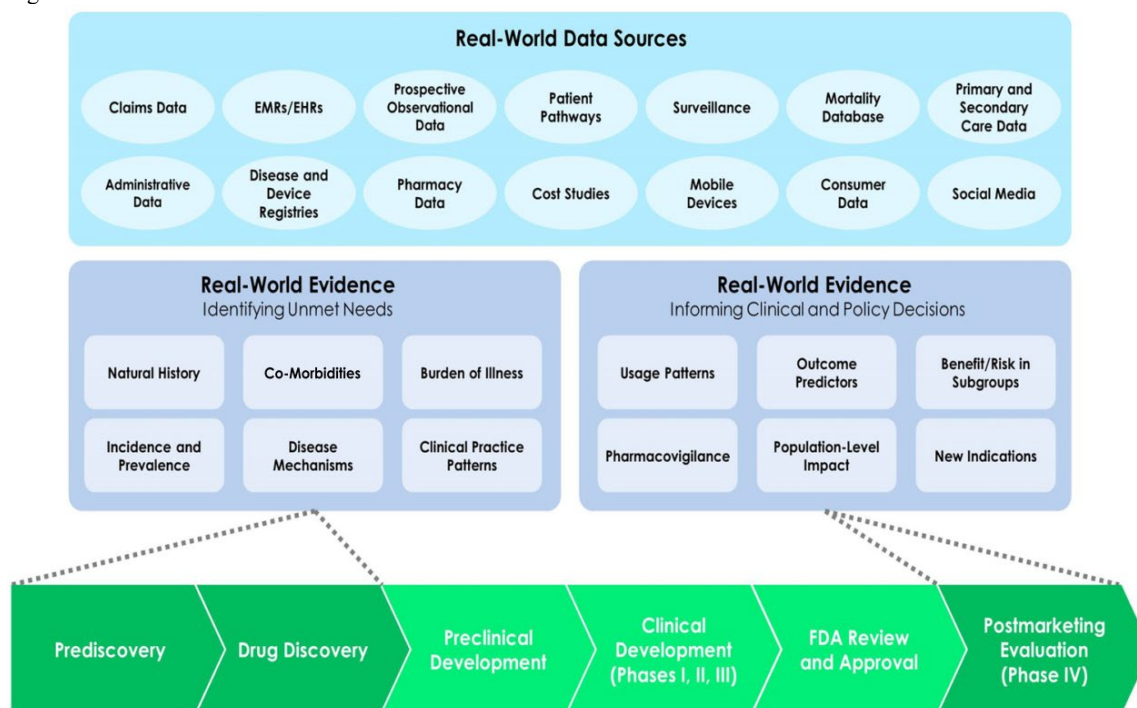
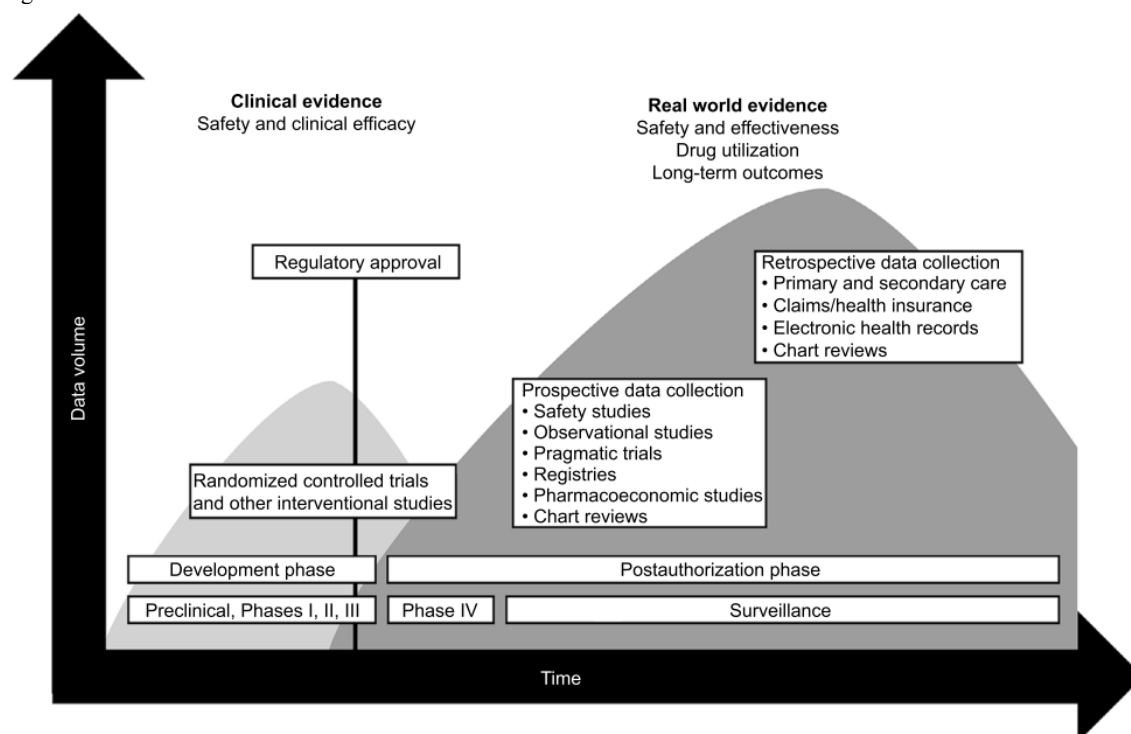


Figure 3.



APPENDIX A – Data Networks

The Sentinel Initiative

The Sentinel Initiative, launched in 2008, began as a Congressional mandate for the FDA to establish a public-private partnership to develop a medical product safety surveillance system using existing data.³⁵ The FDA partnered with over 200 health systems leaders, pharmacoepidemiologists, clinicians, data scientists, patient representatives, and more from 31 health plans and academic organizations to form the network.¹⁵

The principal component of the Sentinel Initiative is the Sentinel System, a multi-site, privacy-preserving, curated distributed data infrastructure, and suite of analysis tools.^{36,37} The FDA has used Sentinel to conduct more than 250 analyses, and it is now embedded in the regulatory review process through the Active Risk Identification and Analysis (ARIA) process.³⁸ ARIA is comprised of pre-defined, parameterized, reusable routine querying tools, and undergoes continuous quality checks and refreshes so analyses can be done quickly and efficiently for medical product safety surveillance.

The FDA recognizes the interest in generating effectiveness evidence and is exploring the potential of the Sentinel System to support studies of efficacy. As a part of this effort, the FDA is funding a study to explore whether observational methods can be used to replicate the results of approximately 30 clinical trials designed to provide evidence about the effectiveness of a drug. This project will assist the FDA in understanding how observational methods can be applied to evaluating drug effectiveness and may have the potential to provide evidence to inform regulatory decision-making.²

Additionally, FDA is increasing the scope of safety signals the Sentinel System evaluates by identifying opportunities to improve data, tools, and methods and has completed or has underway several projects related to patient and product safety:

- Sentinel data have informed regulatory decisions made by the FDA's Center for Drug Evaluation and Research and, in the past 2 years, have eliminated the need for post-marketing studies on nine potential safety issues associated with five products, as an example, ustekinumab and serious infections.¹⁵
- To explore how randomized trials can be conducted in real-world settings, the FDA is supporting the first randomized clinical trial in Sentinel. The IMPACT-Afib trial is testing an educational intervention to address underuse of effective medications to reduce the risk of stroke in patients with atrial fibrillation.^{2,15,39}

FDA released a Sentinel System Five-Year Strategy which details goals for the multi-purpose national data and scientific resource center for evidence-generation that can inform health care decision-making.⁴⁰ The strategy also details several data improvements FDA plans to prioritize including the following:

- Scaling capabilities related to the mother-infant linkage to evaluate in-utero exposure, medical product usage during pregnancy, and post-natal outcomes.
- Working to integrate national and state registry linkages including the National Death Index (NDI), Surveillance Epidemiology and End Results (SEER), and other rare-disease registries.
- Continuing to increase the number of validated Health Outcomes of Interest (HOIs) through medical record review, drawing from increased availability of EHR linkages.
- Expanding linkages to EHR data sources from Sentinel System Data Partners and exploring potential expansion to incorporate other data partners, such as the National Patient-Centered Clinical Research Network (PCORnet).
- Increasing the availability of full medical records, including improved access to the Medicare chart review process, prioritizing electronic sources from integrated delivery systems.

PCORnet

PCORnet originated with, and evolved through funding support from the Patient-Centered Outcomes Research Institute (PCORI) to develop a range of useful resources and partnerships. Currently, PCORnet is a network that supports patient-centered research and answers questions important to patients, caregivers, clinicians, and the broader health care community.⁴¹

PCORnet is a decentralized network that is governed by a steering committee composed of patient representatives and leaders from PCORnet's constituent organizations.⁴² PCORnet supported the largest study of bariatric surgery devices in adolescents.⁴³

MDEpiNet

The Medical Device Epidemiology Network (MDEpiNet) is a global public-private partnership that seeks to advance the collection and use of RWD to improve patient outcomes.⁴⁴ MDEpiNet brings together stakeholders from across the health ecosystem to develop and improve RWD infrastructure and carry out studies to better understand how devices perform in the real-world. MDEpiNet is also focused on developing better methods and medical device registries for medical device surveillance and post-market data collection.

NEST

In 2016, the FDA awarded the Medical Device Innovation Consortium (MDIC) \$3 million to establish the National Evaluation System for health Technology Coordinating Center (NESTcc). The MDIC was in 2012 as the first public-private partnership created with the objective of advancing medical device regulatory science throughout the total product life cycle.⁴⁵ NESTcc aims to support sustainable generation and use of timely, reliable, and cost-effective RWE throughout the lifecycle of medical devices using RWD to support decision-making for: regulatory purposes, patients and clinicians in clinical situations, health systems purchasing, and payer coverage.^{46,47} NESTcc has established partnerships with twelve network collaborators, including MDEpiNet, that represent more than 195 hospitals and 3,942 outpatient clinics to use high-quality RWD from various sources.

The goals of NESTcc include moving from passive surveillance to active, real-time surveillance, leveraging RWE to support regulatory decisions related to medical devices, making better use of data generated in the course of clinical care or by patients themselves, and moving away from lengthy, one-off, cost-prohibitive studies to an ecosystem that supports more routine evidence generation. NEST is setting data quality and methods standards related to observational and randomized studies; designating demonstration projects to assess feasibility and the ability to capture the data needed to support a range of studies and analyses; and offering value through products and services to key stakeholders in the ecosystem.

Registries

Device-specific and condition-specific registries have played an important role in generating clinical evidence on safety and effectiveness by collecting, curating, and analyzing data related to medical product use in routine practice over time.³² Registries collect patient-level data from health systems or physician practices through various pathways and are used for many purposes, including short- and long-term surveillance, fulfillment of post-market observational study commitments for regulatory bodies, and comparative safety and effectiveness assessments, including those in under-studied subpopulations.^{48,49} By linking medical product exposures and long-term outcomes, registries permit follow-up that can span decades.⁴⁸

Others

The TREND Community data collection platform and PatientsLikeMe are examples of online platforms created that allow for the systematic gathering of patient experience data.^{50,51} These online networks of consented patients and caregivers living with diseases are engaged in community discussions and sharing patient experiences. The communities connect scientists, doctors, therapists, research organizations, patients, and caregivers in real time and enable them to directly organize experiments and crowd-source the collection of RWD.

Over the past several years, several companies have emerged that specialize in the collection, curation, analysis of health care technology data. For example, Aetion®, a software platform company delivering the real-world analytics and RWE, recently partnered with the FDA and Brigham and Women's Hospital/Harvard Medical School to use its software platform to re-create RCTs through RWE. The study aims to demonstrate the value of RWE as an accelerant to drug approval, particularly for supplemental indications.⁵²

Box 1. More information on RWD networks

1. [Report an adverse event](#): Any adverse event experience by patients should be reported to the [FDA Adverse Event Reporting System \(FAERS\)](#)
2. [Sentinel](#)
3. [PCORnet](#)
4. [MDEpiNet](#)
5. [NEST](#)

APPENDIX B - RWE Use Cases

Salford Lung Study (Pragmatic (hybrid) Clinical Trial)

The Salford Lung Study assessed the effectiveness and safety of fluticasone furoate in patients with chronic obstructive pulmonary disease (COPD). In this 12 month, open-label, phase 3, multicenter study, 2799 patients with COPD were randomized to a once-daily inhaled combination of fluticasone furoate and vilanterol, or to continuation of their existing therapy. This study analyzed EHR data collected during all interactions of consenting patients with physicians, pharmacists and hospitals.⁵³

ADAPTABLE (Pragmatic (hybrid) Clinical Trial)

The ADAPTABLE (Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-Term Effectiveness) trial compares two commonly used doses of aspirin by randomizing 20,000 patients. The trial is integrated into routine clinical care with minimal inclusion/exclusion criteria and no treatment protocol requirement beyond the assignment to one of the two doses of aspirin. ADAPTABLE is using EHRs and claims data (through PCORnet) to capture primary endpoints such as death, hospitalization for non-fatal myocardial infarction or non-fatal stroke, and secondary endpoints such as coronary revascularization procedures, hospitalization for serious bleeding, and other patient-reported outcomes.^{1,54}

VALIDATE-SWEDEHEART (Pragmatic (hybrid) Clinical Trial)

The VALIDATE-SWEDEHEART (The Bivalirudin versus Heparin in ST-Segment and Non-ST-Segment Elevation Myocardial Infarction in Patients on Modern Antiplatelet Therapy in the Swedish Web System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies Registry) Trial was a registry-based, multicenter trial in which patients were randomized to bivalirudin or heparin during percutaneous coronary intervention. The endpoint was myocardial infarction, all-cause mortality, and major bleeding at 6 months. A national population-based Swedish registry platform was used for continuous enrollment, randomization, data collection, and follow up.^{1,55}

PatientsLikeMe – ALS (Patient Generated RWD)

A PatientsLikeMe community of patients with amyotrophic lateral sclerosis (ALS), a progressive and fatal neurodegenerative condition with no effective treatments, crowdsourced an observational study. Many patients with ALS in the community reported using lithium carbonate, which had shown promise in a small study but did not have regulatory approval for use in ALS. An observational study of drug usage and disease progression from quantitative data recorded by members of the community and matched control patients was conducted. No difference in disease progression was observed after 12 months between the two study groups; similar results were reported in a subsequent RCT. Experts note that these types of observational studies are not a substitute for RCTs, but suggest that data reported by patients in online health communities could be useful for accelerating clinical discoveries and evaluating the effectiveness of drugs in use.⁵⁶

APPENDIX C - Related AMA Policy

H-75.990, “Development and Approval of New Contraceptives”

Our AMA (1) supports congressional efforts to increase public funding of contraception and fertility research; (2) urges the FDA to consider the special health care needs of Americans who are not adequately served by existing contraceptive products when considering the safety, effectiveness, risk and benefits of new contraception drugs and devices; and (3) encourages contraceptive manufacturers to conduct post-marketing surveillance studies of contraceptive products to document the latter's long-term safety, effectiveness and acceptance, and to share that information with the FDA. (BOT Rep. O, I-91 Reaffirmed: Sunset Report, I-01 Modified: CSAPH Rep. 1, A-11)

H-100.968, “Improving the Quality of Geriatric Pharmacotherapy”

Our AMA believes that the Food and Drug Administration should encourage manufacturers to develop low dose formulations of medications commonly used by older patients in order to meet the special needs of this group; require geriatric-relevant labeling for over-the-counter medications; provide incentives to pharmaceutical manufacturers to better study medication effects in the frail elderly and oldest-old in pre- and post-marketing clinical trials; and establish mechanisms for data collection, monitoring, and analysis of medication-related problems by age group. (CSA Rep. 5, A-02 Reaffirmation A-10)

D-100.982, “Enhanced Physician Access to Food and Drug Administration Data”

Our AMA will: (1) urge the FDA to collaborate with physician organizations to develop better risk communication vehicles and approaches; (2) urge the FDA to apply new tools to gather data after drugs are approved for marketing, including a broader use of targeted post-approval studies, institution of active and sentinel event surveillance, and data mining of available drug utilization databases; (3) monitor the design and implementation of any independent drug safety board that may be instituted within the FDA, or external to the agency, and respond as appropriate; and (4) support adequate funding to implement an improved FDA postmarketing prescription drug surveillance process. (CSA Rep. 6, A-05 Modified: CSAPH Rep. 1, A-15)

H-100.992, “FDA”

(1) Our AMA reaffirms its support for the principles that: (a) an FDA decision to approve a new drug, to withdraw a drug's approval, or to change the indications for use of a drug must be based on sound scientific and medical evidence derived from controlled trials and/or postmarket incident reports as provided by statute; (b) this evidence should be evaluated by the FDA, in consultation with its Advisory Committees and expert extramural advisory bodies; and (c) any risk/benefit analysis or relative safety or efficacy judgments should not be grounds for limiting access to or indications for use of a drug unless the weight of the evidence from clinical trials and postmarket reports shows that the drug is unsafe and/or ineffective for its labeled indications.

(2) The AMA believes that social and economic concerns and disputes per se should not be permitted to play a significant part in the FDA's decision-making process in the course of FDA devising either general or product specific drug regulation.

(3) It is the position of our AMA that the Food and Drug Administration should not permit political considerations or conflicts of interest to overrule scientific evidence in making policy decisions; and our AMA urges the current administration and all future administrations to consider our best and brightest scientists for positions on advisory committees and councils regardless of their political affiliation and voting history. (Res. 119, A-80 Reaffirmed; CLRPD Rep. B, I-90 Reaffirmed; Sunset Report, I-00 Reaffirmation A-06 Appended; Sub. Res. 509, A-06 Reaffirmation I-07 Reaffirmation I-09 Reaffirmation I-10)

H-110.986, "Incorporating Value into Pharmaceutical Pricing"

1. Our AMA supports value-based pricing programs, initiatives and mechanisms for pharmaceuticals that are guided by the following principles: (a) value-based prices of pharmaceuticals should be determined by objective, independent entities; (b) value-based prices of pharmaceuticals should be evidence-based and be the result of valid and reliable inputs and data that incorporate rigorous scientific methods, including clinical trials, clinical data registries, comparative effectiveness research, and robust outcome measures that capture short- and long-term clinical outcomes; (c) processes to determine value-based prices of pharmaceuticals must be transparent, easily accessible to physicians and patients, and provide practicing physicians and researchers a central and significant role; (d) processes to determine value-based prices of pharmaceuticals should limit administrative burdens on physicians and patients; (e) processes to determine value-based prices of pharmaceuticals should incorporate affordability criteria to help assure patient affordability as well as limit system-wide budgetary impact; and (f) value-based pricing of pharmaceuticals should allow for patient variation and physician discretion.

2. Our AMA supports the inclusion of the cost of alternatives and cost-effectiveness analysis in comparative effectiveness research.

3. Our AMA supports direct purchasing of pharmaceuticals used to treat or cure diseases that pose unique public health threats, including hepatitis C, in which lower drug prices are assured in exchange for a guaranteed market size. (CMS Rep. 05, I-16 Reaffirmed in lieu of: Res. 207, A-17 Reaffirmed; CMS-CSAPH Rep. 01, A-17 Reaffirmed; CMS Rep. 07, A-18)

H-120.958, "Supporting Safe Medical Products as a Priority Public Health Initiative"

Our AMA will: (1) work through the United States Adopted Names (USAN) Council to adopt methodology to help prevent "look alike-sound alike" errors in giving new drugs generic names;

(2) continue participation in the National Patient Safety Foundation's efforts to advance the science of safety in the medication use process and likewise work with the National Coordinating Council for Medication Error Reporting and Prevention;

(3) support the FDA's Medwatch program by working to improve physicians' knowledge and awareness of the program and encouraging proper reporting of adverse events;

(4) vigorously work to support and encourage efforts to create and expeditiously implement a national machine-readable coding system for prescription medicine packaging in an effort to improve patient safety;

(5) participate in and report on the work of the Healthy People 2010 initiative in the area of safe medical products especially as it relates to existing AMA policy; and

(6) seek opportunities to work collaboratively within the Medicine-Public Health initiative

(H-440.991) and with the Food and Drug Administration (FDA), National Institutes of Health (NIH), United States Pharmacopoeia (USP) and Centers for Disease Control and Prevention (CDC) the Agency for Health Care Policy and Research (AHCPR) and the Centers for Medicare & Medicaid Services (CMS) to provide information to individual physicians and state medical societies on the need for public health infrastructure and local consortiums to work on problems related to medical product safety. (Res. 416, A-99 Appended; Res. 504, I-01 Reaffirmation A-10)

H-315.973, "Guiding Principles for the Collection, Use and Warehousing of Electronic Medical Records and Claims Data"

1. It is AMA policy that any payer, clearinghouse, vendor, or other entity that collects and uses electronic medical records and claims data adhere to the following principles: a. Electronic medical records and claims data transmitted for any given purpose to a third party must be the minimum necessary needed to accomplish the intended purpose. b. All covered entities involved in the collection and use of electronic medical records and claims data must comply with the HIPAA Privacy and Security Rules. c. The physician must be informed and provide permission for any analysis undertaken with his/her electronic medical records and claims data, including the data being studied and how the results will be used. d. Any additional work required by the physician practice to collect data beyond the average data collection for the submission of transactions (e.g., claims, eligibility) must be compensated by the entity requesting the data. e. Criteria developed for the analysis of physician claims or medical record data must be open for review and input by relevant outside entities. f. Methods and criteria for analyzing the electronic medical records and claims data must be provided to the physician or an independent third party so re-analysis of the data can be performed. g. An appeals process must be in place for a physician to appeal, prior to public release, any adverse decision derived from an analysis of his/her electronic medical records and claims data. h. Clinical data collected by a data exchange network and searchable by a record locator service must be accessible only for payment and health care operations.

2. It is AMA policy that any physician, payer, clearinghouse, vendor, or other entity that warehouses electronic medical records and claims data adhere to the following principles: a. The warehouse vendor must take the necessary steps to ensure the confidentiality, integrity, and availability of electronic medical records and claims data while protecting against threats to the security or integrity and unauthorized uses or disclosure of the information. b. Electronic medical records data must remain accessible to authorized users for purposes of treatment, public health, patient safety, quality improvement, medical liability defense, and research. c. Physician and patient permission must be obtained for any person or entity other than the physician or patient to access and use individually identifiable clinical data, when the physician is specifically identified. d. Following the request from a physician to transfer his/her data to another data warehouse, the current vendor must transfer the electronic medical records and claims data and must delete/destroy the data from its data warehouse once the transfer has been completed and confirmed. (CMS Rep. 6, I-06 Reaffirmed; BOT Rep. 17, A-13)

D-315.984, "Ownership of Claims Data"

Our AMA will: (1) encourage physicians to include language designed to buttress rights associated with claims data ownership and access when contracting with health plan payers and other third parties; (2) continue to educate physicians on providing public and private health plan payers the "minimum necessary," as defined in the Health Insurance Portability and Accountability Act (HIPAA) of 1996 and regulations thereunder, protected health information necessary to achieve the purpose of a disclosure; (3) assist physicians wishing to register a complaint against health plan payers that have used claims data to form a database, or that have permitted access to or sale of the database or its contents without explicit patient and/or physician authorization, beyond the scope permitted by HIPAA with the Department of Health and Human Services Office of Civil Rights; (4) advocate to the Department of Health and Human Services, Office of the National Coordinator of Health Information Technology and/or other appropriate agencies for rules and regulations ensuring appropriate physician ownership and access rights to claims data, and appropriate protection of claims data held by various parties; and (5) continue to monitor federal and state activities impacting the exchange of physician-generated health information, including claims data. (BOT Rep. 19, I-06 Modified: CCB/CLRPD Rep. 2, A-14)

H-406.987, "Medical Information and Its Uses"

DATA TRANSPARENCY PRINCIPLES TO PROMOTE IMPROVEMENTS IN QUALITY AND CARE DELIVERY

Our AMA seeks to help physicians improve the quality reporting of patient care data and adapt to new payment and delivery models to transform our health care system. One means of accomplishing this goal is to increase the transparency of health care data. The principles outlined below ensure that physicians, practices, care systems, physician-led organizations, patients and other relevant stakeholders can access and proactively use meaningful, actionable health care information to achieve care improvements and innovations. These principles do not replace but build upon existing AMA policies H-406.990, H-406.989, H-406.991, and H-406.996 that address safeguards for the release of physician data and physician profiles, expanding these guidelines to reflect the new opportunities and potential uses of this information.

Transparency Objectives and Goals

Engaging Physicians - Our AMA encourages greater physician engagement in transparency efforts, including the development of physician-led quality measures to ensure that gaps in measures are minimized and that analyses reflect the knowledge and expertise of physicians.

Promoting New Payment and Delivery Models - Our AMA supports appropriate funding and other support to ensure that the data that are used to inform new payment and delivery models are readily available and do not impose a new cost or additional burden on model participants.

Improving Care Choices and Decisions - Our AMA promotes efforts to present data appropriately depending on the objective and the relevant end-user, including transparently identifying what information is being provided, for what purpose, and how the information can or cannot be used to influence care choices.

Informing Physicians - Our AMA encourages the development of user interfaces that allow physicians or their staff to structure simple queries to obtain and track actionable reports related to specific patients, peer comparisons, provider-level resource use, practice patterns, and other relevant information.

Informing Patients - Our AMA encourages patients to consult with physicians to understand and navigate health care transparency and data efforts.

Informing Other Consumers - Our AMA seeks opportunities to engage with other stakeholders to facilitate physician involvement and more proactive use of health care data.

Data Transparency Resources

Data Availability - Our AMA supports removing barriers to accessing additional information from other payers and care settings, focusing on data that is valid, reliable, and complete.

Access to Timely Data - While some datasets will require more frequent updates than others, our AMA encourages use of the most current information and that governmental reports are made available, at a minimum, from the previous quarter.

Accurate Data - Our AMA supports proper oversight of entities accessing and using health care data, and more stringent safeguards for public reporting, so that information is accurate, transparent, and appropriately used.

Use of Quality Data - Our AMA supports definitions of quality based on evidence-based guidelines, measures developed and supported by specialty societies, and physician-developed metrics that focus on patient outcomes and engagement.

Increasing Data Utility - Our AMA promotes efforts by clinical data registries, regional collaborations, Qualified Entities, and specialty societies to develop reliable and valid performance measures, increase data utility and reduce barriers that currently limit access to and use of the health care data.

Challenges to Transparency

Standardization - Our AMA supports improvements in electronic health records (EHRs) and other technology to capture and access data in uniform formats.

Mitigating Administrative Burden - To reduce burdens, data reporting requirements imposed on physicians should be limited to the information proven to improve clinical practice. Collection, reporting, and review of all other data and information should be voluntary.

Data Attribution - Our AMA seeks to ensure that those compiling and using the data avoid attribution errors by working to correctly assign services and patients to the appropriate provider(s) as well as allowing entities to verify who or where procedures, services, and items were performed, ordered, or otherwise provided. Until problems with the current state of episode of care and attribution methodologies are resolved, our AMA encourages public data and analyses primarily focused at the system-level instead of on individual physicians or providers. (BOT Rep. 6, A-15)

H-406.989, "Work of the Task Force on the Release of Physician Data"

1. Our AMA Council on Legislation will use the Release of Claims and Payment Data from Governmental Programs as a basis for draft model legislation. 2. Our AMA will create additional tools to assist physicians in dealing with the release of physician data. 3. Our AMA will continue to monitor the status of, and take appropriate action on, any legislative or regulatory opportunities regarding the appropriate release and use of physician data and its use in physician profiling programs. 4. Our AMA will monitor new and existing Web sites and programs that collect and use data on patient satisfaction and take appropriate action when safeguards are not in place to ensure the validity of the results. 5. Our AMA will continue and intensify its extensive efforts to educate employers, healthcare coalitions and the public about the potential risks and liabilities of pay-for-performance and public reporting programs that are not consistent with AMA policies, principles, and guidelines. 6. Our AMA: A) opposes the public reporting of individual physician performance data collected by certification and licensure boards for purposes of MOC and MOL; and B) supports the principle that individual physician performance data collected by certification and licensure boards should only be used for the purposes of helping physicians to improve their practice and patient care, unless specifically approved by the physician. (BOT Rep. 18, A-09 Reaffirmed: BOT action in response to referred for decision Res. 709, A-10, Res. 710, A-10, Res. 711, A-10 and BOT Rep. 17, A-10 Reaffirmed in lieu of Res. 808, I-10 Appended: Res. 327, A-11 Modified: CCB/CLRPD Rep. 2, A-14)

H-406.990, "Work of the Task Force on the Release of Physician Data"

Release of Claims and Payment Data from Governmental Programs

The AMA encourages the use of physician data to benefit both patients and physicians and to improve the quality of patient care and the efficient use of resources in the delivery of health care services. The AMA supports this use of physician data only when it preserves access to health care and is used to provide accurate physician performance assessments.

Raw claims data used in isolation have significant limitations. The release of such data from government programs must be subject to safeguards to ensure that neither false nor misleading conclusions are derived that could undermine the delivery of appropriate and quality care. If not addressed, the limitations of such data are significant. The foregoing limitations may include, but are not limited to, failure to consider factors that impact care such as specialty, geographic location, patient mix and demographics, plan design, patient compliance, drug and supply costs, hospital and service costs, professional liability coverage, support staff and other practice costs as well as the potential for mistakes and errors in the data or its attribution.

Raw claims and payment data resulting from government health care programs, including, but not limited to, the Medicare and Medicaid programs should only be released:

1. when appropriate patient privacy is preserved via de-identified data aggregation or if written authorization for release of individually identifiable patient data has been obtained from such patient in accordance with the requirements of the Health Insurance Portability and Accountability Act (HIPAA) and applicable regulations;
 2. upon request of physicians [or their practice entities] to the extent the data involve services that they have provided;
 3. to law enforcement and other regulatory agencies when there is reasonable and credible reason to believe that a specific physician [or practice entity] may have violated a law or regulation, and the data is relevant to the agency's investigation or prosecution of a possible violation;
 4. to researchers/policy analysts for bona fide research/policy analysis purposes, provided the data do not identify specific physicians [or their practice entities] unless the researcher or policy analyst has (a) made a specific showing as to why the disclosure of specific identities is essential; and, (b) executed a written agreement to maintain the confidentiality of any data identifying specific physicians [or their practice entities];
 5. to other entities only if the data do not identify specific physicians [or their practice entities]; or
 6. if a law is enacted that permits the government to release raw physician-specific Medicare and/or Medicaid claims data, or allows the use of such data to construct profiles of identified physicians or physician practices. Such disclosures must meet the following criteria: (a) the publication or release of this information is deemed imperative to safeguard the public welfare; (b) the raw data regarding physician claims from governmental healthcare programs is: (i) published in conjunction with appropriate disclosures and/or explanatory statements as to the limitations of the data that raise the potential for specific misinterpretation of such data. These statements should include disclosure or explanation of factors that influence the provision of care including geographic location, specialty, patient mix and demographics, health plan design, patient compliance, drug and supply costs, hospital and service costs, professional liability coverage, support staff and other practice costs as well as the potential for mistakes and errors in the data or its attribution, in addition to other relevant factors. (ii) safeguarded to protect against the dissemination of inconsistent, incomplete, invalid or inaccurate physician-specific medical practice data.
- (c) any physician profiling which draws upon this raw data acknowledges that the data set is not representative of the physicians' entire patient population and uses a methodology that ensures the following: (i) the data are used to profile physicians based on quality of care provided - never on utilization of resources alone - and the degree to which profiling is based on utilization of resources is clearly identified. (ii) data are measured against evidence-based quality of care measures, created by physicians across appropriate specialties. (iii) the data and methodologies used in profiling physicians, including the use of representative and statistically valid sample sizes, statistically valid risk-adjustment methodologies and statistically valid attribution rules produce verifiably accurate results that reflect the quality and cost of care provided by the physicians. (d) any governmental healthcare data shall be protected and shared with physicians before it is released or used, to ensure that physicians are provided with an adequate and timely opportunity to review, respond and appeal the accuracy of the raw data (and its attribution to individual physicians) and any physician profiling results derived from the analysis of physician-specific medical practice data to ensure accuracy prior to their use, publication or release. (BOT Rep. 18, A-09 Reaffirmed: BOT Rep. 09, A-19 Modified: Speakers Rep., A-19)

H-406.991, "Work of the Task Force on the Release of Physician Data"

Principles for the Public Release and Accurate Use of Physician Data

The AMA encourages the use of physician data to benefit both patients and physicians and to improve the quality of patient care and the efficient use of resources in the delivery of health care services. The AMA supports this use of physician data when it is used in conjunction with program(s) designed to improve or maintain the quality of, and access to, medical care for all patients and is used to provide accurate physician performance assessments in concert with the following Principles:

1. Patient Privacy Safeguards
 - All entities involved in the collection, use and release of claims data comply with the HIPAA Privacy and Security Rules (H-315.972, H-315.973, H-315.983, H-315.984, H-315.989, H-450.947).
 - Disclosures made without patient authorization are generally limited to claims data, as that is generally the only information necessary to accomplish the intended purpose of the task (H-315.973, H-315.975, H-315.983).
2. Data Accuracy and Security Safeguards
 - Effective safeguards are established to protect against the dissemination of inconsistent, incomplete, invalid or inaccurate physician-specific medical practice data (H-406.996, H-450.947, H-450.961).
 - Reliable administrative, technical, and physical safeguards provide security to prevent the unauthorized use or disclosure of patient or physician-specific health care data and physician profiles (H-406.996, H-450.947, H-450.961).
 - Physician-specific medical practice data, and all analyses, proceedings, records and minutes from quality review activities are not subject to discovery or admittance into evidence in any judicial or administrative proceeding without the physician's consent (H-406.996, H-450.947, H-450.961).
3. Transparency Requirements
 - When data are collected and analyzed for the purpose of creating physician profiles, the methodologies used to create the profiles and report the results are developed in conjunction with relevant physician organizations and practicing physicians and are disclosed in sufficient detail to allow each physician or medical group to re-analyze the validity of the reported results prior to more general disclosure (H-315.973, H-406.993, H-406.994, H-406.998, H-450.947, H-450.961).
 - The limitations of the data sources used to create physician profiles are clearly identified and acknowledged in terms understandable to consumers (H-406.994, H-450.947).
 - The capabilities and limitations of the methodologies and reporting systems applied to the data to profile and rank physicians are publicly revealed in understandable terms to consumers (H-315.973, H-406.994, H-406.997, H-450.947, H-450.961).
 - Case-matched, risk-adjusted resource use data are provided to physicians to assist them in determining their relative utilization of resources in providing care to their patients (H-285.931).
4. Review and Appeal Requirements
 - Physicians are provided with an adequate and timely opportunity to review, respond and appeal the results derived from the analysis of physician-specific medical practice data to ensure accuracy prior to their use, publication or release (H-315.973, H-406.996, H-406.998, H-450.941, H-450.947, H-450.961).
 - When the physician and the rater cannot reach agreement, physician comments are appended to the report at the physician's request (H-450.947).
5. Physician Profiling Requirements
 - The data and methodologies used in profiling physicians, including the use of representative and statistically valid sample sizes, statistically valid risk-adjustment methodologies and statistically valid attribution rules produce verifiably accurate results that reflect the quality and cost of care provided by the physicians (H-406.994, H-406.997, H-450.947, H-450.961).
 - Data reporting programs only use accurate and balanced data sources to create physician profiles and do not use these profiles to create tiered or narrow network programs that are used to steer patients towards certain physicians primarily on cost of care factors (450.951).
 - When a single set of claims data includes a sample of patients that are skewed or not representative of the physicians' entire patient population, multiple sources of claims data are used.
 - Physician efficiency of care ratings use physician data for services, procedures, tests and prescriptions that are based on physicians' patient utilization of resources so that the focus is on comparative physicians' patient utilization and not on the actual charges for services.
 - Physician-profiling programs may rank individual physician members of a medical group but do not use those individual rankings for placement in a network or for reimbursement purposes.
6. Quality Measurement Requirements
 - The data are used to profile physicians based on quality of care provided - never on utilization of resources alone -- and the degree to which profiling is based on utilization of resources is clearly identified (H-450.947).
 - Data are measured against evidence-based quality of care measures, created by physicians across appropriate specialties, such as the Physician Consortium for Performance Improvement. (H-406.994, H-406.998, H-450.947, H-450.961).
 - These evidence-based measures are endorsed by the National Quality Forum (NQF) and/or the AQA and HQA, when available. When unavailable, scientifically valid measures developed in conjunction with appropriate medical specialty societies and practicing physicians are used to evaluate the data.
7. Patient Satisfaction Measurement Requirements
 - Until the relationship between patient satisfaction and other outcomes is better understood, data collected on patient satisfaction is best used by physicians to better meet patient needs particularly as they relate to favorable patient outcomes and other criteria of high quality care (H-450.982).

- Because of the difficulty in determining whether responses to patient satisfaction surveys are a result of the performance of a physician or physician office, or the result of the demands or restrictions of health insurers or other factors out of the control of the physician, the use of patient satisfaction data is not appropriate for incentive or tiering mechanisms.
- As in physician profiling programs, it is important that programs that publicly rate physicians on patient satisfaction notify physicians of their rating and provide a chance for the physician to appeal that rating prior to its publication. (BOT Rep. 18, A-09 Reaffirmation A-10 Reaffirmed: BOT action in response to referred for decision Res. 709, A-10, Res. 710, A-10, Res. 711, A-10 and BOT Rep. 17, A-10 Reaffirmation I-10 Reaffirmed in lieu of Res. 808, I-10 Reaffirmed in lieu of Res. 824, I-10 Reaffirmation A-11 Reaffirmed: BOT Rep. 17, A-13 Reaffirmed: Res. 806, I-13 Reaffirmation: A-19)

H-406.996, "Use and Release of Physician-Specific Health Care Data"

- (1) Our AMA advocates that third party payers, government entities and others that use and release physician-specific health care data adhere to the following principles: (a) Physicians under review and relevant physician organizations shall be provided with an adequate opportunity to review and respond to proposed physician-specific health care data interpretations and disclosures prior to their publication or release. (b) Effective safeguards to protect against the dissemination of inconsistent, incomplete, invalid, inaccurate or subjective physician-specific health care data shall be established. (c) Reliable administrative, technical, and physical safeguards to prevent the unauthorized use or disclosure of physician-specific health care data shall be developed. (d) Such safeguards shall treat all underlying physician-specific health care data and all analyses, proceedings, records, and minutes from quality review activities on physician-specific health care data as confidential, and provide that none of these documents shall be subject to discovery, or admitted into evidence in any judicial or administrative proceeding.
- (2) Our AMA supports release of severity-adjusted physician-specific health care data from carefully selected pilot projects where the data may be deemed accurate, reliable, and meaningful to physicians, consumers, and purchaser;
- (3) Our AMA urges that any published physician-specific health care data be limited to appropriate data concerning the quality of health care, access to health care, and the cost of health care;
- (4) Our AMA opposes the publication of physician-specific health care data collected outside of carefully selected pilot studies or where the data are not deemed accurate, reliable, or meaningful;
- (5) Our AMA urges that a copy of the information in any such profile be forwarded to the subject physician, and that the physician be given the right to review and certify adequacy of the information prior to any profile being distributed, including being placed on the Internet; and
- (6) Our AMA urges that the costs associated with creation of any such profiling system should not be paid for by physicians licensure fees. (BOT Rep. Q, I-92 BOT Rep. W, A-92 Reaffirmed: Res. 719, A-93 CMS Rep. 10, A-96 Appended: Res. 316, I-97 Reaffirmation A-01 Reaffirmation A-02 Reaffirmation A-05 Reaffirmed in lieu of Res. 724, A-05 Reaffirmed: BOT action in response to referred for decision Res. 709, A-10, Res. 710, A-10, Res. 711, A-10 and BOT Rep. 17, A-10)

H-406.999, "Goal of Health Care Data Collection"

The AMA (1) continues to advocate that health care data collected by government and third party payers be used for education of both consumers and providers; and (2) believes that government, third party payers and self-insured companies should make physician-specific utilization information available to medical societies. (BOT Rep. W, A-92 Reaffirmed: Res. 719, A-93 BOT Rep. Y, I-85 Reaffirmed CLRPD Rep. 2, I-95 CMS Rep. 10, A-96 Reaffirmed: CMS Rep. 8, A-06 Reaffirmed: CMS Rep. 01, A-16)

H-410.948, "Clinical Pathways"

Our AMA supports the development of transparent, collaboratively constructed clinical pathways that: (1) are implemented in ways that promote administrative efficiencies for both providers and payers; (2) promote access to evidence-based care for patients; (3) recognize medical variability among patients and individual patient autonomy; (4) promote access to clinical trials; and (5) are continuously updated to reflect the rapid development of new scientific knowledge. (Res. 708, A-16 Reaffirmed: CMS Rep. 06, A-18)

H-450.933, "Clinical Data Registries"

1. Our AMA encourages multi-stakeholder efforts to develop and fund clinical data registries for the purpose of facilitating quality improvements and research that result in better health care, improved population health, and lower costs.
2. Our AMA encourages national medical specialty societies, state medical associations, and other physician groups to join the National Quality Registry Network and to participate in efforts to advance the development and use of clinical data registries.
3. Our AMA supports flexibility in the development and implementation of clinical data registries. The following guidelines can help maximize opportunities for clinical data registries to enhance the quality of care provided to patients: a. Practicing physicians must be actively involved in decisions related to the development, maintenance and use of clinical data registries and registry data. b. Data elements, risk-adjustment models and measures used in the registry should be fully transparent. c. Registries should provide timely, actionable feedback reports to individual physicians or entities reporting at the organizational level. d. Registries and electronic health records should be interoperable, and should be capable of sharing and integrating information across registries and with other data sources in a HIPAA-compliant and confidential manner. e. Registry stewards should establish a formal process to facilitate the modification, expansion, or dissolution of the registry in order to accommodate advances in technology and changing clinical data needs to ensure continued utility of their registry.
4. Our AMA encourages physicians to participate in clinical data registries, and will encourage efforts that help physicians identify existing registries suitable for and of benefit to their patient populations and their practices.

5. Our AMA will continue to advocate for and support initiatives that minimize the costs and maximize the benefits of physician practice participation in clinical data registries.

6. Our AMA supports that, with the consent of the participating physician, physician-specific clinical registry data may be used to meet third-party quality reporting requirements, in accordance with the following principles: a. Data should be used to improve the quality of patient care and the efficient use of resources in the delivery of health care services. b. Data related to resource use and cost of care must be evaluated and reported in conjunction with quality of care information. c. Effective safeguards must be established to protect against the dissemination of inconsistent, incomplete, invalid or inaccurate physician-specific medical practice data. d. Case-matched, risk-adjusted quality measure and resource use data are provided to physicians to assist them in determining their relative utilization of resources in providing care to their patients. e. When data are collected and analyzed for the purpose of meeting quality reporting requirements, the methodologies used to create the profiles and report the results are developed in conjunction with relevant physician organizations and practicing physicians, and are disclosed in sufficient detail to allow each physician or medical group to re-analyze the validity of the reported results prior to more general disclosure. (CMS Rep. 8, A-14 Reaffirmed: CMS Rep. 05, I-16 Reaffirmed: CMS Rep. 10, A-17)

H-460.926, "Funding of Biomedical, Translational, and Clinical Research"

Our AMA: (1) reaffirms its long-standing support for ample federal funding of medical research, including basic biomedical research, translational research, clinical research and clinical trials, health services research, outcomes research, and prevention research; and (2) encourages the National Institutes of Health, the Agency for Healthcare Research and Quality and other appropriate bodies to develop a mechanism for the continued funding of translational research. (Sub. Res. 507, I-97 Reaffirmed: CSA Rep. 13, I-99 Modified: Res. 503, and Reaffirmation A-00 Modified: CSAPH Rep. 1, A-10)

H-460.943, "Potential Impact of Health System Reform Legislative Reform Proposals on Biomedical Research and Clinical Investigation"

The AMA, to encourage and support the continuing development of new advances in science and medicine and the development and implementation of meaningful quality assurance programs essential to improving the delivery of medical and health care in the United States, advocates:

- (1) Strong support and funding for medical education programs at all levels to attract and stimulate gifted students and physicians to receive training and experience in, and to participate in, basic science or clinically-oriented research programs.
- (2) Strong financial and policy support for all aspects of biomedical science and research, including: basic science research (investigator initiated grant-funded research) in a wide variety of fields; laboratory-based clinical studies (including surgical studies); clinical studies and therapy trials; clinical outcomes research; behavioral science research, including studies to assess implementation of health promotion and/or disease prevention activities; and technology transfer research, with an emphasis on diffusing information about, training personnel in, and encouraging appropriate use of new technologies.
- (3) Adequate federal funding for biomedical science programs, including an appropriate balance of funding for basic, clinical, health service, and public health/prevention research.
- (4) Support and funding for evaluation and implementation research, including drug and technology assessment, medical device review, and developing and setting standards for computerized medical records. (CSA Rep. 10, A-94 Reaffirmed: CSA Rep. 8, A-05 Reaffirmed: CSAPH Rep. 1, A-15)

D-460.970, "Access to Clinical Trial Data"

Our AMA: (1) urges the Food and Drug Administration to investigate and develop means by which scientific investigators can access original source safety data from industry-sponsored trials upon request; and (2) supports the adoption of universal policy by medical journals requiring participating investigators to have independent access to all study data from industry-sponsored trials. (Res. 503, A-14 Reaffirmed: Res. 907, I-15)

D-460.972, "Creation of a National Registry for Healthy Subjects in Phase I Clinical Trials"

Our AMA encourages the development and implementation of a national registry, with minimally identifiable information, for healthy subjects in Phase I trials by the US Food and Drug Administration or other appropriate organizations to promote subject safety, research quality, and to document previous trial participation. (Res. 913, I-11)

H-525.991, "Inclusion of Women in Clinical Trials"

Our AMA: (1) encourages the inclusion of women, including pregnant women when appropriate, in all research on human subjects, except in those cases for which it would be scientifically irrational, in numbers sufficient to ensure that results of such research will benefit both men and women alike; (2) supports the National Institutes of Health policy requiring investigators to account for the possible role of sex as a biological variable in vertebrate animal and human studies; and (3) encourages translation of important research results into practice. (Res. 183, I-90 Reaffirmed: Sunset Report, I-00 Reaffirmed: CSAPH Rep. 1, A-10 Modified: CSAPH Rep. 05, A-16 Reaffirmed: Res. 909, I-16)

8.8, "Required Reporting of Adverse Events"

Physicians' professional commitment to advance scientific knowledge and make relevant information available to patients, colleagues, and the public carries with it the responsibility to report suspected adverse events resulting from the use of a drug or medical device.

Mandated pre- and post-marketing studies provide basic safeguards for public health, but are inherently limited in their ability to detect rare or unexpected consequences of use of a drug or medical device. Thus spontaneous reports of adverse events, especially rare or delayed effects or effects in vulnerable populations are irreplaceable as a source of information about the safety of drugs and devices. As the professionals who prescribe and monitor the use of drugs and medical devices, physicians are best positioned to observe and communicate about adverse events.

Cases in which there is clearly a causal relationship between use of a drug/device and an adverse event, especially a serious event, will be rare. Physicians need not be certain that there is such an event, or even that there is a reasonable likelihood of a causal relationship, to suspect that an adverse event has occurred. A physician who suspects that an adverse reaction to a drug or medical device has occurred has an ethical responsibility to: (a) Communicate that information to the professional community through established reporting mechanisms. (b) Promptly report serious adverse events requiring hospitalization, death, or medical or surgical intervention to the appropriate regulatory agency.

AMA Principles of Medical Ethics: I,V,VII

Issued: 2016

3. PATIENT USE OF NON-FDA APPROVED CANNABIS AND CANNABINOID PRODUCTS IN HOSPITALS (RESOLUTION 414-A-19)

Reference committee hearing: see report of Reference Committee K.

HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS IN LIEU OF RESOLUTION 414-A-19 REMAINDER OF REPORT FILED

See Policy D-95.969

Resolution 414-A-19, introduced by the Oklahoma Delegation and referred by the House of Delegates asks:

That our American Medical Association offer guidance to medical staffs regarding patient use of non-US Food and Drug Administration approved medical marijuana and cannabinoids on hospital property, including product use, storage in patient rooms, nursing areas and/or pharmacy, with report back to the House of Delegates at the 2019 Interim Meeting.

METHODS

English language reports were selected from searches of the PubMed and Google Scholar databases from January 2009 to August 2019 using the search terms: “hospital policies” and cannabis; “hospital policies” and marijuana. Additional articles were identified by manual review of the reference lists of pertinent publications. Web sites managed by federal agencies and applicable professional organizations, including hospital associations, were reviewed for relevant information.

The Council on Science and Public Health acknowledges that the use of non-FDA approved cannabis and cannabinoid products presents challenges in health care facilities beyond hospitals (e.g., long-term care facilities, mental health and addiction facilities) and patients (e.g., visitors and employees), but those issues were deemed outside of the scope of this report.

CURRENT AMA POLICY

The AMA believes that scientifically valid and well-controlled clinical trials conducted under federal investigational new drug applications are necessary to assess the safety and effectiveness of all new drugs, including potential cannabis products for medical use. Furthermore, cannabis for medicinal use should not be legalized through the state legislative, ballot initiative, or referendum process. The AMA also supports legislation ensuring or providing immunity against federal prosecution for physicians who certify that a patient has an approved medical condition or recommend cannabis in accordance with their state's laws and believes that effective patient care requires the free and unfettered exchange of information on treatment alternatives and that discussion of these alternatives between physicians and patients should not subject either party to criminal sanctions (D-95.969, “Cannabis Legalization for Medicinal Use”).

The AMA urges that marijuana's status as a federal schedule I controlled substance be reviewed with the goal of facilitating the conduct of clinical research and development of cannabinoid-based medicines, and alternate delivery methods. This should not be viewed as an endorsement of state-based medical cannabis programs, the legalization of cannabis, or that scientific evidence on the therapeutic use of cannabis meets the current standards for a prescription drug product (H-95.952, "Cannabis and Cannabinoid Research").

STATUS OF CANNABIS UNDER FEDERAL LAW

Under the U.S. Controlled Substances Act (CSA) of 1970, cannabis is classified as a Schedule I controlled substance, meaning it has no currently accepted medical use in treatment in the United States, a lack of accepted safety for use under medical supervision, and a high potential for abuse.¹ This means that the cultivation, manufacture, sale distribution, and use of medical cannabis violates the CSA and constitutes a federal felony.

Cannabis is not FDA-approved as a safe and effective drug for any indication. However, the agency has approved three drug products containing synthetic versions of the main psychoactive ingredient of cannabis, delta-9 tetrahydrocannabinol (THC). Marinol® and Syndros™, which include the active ingredient dronabinol, are indicated for nausea and vomiting associated with cancer chemotherapy and anorexia associated with weight loss in patients with AIDS.³ Cesamet®, which contains the active ingredient nabilone, is also indicated for the treatment of the nausea and vomiting associated with cancer chemotherapy.²

The Agriculture Improvement Act of 2018 (Farm Bill) removed hemp from the CSA, which means that cannabis plants and derivatives that contain no more than 0.3 percent THC on a dry weight basis are no longer controlled substances under federal law.² However, the law explicitly preserved FDA's authority to regulate products containing cannabis or cannabis-derived compounds.² The FDA has approved one cannabis-derived product, Epidiolex®, which contains a purified form of the drug substance cannabidiol (CBD) for the treatment of seizures associated with Lennox-Gastaut or Dravet syndrome.³ The FDA has expressed concern at the proliferation of products asserting to contain CBD that are being marketed for therapeutic or medical uses that have not been approved by FDA.³ Since CBD has been studied as a new drug, it cannot be legally included in foods or dietary supplements. The FDA is currently considering potential regulatory frameworks for CBD.

STATUS OF CANNABIS UNDER STATE LAW

At the state level, trends in law have moved from decriminalization, to the legalization of medical use of cannabis, to cannabis regulated for adult use.⁴ California was the first jurisdiction in the United States to legalize the medical use of cannabis. Today, 33 states, the District of Columbia, Guam, Puerto Rico, and the U.S. Virgin Islands have legalized the medical use of cannabis through either the legislative process or ballot measures. These laws vary greatly by jurisdiction, from how patients access the product (home cultivated or dispensary), to qualifying conditions, product safety and testing requirements, packaging and labeling requirements, and consumption method (some states prohibit smoking the product). In jurisdictions that have legalized cannabis for medicinal use, physicians can "certify" or "recommend" a qualifying patient for the medicinal use of cannabis, but physicians cannot prescribe cannabis for medical purposes because it is illegal under federal law. In recent years, an additional 17 states have enacted laws allowing access to low THC/high CBD products for children with epilepsy.

In 2012, Colorado and Washington were the first U.S. jurisdictions to legalize the adult use of cannabis for recreational purposes. Today, a total of 11 states and the District of Columbia have legalized cannabis for adult use. Most of these jurisdictions have created for-profit, commercial cannabis production and distribution markets where the product is sold and taxed.

DISCUSSION

The AMA does not approve of state-based medical cannabis programs, the legalization of cannabis, or that scientific evidence on the therapeutic use of cannabis meets the current standards for a prescription drug product. Hospitals are being encouraged to accommodate patient use of cannabis.⁵ The primary argument for allowing patients to use cannabis in hospitals is focused on continuity of care. If patients have had success using cannabis for medicinal purposes, ending that treatment due to a hospital admission disrupts treatment and could lead to worse outcomes.⁵

Risks to Hospitals in Allowing Patient Use of Cannabis Products

Hospitals are subject to federal law because they receive reimbursement from federal programs. Since cannabis is a Schedule I controlled substance, its manufacture, distribution, or possession is a criminal offense. Hospitals that allow patient use of cannabis are at risk of violating federal law, losing their deemed status from Centers for Medicare and Medicaid Services (CMS), exposing themselves to possible penalties or sanctions, and losing federal funding.⁶⁻⁸

Physicians who maintain DEA licensure are also subject to federal law and are not permitted to prescribe a Schedule I substance. In addition to the prohibition on prescribing, the DEA also prohibits a practitioner from administering a Schedule I substance, which means that physicians and other clinicians with DEA licenses cannot administer cannabis. Doing so may jeopardize a clinician's federal DEA registration and their ability to prescribe controlled substances.

In addition to federal law, hospitals must also meet standards for pharmacies and medication management such as those established by hospital accreditation bodies.⁸ For example, The Joint Commission Standard MM.03.01.05 on Medication Management requires that: "[t]he hospital safely controls medications brought into the hospital by patients, their families, or licensed independent practitioners."^{8,9}

This standard includes the following elements of performance:

- The hospital defines when medications brought into the hospital by patients, their families, or licensed independent practitioners can be administered.⁹
- Before use or administration of a medication brought into the hospital by a patient, his or her family, or a licensed independent practitioner, the hospital identifies the medication and visually evaluates the medication's integrity.⁹
- The hospital informs the prescriber and patient if the medication brought into the hospital by patients, their families, or licensed independent practitioners is not permitted.⁹

One of the biggest challenges for hospitals in meeting this standard for cannabis would likely be identifying the medication and visually evaluating the medication's integrity.⁸ Depending on state law, the patient may be enrolled in the state's cannabis for "medicinal use" program and have their own supply from a state licensed manufacturer. However, the hospital would likely not want to assume responsibility for vetting the substance or any adverse effects the patient experiences as a result of the product.

Hospitals would also have to address medication storage concerns, particularly if cannabis products should be stored with the pharmacy department and treated as a controlled substance, by security personnel, or with the patient.¹⁰ There are also complicated logistics for self-administration of cannabis by the patient or caregiver. Many hospitals have policies on self-administration of medicines that permit patients to use their own medications only after identification and labeling by pharmacy personnel.

Since many hospitals have policies prohibiting smoking on facility grounds, hospitals would have to determine what preparations of cannabis would be allowed (e.g., oils or edibles).⁸ Hospitals should also be prepared to provide information to their medical staffs on cannabis withdrawal symptoms as well as possible cannabis or cannabinoid contraindications, drug interactions, or possible adverse effects.

State Laws Addressing Cannabis Use in Hospitals

Some states have tried to address cannabis use in hospital facilities by amending their state laws. Connecticut and Maine permit the use of cannabis by hospitalized patients and give some state-level legal protection for clinicians who administer it. Connecticut law provides that a nurse shall not be subject to arrest or prosecution, or penalized in any manner for administering cannabis to a qualifying patient or research program subject in a hospital or health care facility licensed by the Department of Public Health.¹¹

Maine has enacted protection for hospitals and long-term care facilities for use of edible cannabis products, tinctures, and salves by an admitted patient who has been certified for use of cannabis products under state law.¹² The law provides that hospitals and long-term care facilities are not subject to prosecution, search, seizure or penalty in any manner, including but not limited to a civil penalty or disciplinary action by an occupational or professional licensing board or entity, and may not be denied any license, registration, right or privilege solely because the admitted patient

lawfully engages in conduct involving the medical use of cannabis.¹² These protections also apply to officers or directors, employees or agents of a hospital or long-term care facility.¹²

Minnesota law provides that hospitals may adopt reasonable restrictions on use and storage of cannabis.¹³ The restrictions may include a provision that the provider will not store or maintain the patient's supply of cannabis, that the provider is not responsible for providing cannabis for patients, and that cannabis be used only in a place specified by the provider.¹³ Under Minnesota state law, employees of these facilities are not subject to violations under the statutes for possession while carrying out employment duties, such as providing or supervising care to a registered patient, or distribution of cannabis to a registered patient.¹⁴

The Minnesota Hospital Association (MHA) convened a broad group of stakeholders to discuss the impact of the state's cannabis law on hospital workflows as well as policies and procedures.¹⁵ The group produced template policies on cannabis for MHA members. The policies can be summarized as follows: (1) the hospital will not allow patient use of cannabis, (2) the hospital will allow inpatients to continue use while inpatient in the hospital and cannabis will be treated as self-administered home therapy, and (3) the hospital will allow inpatients to continue while inpatient in the hospital and cannabis will be treated as a medication and integrated within the hospital medical workflows.¹⁵ The templates provide hospitals with a helpful list of issues for consideration.

CONCLUSION

It is the AMA's position that scientifically valid and well-controlled clinical trials conducted under federal investigational new drug applications are necessary to assess the safety and effectiveness of all new drugs, including potential cannabis products for medical use. The AMA does not believe cannabis for medicinal use should be legalized through the state legislative, ballot initiative, or referendum process. Given the growing number of states that have legalized cannabis use, hospitals are increasingly likely to encounter patients who are taking cannabis or cannabis-related products. It has been argued that patients should be allowed to use non-FDA approved cannabis-related products to ensure continuity of care if they are admitted to the hospital. However, hospitals and physicians face legal risks in doing so given cannabis' status as a Schedule I controlled substance. Hospitals should consider the risks associated with allowing the use of non-FDA approved cannabis or cannabis-derived products by patients and develop policies to address this issue so patients and clinicians have clarity on what is permitted. Hospitals that decide to allow the use of non-FDA approved cannabis or cannabis-derived products should provide information to their medical staffs on cannabis withdrawal symptoms as well as possible cannabis or cannabinoid contraindications, drug interactions, or possible adverse effects.

RECOMMENDATIONS

The Council recommends that the following recommendation be adopted in lieu of Resolution 414-A-19, and the remainder of the report be filed.

The AMA encourages hospitals and health systems to: (1) not recommend patient use of non-FDA approved cannabis or cannabis-derived products within healthcare facilities until such time as federal laws or regulations permit its use and (2) educate medical staffs on cannabis use, effects and cannabis withdrawal syndrome.

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