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ADVERSE EVENTS

Surveillance Systems for Adverse Events and Medical Errors

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ADVERSE EVENTS: Surveillance Systems for Adverse Events and Medical Errors

Mr. Chairman and Committee Members:

I am pleased to have the opportunity to testify today as you consider issues related to adverse medical events in the nation's health care system. Adverse events are receiving considerable attention now as a result of the recent Institute of Medicine report on medical errors.[1] Adverse events are injuries to patients caused by medical treatment; medical errors are mistakes in medical care that may or may not lead to harm. Efforts to identify adverse events and evaluate their causes are important components of strategies to reduce harm to patients. Several of our recent reports have considered surveillance systems for medical products, particularly drugs and medical devices. For example, last week we released a report that synthesizes current research on adverse drug events (ADE).[2] We have also evaluated the Food and Drug Administration's (FDA) system for monitoring problems with medical devices.[3]

In summary, I believe that the results of our work have important implications for addressing adverse medical events including the design of surveillance systems to detect adverse events and medical errors. First, while adverse events have been recognized as a serious problem, the full magnitude of their threat to the health of the American public is unknown. Second, gathering valid and useful information about adverse events is extremely difficult. For example, all systems that rely on health care providers to take the initiative to make a report—known as passive or spontaneous reporting systems—have serious limitations. This is true whether or not providers are legally required to report adverse events; that is, both mandatory and voluntary spontaneous reporting systems share this limitation. Furthermore, many of the injuries patients suffer as a result of medical treatment do not stem from errors but reflect the inherent risks of treatments that are administered correctly. It can be difficult both to identify these adverse reactions and distinguish them from medical errors or from the course of a patient's underlying illnesses.

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[1] Institute of Medicine, *To Err Is Human: Building a Safer Health System* (Washington, D.C.: National Academy Press, 1999).

[2] *Adverse Drug Events: The Magnitude of Health Risk Is Uncertain Because of Limited Incidence Data* (GAO/HEHS-00-21, Jan. 18, 2000).

[3] *Medical Device Reporting: Improvements Needed in FDA's System for Monitoring Problems With Approved Devices* (GAO/HEHS-97-21, Jan. 29, 1997).

Little Is Known About The Incidence Of Adverse Events

Relatively little information exists on the incidence of adverse events of all types, including, for example, those caused by drugs, medical device malfunctions, and diagnostic mistakes. Aside from small studies of individual institutions, the best available information comes from two studies of statewide samples of hospitalized patients. The first assessed adverse events in New York in 1984, and the second employed a comparable approach to examine the incidence of adverse events in Utah and Colorado in 1992.[4] The widely cited estimate that 44,000 to 98,000 deaths per year are attributable just to medical errors comes from an extrapolation of the results of these two studies to the United States population as a whole. Although these studies are the best available, national estimates based on them have not taken into account regional variations in clinical practice patterns and patient characteristics.

The largest category of adverse events caused by medical treatment, about one-fifth of the total, consists of those brought about by drugs. Although it is clear that a wide range of commonly used drugs cause adverse drug events with potentially serious consequences for patients, relatively little is known about the frequency of ADEs. In part, this reflects the reality, which we discuss later, that identifying a medication as the cause of an adverse event can often be difficult and uncertain. Consequently, the available information on ADE incidence tends to be fragmentary and inconsistent. Data routinely collected on ADEs during clinical trials or after drugs have been marketed are intended to identify which ADEs are associated with particular drugs and do not focus on how often ADEs take place. Information on the overall incidence of ADEs from all drugs is limited to a few research studies that typically examine the experience of patients in one or two specific institutions—generally hospitals or sometimes nursing homes—leaving the overall incidence of ADEs in outpatient care largely unexplored.

The most broadly based information on ADE incidence comes from the two studies that I mentioned earlier. These studies applied a particularly restrictive definition of ADEs in finding that they occurred at a rate of 0.56 for every 100 patients admitted in Colorado and Utah and 0.72 per 100 admissions in New York. The studies counted only ADEs that resulted in disability, prolongation of a patient's hospital stay, or death, meaning that a significant fraction of the patients less seriously injured by drugs was omitted. Other studies that used broader definitions, but applied them in the context of specific institutions, found a range of 2 to 30 ADEs per 100

[4]T.A. Brennan and others, "Incidence of Adverse Events and Negligence in Hospitalized Patients: Results of the Harvard Medical Practice Study I," *New England Journal of Medicine*, Vol. 324, No. 6 (1991), pp. 370-76, and E.J. Thomas and others, "Incidence and Types of Adverse Events and Negligent Care in Utah and Colorado," *Medical Care*, forthcoming.

hospital admissions. There are still fewer published studies examining ADEs in nursing homes, and all are limited to one or two individual providers. Two of these studies reported an incidence of 0.44 to 0.71 ADEs per patient month, rates roughly comparable to the rate reported in one study of hospital ADEs that presented ADE incidence in terms of time spent in the hospital.

Useful And Valid Information About Adverse Events Is Difficult To Obtain

Recent proposals to increase our understanding of adverse events have focused on improving adverse event reporting systems. However, some of the inherent limitations of these systems are difficult to overcome. Further, it can be difficult to ascertain whether patient injuries or harm come from adverse events or their underlying illness, and many adverse events are not the result of medical errors.

Limitations of Spontaneous Reporting Systems

The Institute of Medicine has recently issued a set of recommendations on measures that the various components of the U.S. health care system can take to reduce the incidence of medical errors. Among their proposals was the suggestion that two types of medical error reporting systems be instituted: a mandatory system focusing on medical errors that resulted in serious injury or death and a voluntary system for reporting events in which errors occurred but led to at most minor injuries. While the proposal for voluntary systems has received widespread support, many provider and professional groups have raised concerns about establishing a national program of mandatory reporting of serious adverse events.

In our recent review of the research on adverse drug events, we learned what is known about the strengths and limitations of adverse event reporting systems of both the mandatory and voluntary variety. It is well known that all spontaneous reporting systems experience a high level of underreporting. For example, FDA believes that its system for gathering information about ADEs, the Adverse Event Reporting System (AERS), receives reports for only about 1 to 10 percent of all ADEs. Indeed, FDA relies on AERS primarily to generate “signals” of new adverse drug events that the agency can then investigate through other data sources.

Even mandatory systems can manifest extensive underreporting. For example, the Institute of Medicine collected detailed information on mandatory adverse event reporting programs in 13 states. According to these data, the state programs receive highly variable numbers of reports. For example, between 15,000 and 20,000 reports are submitted annually in New York, compared with approximately 4,300 in California. The Institute of Medicine did not cite any studies assessing the extent of underreporting

in the various state programs, but it noted the general presumption that to varying degrees all are affected by it. Thus, no one knows at this point what proportion of reportable cases is actually reported to any of the state systems.

There are many possible reasons for underreporting. Among those commonly cited are the fear of being blamed, the potential for legal liability, and an expectation that reports will not have any effect. In addition, depending on the definition of adverse events, and how that definition is interpreted, there may be considerable variability among health care providers and institutions about the kinds of events that are reported. Some of the examples of serious adverse events to be covered by the Institute's proposed mandatory reporting program are relatively unambiguous—a maternal death, for instance. But others, such as "serious injuries associated with the use of a new device, operation, or medication," are not as clear because they are based on judgments of the causes of patient injury, not an easily observed clinical outcome.

Various measures can be taken to address some of these disincentives to reporting and thereby increase the number of reports submitted. These include protecting the confidentiality of reporters and making it easier to file reports. Both were part of a pilot study FDA sponsored of a new system for collecting reports about adverse events for medical devices. That study received adverse event reports at a rate ten times greater than in the current medical device surveillance system, even though the current system mandates the reporting of the same types of events. However, because the reporters may be unknown in a confidential reporting system, it is much harder to follow up reports in order to clarify important information that may be ambiguous or missing. A truly confidential reporting system places a significant burden on adverse event reports to contain all the information that a regulatory agency, or a product's manufacturer, needs or will need in the future to understand the potential public health risk.

Moreover, underreporting is only part of the problem. The bigger difficulty is that the subset of adverse events that are reported does not accurately reflect the universe of all adverse events. The available studies indicate that there is substantial bias in reporting. In the area of drug-related events, we found that a wide variety of factors could affect the likelihood of reporting. For example, more reports are received during a drug's first few years on the market than later, and drug manufacturers with extensive postmarketing surveillance efforts gather more reports than other companies do. Therefore, it is not legitimate to infer that patterns or

trends that emerge in reported events reflect what is happening with adverse events overall.

To get valid information on the incidence of adverse events, we need data that do not come from a spontaneous reporting system. This generally involves a proactive examination of a random sample of patient records, as was done in both the New York and Utah and Colorado studies that I mentioned earlier. In fact, the Institute of Medicine report supports having a new organization, a Center for Patient Safety, collect data on the incidence of adverse events through studies of this type. More such studies are needed if we are to have accurate data on the magnitude of the problem that adverse events represents.

However, studies based on large, representative samples of patient records tend to be expensive and time consuming to complete. Therefore, there will always be the temptation to draw implicit inferences from the more readily available data from the existing adverse event reporting systems about where medical errors are most likely to occur and how much progress, if any, has been made in reducing them. The Institute of Medicine's recommendation to implement standard definitions and formats for the mandatory reporting of serious adverse events is likely to encourage greater reliance and use of those reports. Standardizing definitions cannot overcome the nonrepresentative quality of reported adverse events. Standardized definitions and formats will, however, enhance the utility of adverse reports for other types of analyses that are not concerned with incidence. For example, they will facilitate analyses of multiple instances of a particular type of adverse event. Such analyses can help identify the key underlying factors that explain why these adverse events occur.

Even with the limitations of mandatory and voluntary reporting systems, the information they generate can help in reducing medical errors and associated adverse events. In some cases, the fact that a particular kind of adverse event occurred one or more times and has been reported is sufficient to motivate action and dictate its direction. In those cases, incident reporting systems can function effectively and may have substantial advantages. However, it is often important to understand the frequency of a particular type of error and whether that has changed over time. In these cases, the incomplete data coming from reporting systems may not be sufficient. It is better to rely then, if possible, on data that derive from an examination of a sample of patient records.

Many Adverse Events Are Not Caused by Medical Errors

Efforts to reduce adverse events should not focus exclusively on those caused by errors. The available studies indicate that just over half of adverse events of all types are caused by errors in treatment. The study of New York hospital discharges found that 58 percent of adverse events were preventable, compared with 53 percent in the corresponding study of Utah and Colorado hospital patients. This means that nearly as many adverse events result from appropriate medical treatment as from errors.

The proportion of adverse events involving drugs that is due to medical error is even lower. Available data suggest that one-half to two-thirds of ADEs occur when drugs have been used appropriately. Many of these ADEs are the result of a drug's known pharmacological properties and are often listed on the medication's label. For example, hemorrhaging is the most common adverse reaction for warfarin, a drug that reduces the risk of heart attack, stroke, and other conditions by decreasing the clotting ability of blood. Other adverse reactions, including allergic reactions, are less predictable, caused by sensitivities in individual patients who have no history of adverse reactions to a specific drug. Still other adverse reactions are related to previously undetected risks. These include drug-drug and drug-food interactions that become evident as a drug is used by many types of patients, having many kinds of concurrent illnesses, and taking many other medications, as well as over-the-counter drugs and dietary supplements. FDA's system for collecting voluntary reports on adverse experiences with marketed drugs is designed specifically to uncover these kinds of previously unknown risks.

Many types of drugs can cause adverse reactions. Some drug classes are associated with a substantial number of adverse reactions mainly because they are prescribed to many patients. These include antibiotics, narcotic analgesics, drugs to control hyperglycemia in type II diabetics, psychotropic drugs such as antidepressants and tranquilizers, and nonsteroidal anti-inflammatory drugs (NSAIDs). However, some classes of drugs have notably lower rates of adverse reactions despite high rates of use. Antihistamines and the statin drugs prescribed to lower cholesterol levels are rarely associated with serious adverse reactions.

Patients who are very ill, including those with several concurrent diagnoses, have a greater risk of adverse reaction than others do. Not only are they more fragile but their illnesses may require several simultaneous treatments. In addition, they may be receiving more aggressive treatments that are known to entail significant risks. Some reports have found that elderly persons and women have more adverse reactions than younger persons and men. However, it is possible that age and gender are merely related to other risk factors instead of independently increasing the

likelihood of an adverse reaction. In some studies, controlling for the number of medications being taken substantially diminishes any relationship between age and adverse reactions.

As with medical errors, passive surveillance systems are inadequate for measuring the frequency or rate of adverse drug reactions. Other kinds of studies are required to develop this information. Thus, adverse reactions that develop after the prolonged use of a drug require studies with long follow-up periods to determine whether the adverse events are related to the drug. Similarly, rare adverse reactions require studies with very large numbers of patients to accumulate a sufficient number of problematic cases, and adverse symptoms that mimic those of a patient's underlying condition require carefully controlled clinical trials. For example, the Cardiac Arrhythmia Suppression Trial found that antiarrhythmia medications doubled the risk of cardiac arrest and death in heart attack survivors. This was not detected in clinical practice (nor fully captured in spontaneous reporting systems) because patients with heart disease regularly have arrhythmias and heart attacks, providing a ready alternative explanation that masked the causal role of the drugs. It has been estimated that these medications caused up to 50,000 premature deaths.[5]

In conclusion, surveillance systems that uncover and document adverse events can collect valuable data, but they are not sufficient, by themselves, to improve medical care. The data need to be analyzed and interpreted to create a better understanding of the reasons for adverse events. Sometimes one adverse event, if carefully examined, can provide insights of this sort. At other times, analysts need to assess multiple examples of a particular type of event to discern the critical causal factors. However, for both types of analysis, the quality of the data that are collected is critical. Accurate information on the process of care provided and the patient's response to that care is required to determine the key factors that led to an adverse event. Thoughtful analyses can then use these data to identify specific changes in health care systems and processes that can reduce the likelihood of adverse events caused by both medical errors and the normal risks of adverse outcomes inherent in all medical interventions.

This concludes my prepared statement, Mr. Chairman. I will be happy to respond to any questions that you or members of the committees may have.

[5]See D.S. Echt and others, "Mortality and Morbidity in Patients Receiving Encainide, Flecainide, or Placebo," *New England Journal of Medicine*, Vol. 324, No. 12 (1991), pp. 781-88.

GAO Contact And Acknowledgments

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