

Clarifying Adverse Drug Events: A Clinician's Guide to Terminology, Documentation, and Reporting

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Adverse drug events cause substantial morbidity and mortality, yet they remain underappreciated and misunderstood. The terminology to describe errors and patient harm associated with medications causes much confusion. This article uses the case study of a patient with multiple adverse drug events to clarify key terms, such as *adverse event*, *adverse drug reaction*, *adverse drug event*, *medication error*, and *side effect*. The case discussion illustrates clinical approaches to analyzing the causal connection between a

suspect drug and an adverse event. Examples and rationale for meaningful documentation of adverse drug events are provided, along with an outline of the types of events that should be reported to regulatory agencies.

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Since the early 1990s, adverse drug events have received significant attention from researchers in quality and patient safety (1). Nationally recognized quality experts have identified adverse drug events as a top safety priority (2) because these events are the most common type of iatrogenic injury (3). Studies have indicated that adverse drug events occur almost daily in medium-sized hospitals and outpatient panels (4–6). However, despite the high morbidity and mortality, physicians often do not recognize or appropriately treat instances of drug-related harm (7, 8).

We believe that inadequate recognition and treatment of drug-related harm are, in part, a result of what has been called a Tower of Babel of terminology (1). Terms originally developed in the narrow context of drug effects in a clinical and regulatory setting are now being applied in the broader context of quality improvement in health care delivery systems (9). As might be expected, the expanding role of these terms has been coupled with their use in contradictory ways, even within the same discipline (4, 7, 10–14). In this paper, we use the case of an actual patient as a framework to explain the recognition, treatment, documentation, and reporting of drug-related harm.

ADVERSE EVENTS VERSUS ADVERSE DRUG REACTIONS

Mr. J. was a 70-year-old man with nephrotic syndrome (thought to be related to a congenital single kidney), pneumoconiosis, and a history of gout and myocardial infarction. He presented to the hospital with increasing bilateral leg edema and pain, for which he had been taking over-the-counter ibuprofen, 400 mg three times a day for 3 days and once a day for the preceding 3 weeks. His other outpatient medications were simvastatin, 40 mg at bedtime; aspirin, 81 mg once daily; and metoprolol, 50 mg twice daily. In the emergency department, his serum creatinine level was 680 $\mu\text{mol/L}$ (7.7 mg/dL), much higher than the baseline of 290 $\mu\text{mol/L}$ (3.3 mg/dL) 11 months earlier. He was admitted to the hospital.

The patient experienced an adverse event while using

ibuprofen. Is this event a side effect, an adverse drug reaction, a medication error, or an exacerbation of his underlying renal and cardiac disease?

Terms that initially arose from the field of pharmacovigilance, such as *adverse event* and *adverse drug reaction*, can help physicians relate the edema and renal failure to ibuprofen. Pharmacovigilance is the study of drug-related injuries for the purpose of making warning or withdrawal recommendations for pharmaceutical products. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, of which the U.S. Food and Drug Administration (FDA) and the World Health Organization are members, defines an adverse event as “any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment” (15). The term *adverse event* is not particularly helpful to physicians, but it provides context for the more clinically useful term *adverse drug reaction*. The International Conference on Harmonisation defines an adverse drug reaction as “a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function” (15). Therefore, an adverse drug reaction is an adverse event with a causal link to a drug. Table 1 (16–20) summarizes these key terms.

ASSESSING CAUSAL ASSOCIATIONS

After admission to the hospital, a battery of serologic tests, a microscopic urine examination, and abdominal ultrasonography did not yield specific information about the origin of Mr. J.'s exacerbated renal failure.

Assessing causal connections between agents and disease is fundamental to the practice of medicine and to the understanding of adverse drug reactions (21, 22). In this

Table 1. Summary of Definitions Relevant to Drug-Related Harm

Term	Definition*	Example
Harm occurred		
Adverse event	Harm in a patient administered a drug but not necessarily caused by a drug (16)	Traumatic death while taking lovastatin
Adverse drug reaction	Harm directly caused by a drug at normal dose [†] (16) <i>Unexpected adverse drug reaction: An adverse drug event whose nature or severity is not consistent with the product information (17)</i>	Congestive heart failure from metoprolol
Adverse drug event	Harm caused by the use of a drug (4, 18) <i>Effective definition in common practice: Harm caused by a drug or the inappropriate use of a drug</i>	Hematoma from tirofiban overdose
Harm may have occurred		
Medication error	Inappropriate use of a drug that may or may not result in harm (19)	Failure to renew prednisone order on transfer to medical ward
Side effect	A usually predictable or dose-dependent effect of a drug that is not the principal effect for which the drug was chosen; the side effect may be desirable, undesirable, or inconsequential (17)	(This term should be avoided when considering adverse events)
Harm did not occur		
Potential adverse drug event	Circumstances that <i>could</i> result in harm by the use of a drug but <i>did not</i> harm the patient	Receipt of roommate's felodipine but no resulting hypotension

* Definitions are abstracted from cited sources. See text for original definitions.

† The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use recently dropped the dose limits for adverse drug reactions, but it is not clear whether or when the U.S. Food and Drug Administration will adopt these revised definitions (20).

Table 2. Grades of Certainty That an Event Is Linked to a Drug*

Level	Criteria
Certain	A clinical event, including an abnormal laboratory test result, that occurs in a plausible time relationship to drug administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge) [†] should be clinically plausible. The event must be pharmacologically or phenomenologically definitive, with use of a satisfactory rechallenge [‡] procedure if necessary.
Probable/Likely	A clinical event, including an abnormal laboratory test result, that occurs within a reasonable time sequence to administration of the drug, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal (dechallenge) [†] . Rechallenge [‡] information is not required to fulfill this definition.
Possible	A clinical event, including abnormal laboratory test result, that occurs within a reasonable time sequence to administration of the drug but could also be explained by concurrent disease or other drugs or chemicals. Information on drug withdrawal may be lacking or unclear. [‡]
Unlikely	A clinical event, including an abnormal laboratory test result, whose temporal relationship to drug administration makes a causal relationship improbable and in which other drugs or chemicals or underlying disease provides plausible explanations.

* Adapted with permission from Elsevier (*The Lancet*, 2000;356:1255-9) (16).

† For adverse drug events caused by withdrawal for or reduced dose of a drug, *dechallenge* is restoring the previous drug dose and *rechallenge* is reducing the drug dose or withdrawing the drug again.

‡ Although an adverse drug event may rate only as “possible” soon after discovery, it can be flagged as requiring more information and later be upgraded to probable or certain as appropriate.

case, the treatment and prognosis for Mr. J.’s renal failure largely depend on whether it was exacerbated by ibuprofen or was due to the progression of his underlying disease.

The discipline of pharmacovigilance has yielded tools (16, 23–25) to assess the likelihood of a causal connection between a drug and an adverse event on a case-by-case basis. These tools address the following criteria: time relationships between the drug use and the adverse event, pathophysiology of the adverse event, competing causes for the adverse event, response to dechallenge (for example, discontinuation of therapy with the drug or dose reduction), and response to rechallenge (for example, drug re-administration). Table 2 organizes these criteria to gauge the causal link between a drug and an adverse event in terms of 4 discrete levels of certainty (certain, probable/likely, possible, and unlikely).

The causality criteria listed in Table 2 can be applied to the case of Mr. J. The timing and classic pathophysiologic association of ibuprofen with the edema and worsening renal failure may first seem to result in a *certain* causal association. However, other explanations for the event, such as advancing intrinsic renal failure or cardiac disease, are present, and information on the effect of drug withdrawal is not available at this point in the hospitalization. These conditions result in a *possible* causality rating, which accurately captures the uncertainty in the causal analysis. The strength of a causal association may be revised as more information becomes available.

The day after admission, Mr. J. developed painful, swollen joints. After sodium urate crystals were found in the synovial fluid, polyarticular gout was diagnosed and prednisone therapy was started. Despite administration of a 1-L normal saline challenge and subsequent high-dose furosemide, the patient remained oligo-

ric with an elevated creatinine level. Before dialysis could begin, he became hypertensive; the metoprolol dose was increased to 100 mg twice a day. Within 2 hours of the increased metoprolol dose, the patient developed respiratory distress and was transferred to the medical intensive care unit, where he was intubated and pulmonary edema was diagnosed.

Admitted because of 2 adverse events—edema and renal failure—Mr. J. developed 4 subsequent adverse events: a gout flair, hypertension, pulmonary edema, and respiratory distress. A consideration of pathophysiologic pathways and causal associations can also help the physician identify adverse drug reactions in complex clinical scenarios.

The basic unit of an adverse event is the sequence of pathophysiologically related events originating from one pharmacologic effect of the drug. In Mr. J.'s case, the presumed pharmacologic effect was the inhibited production of prostaglandin in the afferent glomerular arteriole, which led to decreased plasma filtration. The consequent events of uric acid retention, sodium retention, and fluid retention all resulted from ibuprofen's inhibition of prostaglandin production.

In general, a drug may be considered a contributory cause of an adverse event if, had the drug not been administered, 1) the event would not have happened at all, 2) the event would have occurred later than it actually did, or 3) the event would have been less severe. Ibuprofen may have contributed to the edema and may have exacerbated renal failure. The fluid bolus increased the fluid overload and may have caused hypertension. The subsequent increase in metoprolol probably contributed to cardiac decompensation and pulmonary edema. In contrast, the gout flair is a renal failure-mediated secondary or indirect effect (17) of ibuprofen and does not merit consideration as a separate adverse drug reaction.

MEDICATION ERROR

After spending 2 days in the medical intensive care unit and having several liters of fluid removed by dialysis, Mr. J. was extubated and prepared for transfer to the medical ward. Just before transfer, he became tachycardic and diaphoretic; an electrocardiogram showed new precordial T-wave inversions. After consultation with the cardiologist, the intern prescribed 12.5 µg of tirofiban. The pharmacy prepared and the nurse administered 12.5 mg—a thousand-fold overdose. The patient developed a 3-cm hematoma on the back of his hand at a previous venipuncture site and oozing from his dialysis catheter site. He underwent urgent, prolonged dialysis and multiple blood laboratory checks.

Misreading physician orders and preparing a dangerous dose of a drug is a classic medication error. Medication error is commonly defined as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures and systems, including prescribing; order communications; product labeling, packaging and nomen-

clature; compounding; dispensing; distribution; administration; education; monitoring; and use. (19)

Most medication errors do not harm patients. Some authors estimate that less than 1% of medication errors result in harm (26). Some types of errors may present minimal potential for harm, such as a missed dose of simvastatin. Other types of errors pose substantial risk to the patient but are intercepted before reaching the patient; these have been called *near misses*, *close calls*, or *potential adverse drug events* (27). For example, the nurse who was about to administer the tirofiban to Mr. J. might have noticed that the dose was inappropriate and could have returned the drug to the pharmacy.

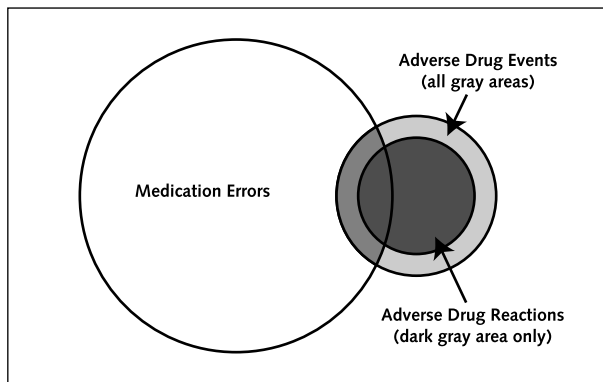
ADVERSE DRUG EVENT VERSUS ADVERSE DRUG REACTION

Several days after Mr. J. was transferred back to the medical ward, his gout recurred. It was discovered that the intern did not include the prednisone prescription when she wrote orders for the patient's transfer back to the medical ward.

The overdose of tirofiban and the recurrence of gout are 2 medication errors that help illustrate the differences between an adverse drug reaction and an adverse drug event. An adverse drug reaction occurs at usual doses and is caused by the action of the drug, such as renal failure due to ibuprofen. Because the hematoma from tirofiban was the result of an abnormally high dose, it does not qualify as an adverse drug reaction. The gout recurrence was a consequence of the unmasking of the underlying disease rather than the action of a drug itself, so this too is not an adverse drug reaction. Pharmacovigilance, as practiced by regulatory bodies, is primarily concerned with adverse drug reactions—the properties of the drug under normal use. The patient safety community is interested in harm resulting from a broader range of events, such as these 2 medication errors. The broader interests of the patient safety movement have reinforced the need for a term other than adverse drug reaction and have led to the adoption of the term *adverse drug event*.

The use of the term *adverse drug event* is consistent both between the pharmacovigilance and patient safety communities and within the patient safety community itself. The FDA recognizes the term *adverse drug event* to be a synonym for *adverse event*, in which a causal association may not exist between the event and the drug (28). In the patient safety literature, the terms *adverse drug event* and *adverse event* usually denote a causal association between the drug and the event (3), but there is a wide spectrum of definitions for these terms, including harm caused by a drug (7, 10), harm caused by drug use (4), and a medication error with or without harm (29).

We recommend the definition of adverse drug event adopted by the Institute of Medicine: “an injury resulting from medical intervention related to a drug” (3, 4), which has been simplified to “an injury resulting from the use of a drug” (18). Under this definition, the term *adverse drug event* includes harm caused by the drug (adverse drug re-

Figure. Relationships of key terms.

The gray areas represent injuries caused by drug use (adverse drug events). The dark gray area represents harm caused by a drug (adverse drug reactions). The light gray area represents harm from appropriate drug use that is generally excluded from studies of adverse drug events. Medication errors are much more common than adverse drug events, but they result in harm less than 1% of the time (30). Conversely, about one quarter of adverse drug events are due to medication errors (4).

actions and overdoses) and harm from the use of the drug (including dose reductions and discontinuations of drug therapy). The term *adverse drug event* does not include failure to use a drug in the first place, which is not a use of a drug. Although this definition is broad, the patient safety literature generally limits adverse drug event by excluding nonserious injuries resulting from appropriate dose titration and disease recurrences resulting from appropriate reductions or discontinuations of therapy with the drug. These implicit limitations according to appropriateness have resulted in a close relationship between the terms *medication error* and *adverse drug event* (medium gray area in the Figure) (30).

RECOGNIZING AND TREATING ADVERSE DRUG EVENTS

The day after the tirofiban overdose, the patient reported lower abdominal pain. Since admission, the patient had been taking narcotics and, when not intubated, calcium carbonate, 1.25 g 3 times a day. Nursing flow sheets and dietary notes indicated almost daily that, despite eating, the patient had not passed stool since admission. On hospital day 13, the patient was given 1 dose of milk of magnesia and began receiving docusate sodium. The patient responded with 1 small bowel movement. Indomethacin was started, presumably to reduce the patient's narcotic requirement. Several days later, Mr. J. vomited and was given droperidol. Otherwise, Mr. J. was improving and was discharged from the inpatient medicine service to the rehabilitation service. The next morning the patient had a second bowel movement—5 days after the first. About an hour later, the patient vomited during breakfast, developed respiratory distress, and was reintubated.

Physicians fail to recognize a majority of adverse drug events (7, 8) for many reasons. Many physicians find nursing notes difficult to read and may ignore these data, but

nursing data may provide the only indication for 40% of all adverse drug events (31). Physicians also commonly classify gastrointestinal adverse drug reactions as “side effects” and believe them to be common and unavoidable consequences of medical care, not clinically significant manifestations of disease. Constipation from narcotics and nausea from antibiotics are examples of adverse drug reactions that frequently occur but seldom cause serious outcomes. However, even though only a small percentage of these events are serious, these “side effects” are so common that serious manifestations, as exemplified by Mr. J.’s case, are not rare (4, 7, 18, 32). The international pharmacovigilance community has recognized that the term *side effect* tends to minimize the injury from drugs and has recommended that this term no longer be used (17).

The failure to recognize an adverse drug reaction as such may lead the physician to inappropriately treat the adverse drug event (33). In this case, the physician did not pursue a diagnosis for the nausea and abdominal pain but instead treated the symptoms with droperidol. The pervasive problem of treating each successive drug-related symptom with another medication exposes the patient to additional drug hazards. In this case, the patient was put at risk for sedation, delirium, or cardiac dysrhythmias from the droperidol. To avoid multiple adverse drug events, the more appropriate action often is to discontinue therapy with the original drug.

DOCUMENTING ADVERSE DRUG EVENTS

The purpose of documenting adverse drug events in a patient’s chart is to help prevent the recurrence of the harm. The more likely an event is to recur and the more serious the event, the stronger the case for documentation and the stronger the incentive to guard against similar use of the drug in the future. Events that are likely to recur are those that have a high causal association with the drug and that result from a common use of the drug. Thus, probable and certain adverse drug reactions are nearly always appropriate to document in the patient chart. For events that are less likely to recur, the physician must consider the seriousness and nature of the event. For example, a life-threatening, possible adverse drug reaction merits documentation. However, documentation is unlikely to prevent the recurrence of an adverse drug event due to an unusual error, such as the tirofiban overdose. These types of errors are better reported through an institution’s incident reporting system.

Documentation is most likely to prevent future adverse drug events when it serves either to caution against the use of a drug at any dose or to establish practical, unsafe dosing ranges. Allergies are common examples of idiosyncratic reactions that make the drug’s use inappropriate at any dose. Dose-dependent reactions are nearly 8 times more frequent than idiosyncratic reactions (7); not including dose information in documentation is a major,

missed opportunity for injury prevention. In Mr. J.'s example, metoprolol was well tolerated at 25 and 50 mg twice a day but not at higher doses. (A second episode of pulmonary edema also occurred after he received two 50-mg doses several hours apart.) Although high doses are more likely to cause adverse drug reactions (4), doses that are too low might also unmask disease. When drugs are suppressing a chronic disease, such as a dysrhythmia or seizure disorder, and the disease recurs after discontinuation of therapy with the drug or dose reduction, the unsafe dose should be documented to avoid unmasking the disease again in the future.

A meaningful and useful record of an adverse drug event combines all 3 of these factors: the severity of the event, the causal association between the drug use and the event, and dosing variables. In this case, for example, intravenous morphine at 2 mg 3 to 4 times daily possibly led to severe constipation (no stool for 13 days) and probably contributed to nausea and vomiting that resulted in aspiration and intubation. Contributors were calcium carbonate for the constipation and indomethacin for nausea and vomiting.

Finally, it is important to document adverse drug events in an accessible part of the medical record. Although many physicians discuss the differential diagnosis of adverse drug events in their progress notes, they may note only the drug's name in the allergy section of the chart. A more detailed description in the allergy section may help another physician decide whether subsequent use of the drug is contraindicated. Because most hospitalizations and clinic visits do not involve an adverse drug event, the burden of improved documentation is small. Table 3 provides other examples of meaningful documentation for some of Mr. J.'s adverse drug reactions. In all, Mr. J. had at least 10 adverse drug events; none of his events were documented in the allergy or adverse drug event section of the medical record.

Mr. J.'s respiratory status rapidly improved, and he was extubated the next day. Shortly afterward he had a dark, guaiac-positive stool; therapy with indomethacin was stopped. Two days later and hours before anticipated discharge, the patient vomited and aspirated his breakfast. He developed extensive bilateral pneumonitis and pneumonia. Mr. J. died the next evening.

REPORTING TO REGULATORY AGENCIES

It might appear that at least one of Mr. J.'s adverse drug events should be reported to the FDA, but this is not the case. Documenting adverse drug events in the patient's chart and reporting adverse drug reactions to regulatory agencies are distinctly different activities (Table 4). The FDA is interested in receiving reports on serious, unexpected adverse drug reactions (not adverse drug events) from marketed drugs. Unexpected reactions are those whose nature or severity is not consistent with the product label (17). The FDA and international regulatory bodies

Table 3. Suggested Components and Examples of Meaningful Documentation of Adverse Drug Events

Components

Drug, dose (for dose-dependent adverse drug events), causality assessment, description of events/outcomes, including contributing factors

Examples

Ibuprofen, 400 mg 3 times daily, possibly exacerbated renal failure, with creatinine level increasing from 290 to 680 $\mu\text{mol/L}$ (3.3 to 7.7 mg/dL) and 3+ edema.

Metoprolol, 100 mg twice daily, probably precipitated congestive heart failure and respiratory failure within 2 hours of the increased dose: once in the setting of renal failure, fluid overload, and aspiration and once in the setting of aspiration alone. Metoprolol, 25–50 mg twice daily, was well tolerated.

Intravenous morphine, 2 mg 3–4 times daily, possibly led to severe constipation and probably contributed to nausea and vomiting resulting in aspiration and intubation. Contributors were calcium carbonate for constipation and indomethacin for nausea and vomiting.

Indomethacin, 50 mg 3 times daily, possibly led to gastritis, nausea, and vomiting, resulting in aspiration and intubation. Prednisone may have contributed to gastritis, and morphine may have contributed to nausea and vomiting.

(The hematoma from the tirofiban overdose and the gout recurrence from the inadvertently discontinued prednisone are medication errors that should not be documented in the adverse drug event section of the patient's medical record.)

define serious events as those resulting in death, life-threatening experiences, prolonged or initial hospitalization, significant or persistent disability, or a congenital anomaly or requiring intervention to prevent one of these outcomes (28). The FDA has discouraged reports on events that are neither unexpected nor serious, except for events associated with newly marketed drugs (34). While nearly all of Mr. J.'s adverse drug events were serious, none is convincingly unexpected in nature or severity.

The FDA has set up a voluntary reporting system for physicians called MedWatch that encourages and facilitates the reporting of serious, unexpected adverse drug reactions. MedWatch forms can be obtained at www.fda.gov/medwatch/report/hcp.htm or through the pharmacy departments at most hospitals. Online reporting is also available at the preceding Web site.

After a drug is marketed, physicians may be the only source of information the FDA has for rare and potentially fatal adverse drug events. However, physicians frequently neglect this crucial role. As few as 1% of serious and unexpected events are estimated to be reported to the FDA (35). Underreporting can lead to substantial delays in dissemination of warnings and product labeling changes (36). Most institutions facilitate reporting by making pharmacists available to complete and submit these reports. If a pharmacist is not available in the outpatient setting, the physician can use online tools to fill out a MedWatch report; personnel at the FDA will communicate with the physician if the report needs clarification or correction.

Table 4. Comparison of Documentation and Reporting of Adverse Drug Events*

Events and Reports	Document in Patient's Chart	Report to FDA
Types of events		
Drug-related injuries	Probable or certain adverse drug reactions Life-threatening, possible adverse drug events Dosing ranges specific to the patient that resulted in adverse drug events Adverse drug events resulting from medication errors that may be repeated with normal drug use	Unexpected and serious adverse drug reactions: Serious reactions result in death, life-threatening experiences, prolonged or initial hospitalization, clinically significant or persistent disability, or a congenital anomaly or require intervention to prevent one of the above (28).
Error/potential adverse drug events	Not relevant	Not usually relevant (Confusing drug labeling is an exception.)
Properties of reports		
Goal	Prevent recurrence of an adverse drug event in one patient	Contribute to labeling or withdrawal recommendations
Determination of causation	Physician determines casual link between drug and event for each case	FDA determines causation from multiple cases. Physician provides information to facilitate this determination.
Where to report	Physician documents in allergy or adverse drug event section of patient chart	Physician (or, for inpatients, usually pharmacist) submits MedWatch report to FDA: www.fda.gov/medwatch
Voluntary or mandatory	Required for good clinical care	Voluntary but encouraged

* FDA = U.S. Food and Drug Administration.

CONCLUSION AND TAKE-HOME POINTS

We propose that a better understanding of terms will help clinicians recognize and treat drug-related injuries (Table 5). Adverse drug reactions are injuries caused by drugs administered at usual doses; they are the primary focus of regulatory agencies and postmarketing surveillance. Adverse drug events are injuries caused by drug use that encompass adverse drug reactions and harm resulting

from medication errors; they are the targets of broader efforts to improve patient safety.

All adverse drug events, including those that are common symptoms, warrant careful attention and evaluation, rather than rote management via standing orders. Nursing documentation is a rich source of information about adverse drug events that manifest as patient discomfort.

The clinical value of accurate documentation of adverse drug events is that it assists future determinations of whether the risks of prescribing a specific drug or drug class outweigh the drug's potential benefits for an individual patient. Providing information on the causal association of the drug and the event is therefore useful. Physicians or pharmacists are strongly encouraged to report unexpected, serious adverse drug reactions to the FDA using the MedWatch system, which requires information similar to but more extensive than that recommended for documentation in a patient's chart (37).

Health care institutions must integrate allergy and adverse drug event reports into the care delivery process. The first step is to expand allergy documentation to accommodate all types of adverse drug events. An important next goal is to integrate the reports electronically into the order-checking process to give nursing and pharmacy personnel the opportunity to intercept potential adverse drug events before they occur.

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Table 5. Key Points for Definitions, Causal Assessment, Documentation, and Reporting

Definitions
<i>Adverse event</i> and <i>adverse drug reaction</i> are regulatory terms; the first does not require a causal link between the drug and the event, the second does.
<i>Adverse drug events</i> extend beyond adverse drug reactions to include harm from overdoses and underdoses usually related to medication errors. A minority of adverse drug events are medication errors, and medication errors rarely result in adverse drug events.
The term <i>side effect</i> should be avoided.
Causal assessment: grades of causation
<i>Certain:</i> dechallenge and rechallenge information corroborates causation
<i>Probable:</i> dechallenge information corroborates causation
<i>Possible:</i> competing explanations are plausible
<i>Unlikely:</i> timeline is improbable
Documentation
Documentation helps determine whether subsequent use of a drug in possibly different circumstances is contraindicated.
Considerations of seriousness and causation should drive the decision about whether to document adverse drug reactions.
Meaningful descriptions of adverse drug events include the grade of causation, a description of the event or outcome, contributing or competing factors, and dose information.
Reporting
Serious and unexpected adverse drug events should be reported to the U.S. Food and Drug Administration.
Information for causal assessment is a crucial and often neglected portion of reports.

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