



Commentary

## Demystifying medication safety: Making sense of the terminology

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### Abstract

*Background:* Although there is a growing interest in medication safety, there remains much confusion about the terminology used to describe the problem. Some have described the classification of medication safety terminology as haphazard.

*Objective:* The purpose of this commentary is to help provide some direction by clarifying the terminology.

*Methods:* A review of the medication safety literature was performed. A description of commonly used terms is provided and the implications of the misuse of terminology are discussed.

*Results:* There are inconsistencies in the definitions of commonly used terms that may affect the accuracy of event rates. This may have an adverse impact on the establishment of medication safety priorities and on the validity of cross-jurisdictional comparisons.

*Conclusions:* As the medication safety literature continues to expand, it is imperative that standardized terminology be adopted and used consistently.

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## 1. Introduction

The medication safety literature has seen unprecedented growth in recent years, and has heralded bold pronouncements of problems associated with medication use. For instance, the Institute of Medicine report, *To Err is Human*, released in November 1999, estimated that between 44,000 and 98,000 people die from medical errors each year in the United States, and approximately 7,000 of these deaths are due to errors associated with medications.<sup>1</sup> The economic consequences are equally compelling. The morbidity and mortality associated with medication use are estimated to cost the American health care system US \$177.4 billion each year.<sup>2</sup>

Despite the growth in interest in medication safety, there remains much confusion about the terminology used to describe the problem. Nebeker et al suggest that the problems with the terminology arise, in part, because the terms that are currently used for patient safety and quality improvement purposes arose out of a much narrower regulatory and clinical context. Application of the terms in a new and broader context has contributed to inconsistencies in their use.<sup>3</sup> The work by Yu et al is highly illustrative in this regard. They electronically searched 160 web sites of organizations associated with medication safety. Of these, 33 sites included some definitions for terms related to medication safety. They found 119 definitions for 25 different terms. Yu et al<sup>4</sup> conclude that “the classification of medication related occurrences using existing terminology can only be described as haphazard.” The purpose of this commentary is to help provide some direction by clarifying the medication safety terminology.

## 2. Types of problems associated with medication use

The differences between the main types of problems associated with medication use are substantial: some are preventable events and some are not, some result in injury and some do not, and reporting systems are in place for some events whereas others lack reporting systems. More specifically, the existence of reporting systems varies depending on the jurisdiction and the type of problem. More detail will be provided later about reporting systems for specific types of medication-related problems. There are a plethora of terms in use in the patient safety literature. In the following text, we have attempted to compare and contrast the major terms used to describe the types of problems associated specifically with medication use.

First, the terminology will be defined broadly to include drug-related (therapy) problems (DRP). Subsets of DRPs include drug-related morbidity (DRM) and medication misadventures. The latter term includes medication errors, adverse drug reactions (ADRs), and adverse drug events (ADEs). Fig. 1 provides a visual depiction of the relationships between these terms. Similar to Otero and Schmitt,<sup>5</sup> we have classified events into those that result in injury and those that do not. By injury, we refer to the definition provided in the text *Injury Prevention and Public Health: Practical Knowledge, Skills and Strategies*.

Injury is damage or harm to the body resulting in impairment or destruction of health.<sup>6</sup>

Hepler makes the distinction between injury and *latent injury*:

If a significant error (or happenstance) is not sufficient to injure a patient, then it causes a latent injury. A *latent injury* or *latent outcome* is a propensity or predisposition for injury that occurs during the processes of care. Latent injury is an attribute of a patient at a particular time. Some latent injuries may be recognizable and correctable at a subsequent time during therapy.<sup>7</sup>

### 2.1. Drug-related (therapy) problems

Beginning with the terms that are broadest in scope, Hepler and Strand's work is important to note because it addresses the breadth of the problems associated with medication use. A DRP can be defined as an event or

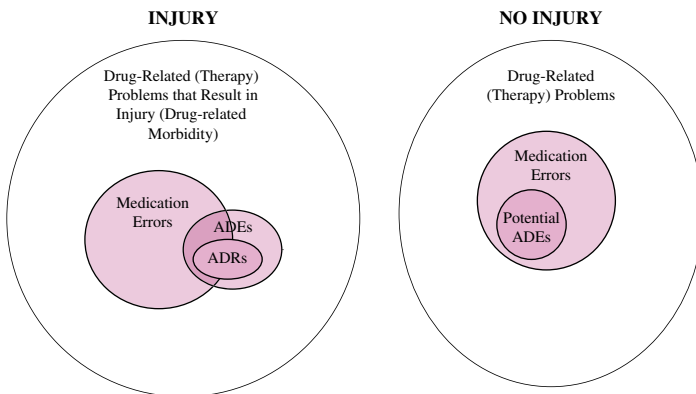


Fig. 1. Relationships between the different types of problems associated with medication use. Adapted from following references: 5, 13, 14. All of the shaded circles are also considered to be medication misadventures. Drug-related morbidity is always the result of some DRP, however, only some DRPs result in injury. All medication errors are classified as ADEs when injury occurs but it is still important to distinguish between medication errors and ADEs for the purpose of this diagram because not all ADRs result from medication errors.

circumstance involving drug treatment that actually or potentially interferes with the patient experiencing an optimum outcome of medical care.<sup>8</sup> The term DRP was originally intended to refer to the process of care, but it is often used as an outcome. Hepler<sup>7</sup> has since suggested use of the term drug-therapy problem (DTP) to identify those events associated with the process of care.

## 2.2. Drug-related morbidity

Drug-related morbidity (DRM) is defined as the failure of a therapeutic agent to produce the intended therapeutic outcome, or the clinical or biosocial manifestation of unresolved DRPs.<sup>8</sup> Hepler further explains the following: “A DRM is an unintended patient injury with a scientifically plausible relationship either to (1) drug therapy or (2) an untreated indication for drug therapy. Plausible means a valid theoretical relationship and chronology.” In helping to distinguish between DRPs and DRMs, Hepler<sup>7</sup> states that the patient injury that occurs as part of a DRM is a “severe, dangerous, injurious, or disabling clinical outcome that was not correctable or required significant additional medical care to correct, eg, emergency treatment or hospitalization.” While a DRP can result in injury, it is clear from the definitions provided above that if that injury is severe, the event would be categorized as a DRM. Thus, all DRMs result in injury whereas only a small percentage of DRPs result in injury, and those injuries would not be serious.

It is possible for undetected DRPs to lead to DRM. For instance, if a person does not fill a prescription for an antidepressant medication because of financial constraints (an unrecognized DRP), that person’s depressive symptoms may precipitate a suicide attempt (a DRM). Many factors could potentially contribute to the manifestation of an injury from a DRP, including the health status and resiliency of the individual. Untreated hypertension (a DRP) may be more likely to result in a stroke (a DRM) in an obese, inactive older person than in a young, fit person of normal weight. In both cases there is a DRP, but personal characteristics of the individual may change the susceptibility to the development of DRM. Eight types of DRPs have been described by Strand et al<sup>9</sup> and these are listed in Table 1. Hepler adds

*A drug therapy problem (DTP) is a detectable (recognizable) latent injury. A latent injury may become recognizable as a DTP long before it actually causes DRM, which is correctable. Other latent injuries may never appear as a DTP. Some latent injuries, including some DTPs, do not become severe enough to be considered DRM. For example, a patient may go for years with an unrecognized side effect. Likewise, a DTP such as somewhat undertreated asthma may go on for years. However, some other event—called a trigger event—may occur during the treatment of the patient that causes the latent injury to become an actual manifest injury.*<sup>7</sup>

Table 1  
Types of DRPs

Drug-related problem	Description
Untreated indications	The patient has a medical problem that requires drug therapy (an indication for drug use) but is not receiving a drug for that indication.
Improper drug selection	The patient has a drug indication but is taking the wrong drug.
Subtherapeutic dosage	The patient has a medical problem that is being treated with too little of the correct drug.
Failure to receive drugs	The patient has a medical problem that is the result of his or her not receiving a drug (eg, for pharmaceutical, psychological, sociological, or economic reasons).
Overdosage	The patient has a medical problem that is being treated with too much of the correct drug (toxicity).
ADR	The patient has a medical problem that is the result of an ADR or adverse effect.
Drug interactions	The patient has a medical problem that is the result of a drug-drug, drug-food, or drug-laboratory interaction.
Drug use without indication	The patient is taking a drug for no medically valid indication.

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Although Fig. 1 does not distinguish between preventable and nonpreventable DRMs, it is estimated that approximately 50% of DRMs are preventable.<sup>10</sup> The term preventability, itself, can cause some misunderstanding. To claim that a particular DRM is preventable, Hepler and Strand state that the following 4 characteristics must be met: given an adverse clinical outcome, a preexisting DRP must have been *recognizable* and the adverse outcome or treatment failure must have been *foreseeable*. In addition, the causes of the DRP and the outcome must have been both *identifiable* and *controllable*.<sup>8</sup>

### 2.3. Medication misadventures

Another “broad” term that captures several different types of adverse outcomes from pharmaceuticals is *medication misadventure*. According to Manasse, a medication misadventure is an iatrogenic hazard or incident that is (1) an inherent risk when drug therapy is indicated; (2) created through either omission or commission by the administration of a drug or drugs during which a patient is harmed, with effects ranging from mild discomfort to fatality; (3) always unexpected and thus unacceptable to the patient and health professional; and (4) attributable to error, immunologic response, or idiosyncratic response. Additionally, its outcome may or may not be independent of the preexisting pathology or disease process.<sup>11,12</sup> An article published in 1998 by the American Society of Health-System Pharmacists demonstrates how the term medication misadventures relates to medication

errors, ADEs, and ADRs.<sup>13</sup> According to Manasse, medication misadventures consist of the sum of (1) medication errors, (2) ADRs, and (3) ADEs. Medication misadventures encompass more events than DRM in that DRM only includes events that result in serious injury while a medication misadventure does not necessitate a serious injury to the patient (ie, may result in discomfort only). Conversely, medication misadventures encompass more events than DRPs because DRPs do not necessarily include events that result in serious injury to the patient while medication misadventures do include these events. However, in another sense both DRMs and DRPs are broader than medication misadventures because the former terms include more events than only medication errors, ADEs, and ADRs.

#### 2.4. Adverse drug events

An ADE is any injury that is caused by a medication (or lack of an intended medicine).<sup>14,15</sup> Its origins come from the Harvard Medical Practice Study, where adverse events were defined as “unintended injury that was caused by medical management and that resulted in measurable disability.”<sup>16</sup> A subset of ADEs can happen despite proper use of the medication by the patient, and these would be considered ADRs. Not all ADEs are caused by error. This would include, for instance, the case of a patient developing a rash due to an unknown allergy to a medication. All ADEs result in patient injury. Bates et al<sup>14</sup> suggest that most of the ADEs that are caused by errors are usually predictable and preventable (eg, excessive dose). Other examples of preventable ADEs caused by error include administering the wrong drug to the right person, the right drug to the wrong person, using the wrong route of administration and so on.<sup>17</sup> It is important to note that DRM includes injury caused by nontreatment or undertreatment, whereas ADEs have not always included these events in past studies.<sup>7</sup> Other events often excluded from ADE studies include dose-related therapeutic failure, failure to accomplish intended purpose of treatment, lack of necessary drug therapy, long-term undertreatment, patient noncompliance, suboptimal management, and treatment failure.<sup>7</sup> These events would all be included under the term DRM. As previously discussed, problems associated with the medication use system can result in direct harm to the patient (injury) or not. Bates et al define medication errors with the potential for injury, but in which no injury occurs, as potential ADEs. An example of a potential ADE is the case of a person prescribed a medication in a dose range that could cause toxic effects, but the pharmacist recognizes this before the medication is administered.<sup>14</sup>

#### 2.5. Medication errors

Error is defined by the Institute of Medicine as “the failure of a planned action to be completed as intended or use of a wrong plan to achieve an aim.”<sup>1</sup> Medication errors are specific types of errors in that they are preventable

events that can occur at any stage in the medication use process that lead to patient harm or inappropriate medication use. Only a very small percentage of medication errors actually result in injury. All of those that do result in an injury would also be classified as ADEs. However, not all ADEs are classified as medication errors, such as ADRs that do not occur as a result of error.

### *2.6. Adverse drug reactions*

The World Health Organization has defined an ADR as a “response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of a disease, or for modification of physiologic function.”<sup>18,19</sup> This definition does not include therapeutic failures, drug abuse, errors in drug administration, noncompliance with directions for drug use, or intentional and accidental poisonings. However, most would argue that some ADRs do result from medication errors (also known as preventable ADRs). Some examples include a hypotensive flushing reaction resulting from administering vancomycin too fast and an injury resulting from administering penicillin to a patient known to be allergic to penicillin.<sup>13</sup> ADRs can also be thought as a subset of ADEs. All ADRs result in injury, although the injury can be temporary or permanent. Both allergic and idiosyncratic reactions are considered to be ADRs.<sup>13</sup>

## **3. Reporting systems**

We are not aware of any reporting programs in existence that include all DRPs and DRMs. In some cases, DRPs are not recognizable until a DRM has become apparent. Even then, it is not always possible to determine if the injury is medication related. There are reporting mechanisms for *some* types of DRM.

In Canada, for example, there is a national reporting scheme for ADRs managed by Health Canada, however, reporting is not mandatory.<sup>20</sup> The Canadian Medication Incident Reporting and Prevention System is an anonymous, voluntary reporting system under development by Health Canada, the Institute for Safe Medication Practices—Canada, and the Canadian Institute for Health Information aimed at improving the medication use system. The Canadian Medication Incident Reporting and Prevention System will establish a standardized minimum data set.<sup>21</sup> In addition, many Canadian hospitals also have a mechanism for reporting ADEs, but this information is not routinely shared with other hospitals or regulatory agencies.

## **4. Implications of misuse of terminology**

The manner in which adverse medication-related events are classified by organizations has significant clinical-, policy-, and research-related

implications. Establishing accurate event rates is determined by the case definition. These rates subsequently help organizations to identify priority areas for, and the nature of, interventions. Policy development is likely to be influenced by identified priorities. Event rates also provide a measure with which to evaluate the effectiveness of prevention strategies. Comparisons across jurisdictions have little meaning if there are different definitions of what constitutes an event.<sup>22</sup> For example, in the work by Yu et al,<sup>4</sup> they developed a scheme to classify the functional meanings of the 119 different definitions they identified. The definitions of many commonly used terms created more than one functional meaning per term, thus making the comparability of studies using those terms problematic. Schneitman-McIntire et al examined the prevalence of medication misadventures resulting in an Emergency Department visit to a health maintenance organization medical center. Their definition included noncompliance and inappropriate prescribing, but excluded intentional overdoses and substance abuse.<sup>23</sup> To make valid comparisons with the prevalence in other emergency departments, the same case definition would have to be used. The prevention strategy for noncompliance would be completely different for that used with substance abuse, thus suggesting that the elements of the case definition are critical. Easton-Carter et al report that emergency department visits associated with DRPs range from 1.7% to 28.1%. They suggest that these significant discrepancies are related in part to the differences in case definitions.<sup>24</sup>

In their study examining methods for estimating rates of adverse events, Michel et al determined that “the under identification of cases was mostly due to medical staff inadequately grasping the concept of adverse events. For example, they did not consider events as adverse if they were frequent or the patient recovered without sequelae.”<sup>25</sup> In this case, a clear definition of an adverse event could facilitate consistent and accurate recognition. Tamuz et al argue that the definition and classification of events can also result in underreporting or misclassification related to incentives for reporting. More importantly, the authors suggest that classification can affect organizational functions that respond to events and those that promote opportunities to learn from events. Specifically, pharmacists who were interviewed did not consider prescribing errors to be reportable if they were corrected in the Pharmacy Department. This was considered to be an intervention, rather than a medication error. This, in turn, led to a systematic underestimation of medication errors for the organization, and a lost opportunity to learn from potential errors.<sup>22,26</sup>

As patient safety initiatives strengthen and reporting systems are put in place, the consistent definition of events is essential. For example, the Canadian Medication Incident Reporting and Prevention System is designed to identify areas of concern, potential intervention strategies, and to evaluate the effectiveness of any strategies that are implemented. However, unless there are clear case definitions for inclusion in the system, it will be difficult to make meaningful comparisons of event rates over time. With voluntary

reporting by health professionals and laypersons, any system runs the risk of erroneously including or excluding events if the definitions of what types of events should be reported are not clear to those people doing the reporting.

## 5. Research agenda

Laudably, there is growing research activity on medication safety. The most imminent challenge within this expanding research agenda is to establish internationally accepted standards for terminology, much as the Anatomic Therapeutic Chemical (ATC) and Defined Daily Dose (DDD) systems have created a shared standard that has permitted meaningful cross-jurisdictional comparisons in drug utilization studies. Moreover, while some work has been done on the development of indicators, or performance measures, of adverse events related to medication use, more research is needed in the development and validation of further indicators that work in a variety of practice settings (such as inpatient, ambulatory, and long-term care).

## 6. Conclusion

The need to understand the terminology used in the medication safety literature is not merely academic. The development of appropriate prevention strategies is predicated on a clear understanding of the problem. For instance, interventions designed to prevent ADEs caused by an untreated indication will be far different than those aimed at reducing medication errors caused by inaccurate transcription. Because the medication safety literature continues to expand, it is imperative that standardized terminology be adopted and used consistently.

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