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# Patient safety and medication errors

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## Abstract

The morbidity and mortality of drug-related problems has most recently been estimated to cost $177.4 billion annually within the United States alone. Empirical investigations have also suggested that almost one-fifth of all medical errors are drug-related within hospital settings, with over half of these being of a preventable nature. As such, minimizing medication errors has emerged as a priority area to ensure patient safety within healthcare systems worldwide, as several nations have implemented broad initiatives to improve the medication use system. Due to the numerous complexities involved, multifaceted and system-wide approaches to redesigning processes are most often advocated. Given the importance of appropriate medication use in achieving optimal patient outcomes, this paper addresses the various nomenclature and taxonomies of error within healthcare as well as the incidence, risk factors, causes, and prevention of medication errors.

*Key words: patient safety, medication errors*

### Introduction

In light of numerous reports and commentary concerning patient safety, a critical component of quality in healthcare now centers upon reducing error throughout the world's healthcare systems. Within the United States, the Institute of Medicine (IOM) has addressed this major public health concern by explicitly identifying and prioritizing patient safety as one of the areas that must be improved in the 21st century healthcare system.[1] Globally, numerous countries have also shared similar concerns about patient safety and error.[2-6]

The morbidity and mortality associated with medication errors and other inappropriate use represents a large clinical and economic burden for patients, providers, and society. Based upon prior epidemiological investigations, the landmark IOM report *To Err is Human* (2000) estimated that between 44,000 and 98,000 deaths per year were caused by medical errors in hospitals within the United States.[1] As such, medical errors ranked between the fourth and seventh leading cause of death, essentially exceeding the mortality attributed to either breast cancer, AIDS, or highway accidents.[1] In addition to this estimate of mortality, injury as a result of medical error was approximated to impact 1 million individuals.[7-9] Johnson and Bootman (1995) reported that the annual cost of drug-related morbidity and mortality was $76.6 billion in ambulatory care settings within the United States, while an update conducted by Ernst and Grizzle (2003) noted a cost of $177.4 billion.[10,11] Within nursing facilities, these costs were found to be $7.6 billion, which essentially equated to $1.33 spent on drug-related problems for every dollar used for medications.[12] Bates and colleagues (1997) indicated that preventable adverse drug events requiring a hospital admission were associated with an average increases in lengths of stay of 4.6 days and costs of $4600.[13]

The IOM identified medication errors as a major source of error in healthcare which may negatively impact patient safety.[1] While almost one-fifth of all medical errors in hospital settings were deemed to be drug-related, over half of these were considered preventable. As such, the IOM has placed medication error reduction as a priority area within the reports *To Err is Human* (2000), *Crossing the Quality Chasm* (2001), *Priority Areas for National Action* (2003), and *Patient Safety* (2004).[1,14-16] The response to this work has resulted in numerous leadership initiatives to reduce error and improve safety spanning across nations.[16-18] Illustrating this, broad safety and quality reporting systems have been implemented in countries such as New Zealand, Australia, the United Kingdom, Denmark, Italy, Germany, and France; communication and collaboration between nations has also been accelerating.[19-22] Additionally, within the United States, efforts

directed by the Agency for Healthcare Research and Quality (AHRQ) are reporting findings of quality assurance demonstration projects in hospital and ambulatory settings.[22] The Centers for Education and Research on Therapeutics (CERT), which is a national initiative administered by AHRQ in consultation with the Food and Drug Administration (FDA), also aims to advance the optimal use of drugs, medical devices, and biological products.[23] The passage of the Medicare Prescription Drug Act (2003) within the United States that seeks to increase the access of prescription drugs to older persons, also addresses issues of complex medication therapy management and medication error (e.g., MMA section 107(c)).[24] Prior to these aforementioned initiatives, scientific investigation concerning medication errors had focused primarily upon drug distribution systems and medication administration, whereas more recent studies have centered upon prescribing practices and system-wide analyses which more consistently address the sentiments of the IOM reports.[22,25]

The increasing complexities associated with pharmacotherapy and the current medication use system used to describe the process of drug ordering or prescribing, transcribing, dispensing, administering, or monitoring presents numerous and substantial barriers to improve safety within healthcare. Given this, the purpose of this paper is to discuss the incidence, risk factors, causes, and prevention of medication errors. As no consensus exists concerning the basic definitions of error, an initial presentation of the various nomenclature and taxonomy is also offered. Eliminating preventable errors and increasing the awareness of the multifaceted aspects associated with the appropriate use of medications has emerged at the forefront of patient care. Although reaching these efficiencies often involves challenging and diverse interprofessional, interdisciplinary, and system-wide approaches, achieving these goals is of paramount importance in achieving optimal patient outcomes.

## Nomenclature

As discussed by Aronson and Ferner (2005), a consistent nomenclature has not been uniformly adopted to assess elements of drug safety.[26] Although several definitions have been proposed or adopted, these authors commented that ultimately reaching consensus may allow for a more robust assessment and communication of the frequency, intensity, and seriousness of negative events. For purposes of illustration, the forthcoming definitions represent some of the widely-adopted or proposed descriptions appearing within the scientific literature.

*Errors* involve a broad characterization within healthcare, often defined simply as "the failure of planned action to be completed as intended (i.e., error of execution) or the use of a wrong plan to achieve an aim (i.e., error of planning)."[1] Thus, errors may involve an act of *commission* (e.g., prescribing a drug with a known fatal drug-drug interaction) or an act of *omission* (e.g., failing to prescribe a drug for a patient's underlying disease state).[16] *Medication errors* are considered a specific subcategory of *medical errors*, often defined as "any error in the process of prescribing, dispensing, or administering a drug, whether there are adverse consequences or not."[27] Medication errors may be coincidental in nature or may relate to the circumstances associated with the utilization of a given drug, including events that are preventable and revolve around the broader medication use system.[28,29]

Perhaps the most general description of medication errors fall within the guise of *drug-related problems* (DRPs), which include medication errors, adverse drug reactions, noncompliance, and treatment failure.[30] Johnson and Bootman (1995) defined a DRP as "a circumstance that involves a patient's drug treatment that actually, or potentially, interferes with the achievement of an optimal outcome."[10] Strand and colleagues (1990) categorized DRPs as inappropriate medication use through either commission or omission including: a) an untreated indication; b) drug use without indication; c) improper drug selection; d) subtherapeutic dosage; e) overdosage; f) failure to receive drugs; g) drug interactions; or h) adverse drug reactions.[31] The more specific term, an *adverse drug reaction* (ADR) is defined by the World Health Organization (WHO) 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 disease, or for modification of physiological function."[32] Rawlins and Thompson (1977) proposed one of the more commonly-used classification systems for ADRs as: 1) Type A, which denoted reactions that were considered predictable and dose dependent (i.e., "the result of an exaggerated, but otherwise normal, pharmacological action of a drug given in the usual therapeutic doses"); and 2) Type B, which were deemed unpredictable and not related to dose (i.e., "totally aberrant effects that are not to be expected from the known pharmacological actions of a drug when given in the usual therapeutic doses to a patient whose body handles the drug in the normal

way"); this classification has been since described as 'augmented' or 'bizarre' for Type A and B reactions, respectively.[33,34] Extensions to this system have been offered to include Type C (i.e., long term or 'continuous'), Type D (i.e., 'delayed'), Type E (i.e., 'end of use' or withdrawal), Type F (i.e., 'failure'), and Type G (i.e., 'genetic/genomic').[35-38] Importantly, several taxonomies exist other than that which was proposed by Rawlins and Thomson, and no uniform method is necessarily used in reporting. An additional system used for categorizing medication errors was developed by the United States Pharmacopeia National Coordinating Council for Medication Error Reporting and Prevention, wherein errors are reported based upon an assessment of potential severity and actual degree of patient harm that was incurred.[39,40]

While an ADR purports that a causal relationship exists between the use of the drug and a subsequent toxic or side effect and often excludes error within various definitions, an *adverse drug event* (ADE) differs in that it involves an injury or iatrogenic outcome either during or after the use of a medication and does not necessarily purport a cause-effect relationship.[26,28,41,42] Explained differently, an ADE is often used to describe harm that results from medication use that can include both ADRs which may be expected from the utilization of a drug as well as those associated with error or improper use.[27] Aronson and Ferner (2005) noted that all ADRs are considered ADEs, although the opposite does not necessarily hold true; the distinction may become particularly important when considering causation versus association within studies that seek to assess efficacy (e.g., use within controlled, experimental clinical trial settings) versus effectiveness (i.e., use observed within real world practice settings).[44] An ADE may also be specified as either *preventable* (e.g., dispensing misfill) or *nonpreventable* (e.g., certain side effects or adverse drug reactions). A *potential* ADE (or "*near miss*") involves a medication error wherein an injury or deleterious event had the potential to occur but was subsequently avoided or circumvented, defined by the IOM as "an act of commission or omission that could have harmed the patient but did not do so as a result of chance, prevention, or mitigation."[1]

### Incidence

Due to the diverse methodologies, taxonomy, nomenclature, classification systems, and outcomes adopted within drug safety research, there is currently no benchmark concerning the occurrence of medical or medication errors in all healthcare settings or amongst all patient populations.[25,45] As such, differences in the incidence of DRPs have been found to vary based upon the practice setting, reporting system used, and populations of interest. To illustrate, researchers have estimated that voluntary reporting systems designed to measure errors may underestimate the true number of ADEs or medication errors by up to 90%.[9,46-48] Flynn and colleagues (2002) also noted that measuring and reporting medication errors varies according to numerous factors including geographic location and accreditation status of a healthcare organization.[49]

Within institutional settings, reviews of research concerning ADRs that exclude errors have found the incidence ranges from 1.5 to 35%, with between 0.3 and 7% of hospital admissions deemed attributable to ADRs.[50-52] A meta-analysis of 39 studies conducted by Lazarou and colleagues (1998) reported the incidence of ADRs to be 10.9% within hospitals, with 4.7% of admissions being caused by an ADR.[53] Van de Bemt and colleagues (2000) found studies observing the rate of medication errors within these settings to range between 1.7 and 59%; prescribing errors accounted for an additional 0.3 to 2.6%.[30] ADEs have been observed to range between 0.7 and 6.5%, though several studies that followed strict definitions of an ADE that may have underestimated their true incidence.[30] Regardless of the associated discrepancies, estimates of ADEs that are suggested to be preventable range from 28 to 56% or higher.[7,13,28,54]

Amongst selected and more frequently-cited research studies, the extensive Harvard Medical Practice Study with which the IOM based several of its projections in the IOM's *To Err is Human* found a 3.7% rate of injury relating to medical errors amongst hospitalized patients.[2,55] Preventable medical errors occurred in 58% of instances and negligence accounted for 27.6%; complications related to pharmacotherapy occurred in 19% of these events, marking the most common form of error observed. The IOM noted that these general findings were also found in an additional large investigation conducted by Thomas and colleagues (1999) of hospitals in Colorado and Utah.[3]

Efforts to identify and minimize medication errors have generally directed toward institutional rather than ambulatory practice settings. Regardless, research indicates that ADRs range

from 2.6 to 50.6% in an outpatient environment.[56] The occurrence of medication errors also appears to be increasing at a higher rate in community settings than within institutions.[57,58,59] Illustrating this, ambulatory visits in the United States have increased over 75% from 1983 to 1993 while inpatient days have decreased by 25%; some 81% of adults are noted to receive at least one prescription per year.[58,60,61] Potential drug-drug interactions (DDIs) have also been observed to occur between 9 and 70% in community practice.[62] In a large study assessing over 60,000 emergency department visits, Schneitman-McIntire and colleagues (1996) reported that 1.7% of incidents were related to drug-related problems within ambulatory health maintenance organization patients.[63] Both Sullivan and colleagues (1990) and Einarson (1993) also reported from meta-analyses that noncompliance was associated with 5.5% of hospital admissions.[64,65] More recently, Gurwitz and colleagues (2000, 2003) found 277 adverse drug events per 1,000 person years within nursing homes and 50.1 adverse drug events per 1,000 person years in ambulatory settings amongst Medicare recipients.[66,67] Ghandi and colleagues (2003) reported that 25% of the ambulatory care patients that received at least one prescription had an ADE, with several of events being able to be improved or prevented.[68] Concerning errors of omission, McGlynn and colleagues (2003) estimated that over half of patients do not receive recommended preventative, acute, or chronic care in the United States.[69]

### Risk factors and causes

The medication use system involves numerous characteristics of patients, products, professionals, and processes that may either individually or collectively contribute to errors when a drug is ordered or prescribed, transcribed, dispensed, administered, or monitored.[29,70] Earlier research concerning medication errors of commission sought to identify medications associated with the highest incidence of error, working conditions, and characteristics of healthcare professionals. Furthermore, traditional methods of preventing or avoiding errors in healthcare have most often centered upon elements of training or guideline compliance, with litigation serving as one method of attributing negligence upon an individual.[71] More recently, efforts have shifted to advocate broad system-based approaches to increasing safety which stress the overall redesign of processes associated with the medication use system and addressing both errors of commission and omission.[72]

In research relating to the processes of medication use, Leape and colleagues (1995) and Classen (1997) found that wrong prescriptions accounted for 56% of medication errors while 44% were associated with drug administration.[7,73] For the 19% of medication errors observed by Barker and colleagues (2002), 43% involved the wrong time of administration, 30% involved omission of the medication, and 17% involved the wrong dose.[74] Leape and colleagues (1993) categorized general medical errors that most frequently impacted patient safety as involving diagnosis, treatment, prevention, and other (e.g., equipment or system failures).[75] Specifically relating to the medication use process, Cohen (2000) identified six predominant system causes of specific medication errors as involving: a) communication; b) drug distribution; c) dosage calculation; d) administration; e) patient education; and f) specific attributes of the drug or drug devices themselves.[76] Empirically, Leape and colleagues (1995) reported that preventable ADEs within hospital settings occurred during ordering (49%), administration (34%), transcription (6%), and dispensing (4%).[73] While 16 overall system causes were identified, 78% were deemed to be related to medication delivery process itself, particularly relating to drug knowledge dissemination (29%), dosage and identity checking (12%), patient information availability (11%), order transcription (9%), allergy information availability (7%), order tracking (5%), and interservice communication (5%).[73] Importantly, prevention of these was viewed as being able to be incurred at the initial stages of the medication use process.[77] In earlier research conducted by Bates and colleagues (1995), most preventable medication errors in hospital settings were noted to occur during ordering or administration.[28] The United States Pharmacopeia has reported that the most common medication errors were associated with omissions, incorrect doses, or a wrong drug.[78] Studies investigating the types of medications associated with medication errors are numerous, with findings indicating that antibiotics or antivirals, parenteral nutrition or intravenous fluids, cardiovascular medications, narcotics, anticoagulants, nonsteroidal anti-inflammatory drugs, and chemotherapeutic agents to be associated with greater incidence of error;

specific products identified from empirical studies include heparin, lidocaine, potassium, and xanthines.[6,79,80,81]

Lesar and colleagues (1997) noted that the most common factors associated with errors included decreased renal or hepatic function which warranted changes in drug therapy (13.9%), patient history of allergy to agents within similar medication classes (12.1%), incorrect medication name, dosage form, or abbreviation (11.4%), incorrect calculation of dosages (11.1%), and dosage frequency concerns which were atypical or unusual in nature (10.8%).[82] The factors most commonly associated with errors were grouped as relating to knowledge and the application of knowledge regarding drug therapy (30%), knowledge and use of knowledge regarding patient factors that affect drug therapy (29.2%), use of calculations, decimal points, or unit and rate expression factors (17.5%), and nomenclature such as medication name, dosage forms, or abbreviations (13.4%).[82]

***Specific Populations: Pediatrics and Older Persons***

Both the very young and very old have been found to be at increased risk for medication errors. Studies involving pediatric populations have observed a rate of medication error three times that of adults, with the types of error differing substantially between groups (i.e., dosing errors being the most common form of medication errors within pediatric populations).[83-85] Settings with the highest rates of error typically involve pediatric or neonatal intensive care units.[86,87] Quality assurance efforts for pediatrics often focus upon education concerning differences in pharmacokinetics and pharmacodynamics in addition to other strategies such as computerized physician order entry and quality review systems.[88]

A higher incidence of drug-related problems in older patients has also brought increased attention to quality improvement for medication use within this group.[89,90] In a large investigation of older individuals within an outpatient setting, Gurwitz and colleagues (2003) reported 13.8 preventable ADEs per 1000 person years.[67] Notably, over one-fifth of these were attributed to poor patient adherence. In earlier research, Beard (1992) reported that 3 to 11% of hospital admissions were related to ADEs amongst older persons.[91] Inappropriate drug use and ADEs may occur more frequently in this population due to polypharmacy or the overuse of medication, inappropriate prescribing, underuse or omission of medications, and patient non-adherence with therapeutic regimens.[92] While substantial debate exists whether age itself is a risk factor for DRPs, many older individuals present with multiple disease states that require numerous drugs for treatment; over 75% utilize prescription medications and 82% use nonprescription drugs frequently.[93-95] Addressing patient safety concerns, Beers and colleagues (1991) and Beers (1997) initially published several criteria for determining inappropriate drug use with older patients which has since been updated by Fick and colleagues (2003); 'Beers criteria' exists as one of the more widely-used guidelines for medications to be avoided within these patients due to either high risk or ineffectiveness.[96-98]

***Prevention***

Given the complexity of the medication use system, multifaceted approaches to increase patient safety are most often recommended. Although innovative applications of methods used within sectors other than healthcare are of key importance in minimizing error (e.g., total quality management, reengineering, failure mode and effect analysis), achieving a fail safe healthcare system requires an concerted interdisciplinary and interprofessional approach to both identify and remove underlying system errors and to establish mechanisms for continuous improvement.[14] Pharmacoeconomics and outcomes research may also be employed to improve the medication use process, particularly with its focus upon population-based approaches to optimize economic, clinical, and humanistic outcomes.[44,99]

In *Crossing the Quality Chasm*, the IOM noted that the provision of patient care has not kept pace with other rapid advances in the health sciences, with the organizational changes of the most recent time period referred to as an "era of Brownian motion."[14] The 21st century healthcare system was recommended by the IOM to be safe, effective, patient-centered, timely, efficient, and equitable.[14] In achieving these goals, rather than relying upon incremental change to improve safety, it has been advocated that broad reform be implemented, noting that the actual process of change be managed appropriately to maximize the acceptance and adoption of redesign.[1,14,100,101] Support is ultimately required between all stakeholders within the healthcare system in addition to organizational and systems redesign and the use

of technology. Given that the IOM has worked toward making patient safety a standard of care, nine broad recommendations relating specifically to patient safety appearing in Box 1 have been offered to facilitate future efforts to reduce general medical errors in healthcare.[1]

Specifically addressing medication errors, empirical research has shifted from initially identifying and categorizing medication errors associated with either dispensing or administration to those involving more systems-based approaches (e.g., errors of prescribing).[14,25] Subsequent to these studies, particular patient management during transitions of care may minimize preventable errors of either commission or omission. In all, general recommendations to reduce medication error include: a) implementing computerized physician order entry (CPOE); b) emphasizing elements of safety to prescribers; c) improving dispensing activities of pharmacists; d) augmenting administration activities by nurses; and e) empowering patients.[14,43,102-104] Summarized in Box 2, the IOM has more comprehensively offered recommendations to decrease medication errors.[1]

While the implementation of improved decision support and information systems has been recommended to achieve improvements in patient safety, the mere presence of computer

**Box 1. Recommendations for reducing errors in healthcare and improving patient safety offered by the Institute of Medicine[1]**

| Institute of Medicine Recommendations and Descriptions | |
|---|---|
| Recommendation 4.1 | • Congress should create a center for patient safety within the Agency for Healthcare Research and Quality |
| Recommendation 5.1 | • A nationwide mandatory reporting system should be established that provides for the collection of standardized information by state governments about adverse events that result in death or serious harm. Reporting should initially be required of hospitals and eventually be required of other institutional and ambulatory care delivery settings |
| Recommendation 5.2 | • The development of voluntary reporting efforts should be encouraged |
| Recommendation 6.1 | • Congress should pass legislation to extend peer review protections to data related to patient safety and quality improvement that are collected an analyzed by health care organizations for internal use or shared with others solely for purposes of safety and quality |
| Recommendation 7.1 | • Performance standards and expectations for healthcare organizations should focus greater attention on patient safety |
| Recommendation 7.2 | • Performance standards and expectations for health professionals should focus greater attention on patient safety |
| Recommendation 7.3 | • The Food and Drug Administration (FDA) should increase attention to the safe use of drugs in both premarketing and postmarketing processes |
| Recommendation 8.1 | • Healthcare organizations and the professionals affiliated with them should make continually improves patient safety a declared and serious aim by establishing patient safety programs with defined executive responsibility |
| Recommendation 8.2 | • Healthcare organizations should implement proven medication strategies |

**Box 2. Selected medication safety strategies offered by the Institute of Medicine[1]**

**Institute of Medicine Tactics to Improve Medication Safety**

- Adopt a system-oriented approach to medication error reduction
- Implement standard processes for medication doses, dose timing, and dose scales in a given patient care unit
- Standardize prescription writing and prescription rules
- Limit the number of different kinds of common equipment
- Implement physician order entry
- Use pharmaceutical software
- Implement unit dosing
- Have the central pharmacy supply high-risk intravenous medications
- Use special procedures and written protocols for the use of high-risk medications
- Do not store concentrated solutions of hazardous medications on patient care units
- Ensure the availability of pharmaceutical decision support
- Include pharmacists during rounds of patient care units
- Make relevant patient information available at the point of patient care
- Improve patient knowledge about their treatment

systems do not necessarily protect against errors.[105] For example, although sophisticated hardware may be available at specific points of patient care, computer systems in healthcare are often stand-alone and lack much of the required data that is required to assess appropriate prescribing. As such, the Institute for Safe Medication Practices (ISMP) reported that almost one-third of serious errors were not detected by existing computers or processes, and that errors were often attributed to broader issues such as the lack of computer integration and a lack of data exchange.[100] While numerous studies have indicated that technology (e.g., computerized order entry, alerting systems, decision support) can improve the medication use system as well as positively affect costs and outcomes, again, comprehensive organizational changes are often warranted to ensure the adoption and success of these systems.[43,106-108] Pragmatically, Anderson (2004) stated that the rapid diffusion and acceptance of successful information systems would minimize both the complexity and time associated with their use.[72] Establishing robust reporting systems for errors are also critical both during and after change implementation. Currently, the concern for underreporting of adverse events is high, as Cullen (1995) noted that for every error that is reported, 20 are not.[9] The development of non-punitive methods to report either averted or actual errors has also been supported.[109] Augmenting the basic presence of technology, consideration must also occur relating to the interprofessional and team-based provision of care, noting particularly that several studies have reported a benefit in increasing patient-care responsibilities for pharmacists. For example, Fortescue and colleagues (2003) found that pharmacists present on patient rounds, in addition to CPOE and enhanced interprofessional communication, could possibly prevent 98.5% of medication errors in pediatric inpatients alone.[110] Finally, in addressing an important area required for the diffusion of innovation, the IOM has worked toward creating a national health information infrastructure by recommending standards for data exchange between institutions for the collection, coding, and classification of patient safety information.[16]

Although several operational hurdles are required to improve the current status of the medication use system, consideration of the broader strategic vision is helpful in achieving the goal of decreasing DRPs. As noted by Walsh and colleagues (2005), an initial step would be to recognize that errors occur to a much higher frequency than is acceptable.[29] Furthermore, based upon the recommendations of the IOM, improving patient safety and reducing error must be viewed as a priority wherein it is integrated as a fundamental standard of practice.[1] Rather than proceeding forward with incremental steps, improvement initiatives require open communication and a comprehensive approach which will ultimately assess, redesign, change, and monitor processes within healthcare to the highest level of quality achievable.[1,14,16]

## Conclusions

Errors associated with the medication use system have been reported to exact a tremendous clinical and economic burden upon patients, providers, and society. Although the incidence of these errors differ between patient care settings and amongst various populations, the recommendations to minimize drug-related problems remain relatively consistent. While robust assessments of current processes are required, leaders that seek to improve patient safety are advocated to develop and implement strategies which consider comprehensive system-wide redesign in a manner that appropriately addresses the dynamics and complexities associated with technological innovations, stakeholders, and organizations within healthcare.

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