

The Incidence of Adverse Events and Medical Error in Pediatrics

Paul J. Sharek, MD, MPH^{a,b,*},
David Classen, MD, MS^c

^a*Division of General Pediatrics, Department of Pediatrics, Stanford University School of Medicine, 750 Welch Road, Suite #325, Palo Alto, CA 94070, USA*

^b*Lucile Packard Children's Hospital, 725 Welch Road, Palo Alto, CA 94304, USA*

^c*Division of Infectious Diseases, Department of Medicine, University of Utah School of Medicine, 561 East Northmont Way, Salt Lake City, UT 84103, USA*

In its 2000 report, *To Err is Human* [1], the Institute of Medicine (IOM) concluded that between 44,000 and 98,000 deaths per year occur in United States hospitals as a result of error. These rates are higher than death rates from motor vehicle accidents and place adverse medical events as the eighth most common cause of death in the United States [1]. This estimate was developed in part from results of the seminal work, the Harvard Medical Practice Study, published in 1991, which estimated 3.7% of all hospitalized adult and pediatric patients in a 1984 New York State cohort experienced an adverse event (AE) related to medical therapy [2]. Similar results using similar detection methodologies were found in a report of a 1992 cohort of Colorado and Utah patients published in 2000 [3]. Recently developed detection methods have identified even higher rates of AEs than these [4–9], including one report revealing 52 adverse drug events (ADEs) per 100 adult inpatient admissions [4]. These data have captured the attention of the nation [10,11] and resulted in aggressive calls for further research [12,13], regulatory interventions [14–16], third-party payer involvement [17,18], and health care organization initiatives to improve these rates.

This article discusses the important differences between error and harm and discusses the various ways that harm is measured in the medical literature. A full appreciation of the impact of medical error in pediatrics first requires an understanding of the differences between error and harm and

* Corresponding author. Division of General Pediatrics, Department of Pediatrics, 700 Welch Road, Suite #227, Palo Alto, CA 94070.

E-mail address: psharek@lpch.org (P.J. Sharek).

of the limitations of available methods for quantifying the incidence of harm. The available evidence regarding the incidence of ADEs and adverse medical events in pediatric inpatients is summarized along with the less frequently studied incidence of adverse medical events in pediatric outpatients. Discussion of potential solutions to prevent AEs are provided elsewhere [19,20], as well as in articles by Curley and colleagues, Lehmann and Kim, and Streitenberger and colleagues elsewhere in this issue.

Harm versus error

The ultimate goal of the patient safety movement in health care is to reduce patient harm [1,7]. Early efforts to improve patient safety, however, frequently focused on eliminating error [21–23]. The assumption in this context was that reducing error would translate directly into reducing harm. Unfortunately, experience suggests that error reduction often is not linked to harm reduction in health care, as most medical errors never cause harm to patients [7,8,24–26]. It was necessary, therefore, for a paradigm shift to occur to accelerate improvement in the outcomes central to the patient safety movement.

Medical error, defined as “the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim” [7], often is either intercepted by redundancies in the system before it makes it to patients or frequently is not clinically significant. For example, providing a dose of acetaminophen 1 hour late technically is a medication error, yet this error is unlikely to translate into patient harm. AEs, however, defined as “injuries, large or small, caused by medical management rather than the underlying condition of the patient” [7,25–27], are, by definition, linked to harm and, thus, the ultimate outcome that patient safety interventions aim to decrease. It is critical to understand that AEs not always are the result of error [24–26], such as in the case where a patient has anaphylaxis for the first time after administration of an appropriate dose of penicillin. Medical error and adverse medical events are not synonymous and, therefore, require different intervention strategies to impact their rates [26]. The advantages of focusing on harm rather than error include focusing on the health care system rather than individuals within the system [8,24–27], thus reducing punitive concerns and encouraging better compliance [28,29]; grounding safety in patient experience rather than hospital-based processes; and acknowledging that some harm currently is unpredictable and unavoidable [7,25].

One of the clearest examples in the medical literature highlighting the differences between error reduction and harm reduction is the group of studies evaluating the effect of computerized physician order entry (CPOE) on medication safety. Several studies show CPOE reduces medication errors significantly after implementation [30–35], yet few studies to date have linked CPOE with significant reductions in AEs [30–32,35–37]. At least one study suggests that CPOE, when not implemented effectively,

can increase patient harm [38]. Although this study had significant methodologic flaws [39–42], it is a reminder that error reduction often is not associated with meaningful patient harm reduction. For all these reasons, the Institute for Healthcare Improvement (IHI), an influential nonprofit organization that focuses on improving health care quality and patient safety, and the IOM recommend that patient safety efforts transition from focusing on decreasing error to decreasing harm [7–9,43]. It is possible that the initial focus on error reduction rather than harm reduction has been a major factor in the lack of substantial improvements in patient safety outcomes despite aggressive efforts undertaken during the first 5 years since the IOM report was released [44,45].

Measuring harm

A brief discussion of the most frequent approaches to patient safety measurement is worth pursuing, as dramatically different AE rates are identified depending on the methods used to identify and measure harm.

Occurrence reports

The most well-known strategy to identify and measure patient safety concerns in hospitals in the United States is the use of occurrence (incident) reports. Although these data are relatively easy and inexpensive to obtain, evidence suggests that occurrence reports are underused [7,8,24,25] and, as a result, identify only between 2% and 8% of all AEs in inpatient settings [5,6,8]. This underuse results from the fact that occurrence reports are voluntary, time intensive, and frequently perceived by staff to be potentially punitive [7]. Occurrence reports, although identifying important clues to process flaws, generally identify near misses but rarely are reflective of the spectrum of AEs [46,47].

Retrospective or concurrent chart review

The Harvard Medical Practice Study and several other influential patient safety studies identified AEs and ADEs using a combination of voluntary and verbally solicited reports from house officers, nurses and pharmacists along with reviews of medication orders, medication administration records, and charts for other parts of the hospital [2,3,48]. Three studies using this methodology [2,3,48] revealed AE rates of 3.7, 2.9, and 2.3 per 100 admissions. This methodology suffers from a lack of consistency in what constitutes an AE; frequently results in an inability to extract meaningful data from the medical record related to poor, incomplete, confusing, or conflicting entries; and is extremely resource intensive. This methodology was valuable in highlighting the major patient safety risks present in inpatient health care settings but now increasingly is perceived by many as obsolete given the

newer, more efficient, and more sensitive methodologies currently available. One of the most widely adopted of these new approaches is known as the trigger methodology [5–9].

Trigger-based chart review

The use of trigger tools has emerged as the next generation of AE detection methods. Triggers, defined as “occurrences, prompts, or flags found on review of the medical record that ‘trigger’ further investigation to determine the presence or absence of an adverse event” [7,27], are shown to identify efficiently higher rates of AEs than any other published detection method [5–9]. For example, a recent study using a neonatal ICU (NICU) population–focused trigger tool revealed an AE rate of 74 events per 100 patients in the NICU [5] compared with a study using a nontrigger chart review method that revealed an AE rate in hospitalized children ages 0 to 1 year old to be 0.63 AEs per 100 patients [49]. Another study that looked at ADE rates for inpatient pediatric patients showed substantial differences in ADE rates in inpatient pediatric patients between the Harvard Medical Practice Study method (rate of 2.3 per 100 admissions) [44] and the Child Health Accountability Initiative–developed pediatric ADE trigger tool method (11.1 ADEs per 100 patients) [6]. It is becoming increasingly clear that the more traditional methods of identifying AEs using unfocused chart review or chart review with voluntary reports are less sensitive than the strategies that incorporate the trigger method.

Incidence of inpatient pediatric adverse drug events

Published estimates of ADE rates in pediatrics are few [6,48,50] compared with those of adults [2–4,25–27,51,52]. Two of the earliest and most influential pediatric studies used the Harvard Medical Practice Study method described above to identify ADE rates [48,50]. In one study, Kaushal and colleagues [48] reported ADE rates in children on inpatient wards at two urban teaching hospitals to be 2.3 per 100 admissions (26 events), with an additional potential ADE rate of 10 per 100 admissions (115 events). Of the 26 true ADEs, five (19%) were classified as preventable. In the second study, Holdsworth and coworkers [50] reported an ADE rate in pediatric inpatients (pediatric ICU and general care unit at a university hospital) of 6 per 100 admissions (76 events), with 61% classified as preventable, and a potential ADE rate of 8 per 100 patient days (94 events).

The only study to date using the trigger methodology to identify pediatric ADE rates was undertaken by Takata and Currier as part of a 12-site children’s hospital quality and safety collaborative study [6]. In this study, 960 inpatient pediatric admissions were reviewed using a trigger tool, revealing a rate of 11.1 ADEs per 100 admissions. Twenty-two percent of these AEs

were deemed preventable, and the ratio of ADEs detected by the trigger tool compared with ADEs detected by occurrence reports was 22 to 1. Assuming that all ADEs identified in each of these 3 studies were identified accurately, the pediatric ADE trigger tool identified between 1.8- and 4.8-fold more ADEs than the studies that used the Harvard Medical Practice Study method. The trigger tool used in this study was modified for pediatrics from the IHI-developed general adult ADE trigger tool, which identified an ADE rate in the adult population of 24 per 100 admissions [8].

Severity of inpatient pediatric adverse drug events

Fortunately, the majority of ADEs in inpatient pediatric patients appear to be of relatively low severity. In the study by Kaushal and colleagues, the 26 ADEs identified were categorized as significant (66%), serious (24%), or fatal/life threatening (10%) [48]. In the study by Holdsworth and colleagues, the 76 ADEs were classified as 76% significant, 13% serious, and 11% life threatening [50]. Severity in these two studies was defined on the basis of actual outcomes using a previously published scale [20,53]. Finally in Takata's study [6], using the more detailed harm scale (Fig. 1) published by the National Coordinating Council for Medication Error Reduction and Prevention [54], 97% were classified as "contributed to or resulted in temporary harm to the patient and required intervention" (severity level E), whereas

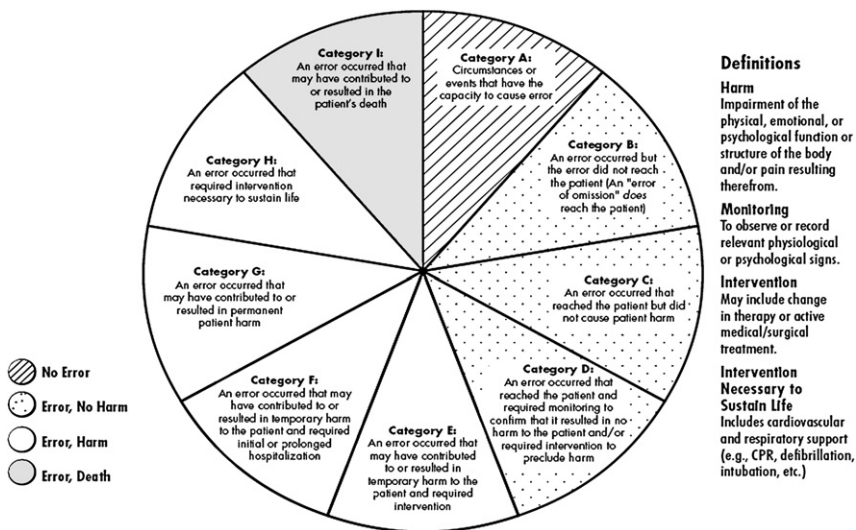


Fig. 1. National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) categories of medication errors. (Courtesy of NCC MERP, Rockville, MD. © 2001 National Coordinating Council for Medication Error Reporting and Prevention. All Rights Reserved.)

only 3% were classified as “contributed to or resulted in temporary harm to the patients and required initial or prolonged hospitalization” (severity level F). None was associated with permanent harm or death. When the severity of ADEs is compared with AEs as a whole (discussed later), the evidence suggests that medication-related harm is far less severe than nonmedication-related harm in inpatient settings.

Incidence and severity of inpatient pediatric adverse events

To date, there are only a few studies published that quantify AE rates in pediatric inpatients. Woods and colleagues, using retrospective chart review of 3719 randomly selected discharges of patients between 0 and 20 years old hospitalized in Utah and Colorado in 1992, report AE rates of 1 per 100 patients (39 events), with 59% classified as preventable [49]. The severity of these 39 events was not described. Miller and colleagues applied the first generation of the Agency for Healthcare Research and Quality (AHRQ) patient safety indicators (PSI) [55] to the administrative data from 3.8 million discharges, ages 0 to 19 years in 22 states in 1997, and, from the data presented, an AE rate of 1.2 per 100 discharges can be calculated. Miller and colleagues state clearly, however, that “the PSIs are not a comprehensive catalog of all medical errors that can occur in the hospital setting”; hence, they suggested that this number likely is a significant underestimate of the true AE rates in pediatric inpatients. Preventability and severity are not assessed in this study; however, patients who had a PSI-defined AE had longer lengths of stay and in-house mortality than those who did not have an AE, reflective of substantial associated morbidity. Similar overall AE rates can be estimated using the data published by Miller and Zhan [56], using the second-generation AHRQ PSIs on 5.7 million discharges, ages 0 to 18 years in 27 states in 2000 (0.9 AEs per 100 discharges). This study included AE related to obstetric trauma in mothers younger than 19 years old. Finally, a study published by Sharek and colleagues used a NICU-specific trigger tool to identify AEs for patients in NICU settings [5]. This study included 50 patients from each of 15 sites in the United States and Canada and incorporated 17,106 NICU days. Sharek and colleagues reported AE rates for the NICU population, clearly a high-risk population, of 74 per 100 admissions (range of birth weight-adjusted AE rates between hospitals of 0.18 to 1.28 per patient), with 56% judged preventable, 16% judged as “could have been identified earlier,” and 6% classified as “could have been mitigated more effectively.” Of the 554 AEs identified, 60% were defined as category E, 17% category F, 6% category G, 6% category H, and 10% category I (Fig. 1) [54]. The AEs identified most frequently included nosocomial infection (27.8% of all AEs), catheter infiltration/burn (15.5% of all AEs), and abnormal cranial imaging (10.8% of all AEs).

Incidence and severity of outpatient pediatric adverse events and adverse drug events

Far less research and information are available regarding the incidence of AEs and ADEs in outpatient settings. Gurwitz and colleagues report an ADE rate of 50.1 per 1000 person-years in a large adult outpatient population, with 38% categorized as serious, life threatening, or fatal and 27.1% classified as preventable [57]. In this study, the most common drug classes associated with outpatient ADEs were cardiovascular medications (24.5%), diuretics (22.1%), and nonopioid analgesics (15.4%). Similar to research of inpatient settings, the majority of initial research efforts focused on medication errors rather than ADEs [58,59]. In another adult-based study, Honigman and coworkers used a computer-based strategy to identify ADEs in an outpatient setting and found ADE rates of 5.5 per 100 patients presenting for care, with 23% classified as life threatening and 38% deemed preventable [60]. A third study, by Gandhi and coworkers, evaluated 662 adult outpatients at four ambulatory clinics and identified an ADE rate of 27 per 100 patients within 3 months of the initial visit based on survey and chart review [61]. Thirteen percent were deemed serious (none fatal or life threatening), and 11% were classified as preventable. The only significant risk factor for an ADE identified in this study was the number of medications prescribed. The drug classes associated with the most ADEs in this study were serotonin-reuptake inhibitors (10%), β -blockers (9%), and angiotensin converting enzyme inhibitors (8%).

In pediatrics, there are few studies that assess error or harm in outpatient settings. A recent study of a pediatric population by McPhillips and colleagues focused on medication errors in an outpatient setting and revealed 15% of all prescriptions dispensed contained a medication error; 8% of these prescriptions reflected an overdose and 7% reflected an underdose [62]. In this study, children at particular risk for an outpatient medication error included those less than 35 kg in weight (33% of prescriptions dispensed contained an error; no odds ratio [OR] provided), children between 0 and 3 years of age (OR 1.7), and children who had 6 or more medications dispensed (OR 3.3). The medication classes most at risk for errors included antiepileptic medications (errors 21% of the time), asthma and allergy medications (errors 19% of the time), and analgesics (errors 16% of the time). ADEs were not evaluated in this study. A study by Gandhi and colleagues [63] reviewed medication errors and potential ADEs in adult and pediatric outpatients receiving outpatient chemotherapy and found that medication errors occurred in 3% of medication orders in this pediatric population, with 60% of these errors classified as potentially causing an ADE. None of these medication errors was considered life threatening, and none resulted in a true AE.

Summary

Since the 2000 IOM report, *To Err is Human*, patient safety has vaulted into the consciousness of patients, health care providers, regulators, insurance companies, researchers, and the lay press. Early efforts to improve patient safety focused on preventing error, with more recent strategies focusing on decreasing patient harm. Efforts to improve patient safety have been hampered by relatively inaccurate measurement techniques; however, recent evidence suggests detection of AE is improving with the aid of the more focused and efficient trigger tool measurement methodology. Use of this methodology has provided estimates of ADE rates for hospitalized children of 11.1 per 100 patients and AE rates in NICU-based patients of 74 per 100 patients. The extent of medication- and nonmedication-related harm in pediatric outpatients currently is unknown. Future efforts should focus on continued development of a reliable measurement strategy (including developing population-specific trigger tools and automation of these tools using electronic medical records), identification of pediatric populations at most risk for AEs, and a more extensive evaluation of pediatric AEs in outpatient settings. These data then can be used to target the highest risk populations and highest risk classes of AEs in children so that appropriate interventions can be implemented.

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