

Medication Errors and Adverse Drug Events in Pediatric Inpatients

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IATROGENIC INJURIES OCCUR FREQUENTLY in hospitalized patients and often have serious sequelae.¹ The Harvard Medical Practice Study estimated that 3.7% of hospitalized patients experienced an adverse event related to medical therapy in New York State in 1984.¹ Of these iatrogenic injuries, 69% were preventable.² A more recent study reached similar estimates.³ An Institute of Medicine report in 1999 estimated that 44 000 to 98 000 people die each year at least in part because of medical error.⁴ Although there has been some controversy about the accuracy of these extrapolated estimates,⁵⁻⁷ the report dramatically increased awareness of the problem of medical errors.

In the Harvard Medical Practice Study, the most common adverse events were complications of medication use (19.4% of all events).⁸ Thirty percent of patients with drug-related injuries died or were disabled for more than 6 months, although not all morbidity and mortality was directly attributable to these drug-related injuries.¹ In response to these concerning findings, the Adverse Drug Event Prevention Study was performed, which addressed medication errors and adverse drug events (ADEs) in hospitalized adults in more detail.^{9,10} It found that ADEs were com-

Context Iatrogenic injuries, including medication errors, are an important problem in all hospitalized populations. However, few epidemiological data are available regarding medication errors in the pediatric inpatient setting.

Objectives To assess the rates of medication errors, adverse drug events (ADEs), and potential ADEs; to compare pediatric rates with previously reported adult rates; to analyze the major types of errors; and to evaluate the potential impact of prevention strategies.

Design, Setting, and Patients Prospective cohort study of 1120 patients admitted to 2 academic institutions during 6 weeks in April and May of 1999.

Main Outcome Measures Medication errors, potential ADEs, and ADEs were identified by clinical staff reports and review of medication order sheets, medication administration records, and patient charts.

Results We reviewed 10 778 medication orders and found 616 medication errors (5.7%), 115 potential ADEs (1.1%), and 26 ADEs (0.24%). Of the 26 ADEs, 5 (19%) were preventable. While the preventable ADE rate was similar to that of a previous adult hospital study, the potential ADE rate was 3 times higher. The rate of potential ADEs was significantly higher in neonates in the neonatal intensive care unit. Most potential ADEs occurred at the stage of drug ordering (79%) and involved incorrect dosing (34%), anti-infective drugs (28%), and intravenous medications (54%). Physician reviewers judged that computerized physician order entry could potentially have prevented 93% and ward-based clinical pharmacists 94% of potential ADEs.

Conclusions Medication errors are common in pediatric inpatient settings, and further efforts are needed to reduce them.

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mon (occurring at a rate of 6.5 per 100 adult admissions), costly, and often had severe sequelae.^{9,11} Other studies largely confirmed these findings.^{12,13}

Several studies suggest that about one third of ADEs are associated with medication errors and are thus preventable.^{9,14} Bates et al¹⁵ found that medication errors were common, occurring at a rate of 5 per 100 medication orders. However, only 7 in 100 medication errors had significant potential for harm, and 1 in 100 actually resulted in an injury.¹⁵

Analysis of the origin of errors has suggested that specific improvements in the medication ordering and processing system might reduce the risk of error.¹⁰ Several studies have demon-

strated that some of these interventions can be effective. In particular, physician computer order entry reduced medication errors significantly in an academic medical center,¹⁶ as did a dedicated clinical pharmacist in an academic intensive care unit (ICU).¹⁷ Similarly, a computerized clinical decision support program dramatically de-

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creased antibiotic-associated medication errors and ADEs, as well as total costs for patients in an ICU.¹⁸

Less information is available regarding the epidemiology and prevention of medication errors and ADEs in pediatric inpatient settings.¹⁹ Children pose unique challenges to the system for ordering, dispensing, administering, and monitoring medications. For example, since weight-based dosing is needed for virtually all drugs in pediatrics, ordering medications typically involves more calculations than for adults. Dispensing drugs in pediatrics is also error-prone because pharmacists often must dilute stock solutions. Young children do not have the communication skills to warn clinicians about potential mistakes in administering medications, or about adverse effects that they may experience. Finally, all children, especially neonates, may have more limited internal reserves than adults with which to buffer errors. For example, the cardiovascular system of a premature baby may be unable to cope with even a small error in the dosage of an inotropic agent.

To assess the epidemiology of medication errors, potential ADEs, and ADEs in hospitalized children, we performed a prospective cohort study in 2 academic institutions. Our goals were to (1) determine the rates of medication errors, potential ADEs, and ADEs; (2) compare rates in a pediatric hospital setting with previously reported rates in adult hospitals; (3) analyze the major types of errors; and (4) assess the potential impact of prevention strategies.

METHODS

Study Sites

The study was conducted at 2 urban teaching hospitals with socioeconomically diverse patient populations. One hospital (hospital A) is a freestanding pediatric institution. The other hospital (hospital B) treats both adult and pediatric patients, but has a geographically and administratively distinct pediatric service. Adults comprise less than 5% of patients treated on the pediatric wards. They generally have complex long-

term medical and surgical conditions, such as congenital diseases (eg, cystic fibrosis, cardiac anomalies, metabolic diseases, sickle cell disease), multiple disabilities, immunosuppressive conditions, and eating disorders.

At hospital A, we studied 2 randomly selected general medical wards, 1 randomly selected general surgical ward, the short-stay medical ward, and the pediatric medical/surgical ICU (which has few cardiac patients because there is a separate cardiac ICU). The oncology ward and neonatal ICU (NICU) were not studied at this hospital because these units were preparing for possible introduction of computerized order entry. At hospital B, all pediatric wards were studied, including the general medical/surgical wards (including oncology patients), the pediatric medical/surgical ICU, and the NICU. In total, we studied 9 wards. There were clear differences in case mix, as well as staffing, among individual wards of the 2 hospitals.

Medication Systems

Physicians at both hospitals currently handwrite orders, copies of which are sent to the pharmacy. At hospital A, nurses transcribe orders into the medication administration record (MAR). Hospital A has satellite-based pharmacists who dispense ready-to-administer doses to the floor, but do not actively participate in other activities, such as ward-based rounds.

At hospital B, clerks transcribe orders into the MAR. A supply of medications is provided to the units, with nurses subsequently performing dose calculations and drug administration. Pediatric clinical pharmacists attend work rounds, monitor transcriptions, and assist nurses with calculations. Since these pharmacists are assigned to multiple units daily, they have limited time to spend on each unit.

Definitions

Medication errors were defined as errors in drug ordering, transcribing, dispensing, administering, or monitoring. An example is an order written for

amoxicillin without a route of administration. Some medication errors have significant potential for injuring a patient and are considered potential ADEs. Potential ADEs may be intercepted before reaching the patient. An example of an intercepted potential ADE would be an order written for a 10-fold overdose of morphine that is intercepted and corrected by a pharmacist before reaching the patient. A nonintercepted potential ADE would be an overdose of acetaminophen administered to a patient who does not experience any sequelae. ADEs are injuries that result from the use of a drug. Some ADEs are associated with a medication error and therefore are considered preventable, while some are not associated with a medication error and therefore are considered nonpreventable. An example of a preventable ADE is the development of rash after the administration of ampicillin/sulbactam to a patient known to be allergic to penicillin. In contrast, a nonpreventable ADE would be development of *Clostridium difficile* colitis after appropriate antibiotic use. Finally, rule violations are faulty medication orders with little potential for harm or extra work because nursing and pharmacy staff typically interpret them correctly without additional clarification. An example is a pain medication ordered on a per need basis for a postoperative patient without an explicit reason for administration stated. Rule violations were not considered medication errors.

Case Finding

One physician (R.K.) trained all data collectors, who were nurses, pharmacists, and physicians, in an identical manner. During the 2-week training period, the unique perspectives of these different disciplines were shared to maximize appreciation of potential error types and to develop a comprehensive, uniform approach to error detection. We determined inter-rater reliability by a random sampling of 10% of the data collected at each institution by a data collector from the other institution.

Data collectors identified medication errors, potential ADEs, and ADEs

Table 1. Rates of Medication Errors and Adverse Drug Events (ADEs)*

	Total	No. per 100 Orders	No. per 100 Admissions	No. per 1000 Patient-Days
Medication orders	10 778	NA	962	2741
Medication errors	616	5.7	55	157
Potential ADEs	115	1.1	10	29
ADEs	26	0.24	2.3	6.6
Preventable ADEs	5	0.05	0.52	1.8
Nonpreventable ADEs	21	0.20	1.9	5.3

*NA indicates data not applicable.

by voluntary and verbally solicited reports from house officers, nurses, and pharmacists; and by medication order sheet, MAR, and chart review of all hospitalized patients on study wards. On a given day, 1 data collector was assigned to each study ward based on individual availability. Data collected for each incident included name, dose, route and category of drug, point in the system where the error occurred, and type of error. Data collectors worked 5 days per week, with recording of week-end data on Mondays for patients still hospitalized. At the end of the study, we obtained administrative data for each patient hospitalized on the study wards, including age, sex, and race.

Reliable detection of medication errors requires cooperation and engagement of the staff, which depends in large measure on reducing suspicion and fear of reporting. Before initiating this study, we gained the support of the leadership of nursing, pharmacy, medical staff, and administration at each hospital. House staff, nurses, and pharmacists received informal seminars that emphasized the roles of complex systems and human factors in predisposing to error, as opposed to individual blame. We stressed the importance of understanding the epidemiology and causes of error, and reinforced the multidisciplinary nature of systems improvement. We performed the study over 6 weeks in April and May of 1999, after obtaining institutional review board approval at each institution.

Review Process

Two physicians (D.W.B. and D.A.G.) independently reviewed suspected ADEs and potential ADEs and classi-

fied them as ADEs, potential ADEs, medication errors, and rule violations. The physician reviewers rated ADEs and potential ADEs according to the severity of injury to the patient using a 4-point Likert scale. They also rated ADEs on preventability using a 5-point Likert scale and attribution (ie, the likelihood that the incident is due to the specific drug) using the Naranjo algorithm.²⁰ The 2 evaluators resolved all disagreements through discussion and consensus.

Statistical Methods

We report rates of errors per 100 orders, 100 admissions, and 1000 patient-days. We did subanalyses of preventable and potential ADEs. We measured age-specific rates per 100 admissions, and analyzed them assuming that the number of errors occurring during an admission followed a Poisson distribution. We measured ward-specific rates per 100 orders and compared them using the χ^2 test for categorical variables since it was extremely rare for more than 1 error to occur during a single order. Similarly, we compared rates per 100 orders between adult and pediatric hospital settings and analyzed them using the χ^2 test. When we assumed that the number of errors per order followed a Poisson distribution, we obtained similar results, so we report only the χ^2 test results. The SAS statistical package (for Windows 6.12) was used (SAS Institute Inc, Cary, NC).

We calculated inter-rater reliabilities using the percentage of agreement and the κ statistic. The data collectors and physician reviewers had moderate-to-excellent agreement with 87%-to-100% agreement and κ statistics of 0.65 to 1.0.

RESULTS

The 36-day study period included 1120 admissions and 3932 patient-days, during which 10 778 orders were written. The patients included 183 (16%) neonates, 326 (29%) infants, 223 (20%) preschoolers, 161 (14%) school-aged children, 191 (17%) teenagers, and 36 (3%) adults. Of the children, 525 (49%) were female, 731 (65%) were white, 139 (12%) were Hispanic, and 79 (7%) were black.

There were 616 medication errors (5.7%) or 55 medication errors per 100 admissions (TABLE 1). In total, 320 patients accounted for these medication errors and 64 patients had 3 or more errors. We found 26 ADEs (0.24%), of which 5 (19%) were preventable. In addition, we identified 115 potential ADEs (1.1%), which occurred at a rate of 10 potential ADEs per 100 admissions.

Medication errors occurred more frequently in adults compared with other age groups (86 vs 62 for neonates, 41 for infants, 48 for preschoolers, 58 for school-aged children, and 63 for teenagers per 100 admissions; $P = .006$). The rate of potential ADEs was considerably higher in neonates than in other age groups (20 vs 5 for infants, 8 for preschoolers, 12 for school-aged children, 11 for teenagers, and 14 for adults per 100 admissions; $P < .001$).

Given the high rate of neonatal potential ADEs, we performed a subanalysis comparing the 54 neonatal patients in the NICU with the 129 neonatal patients in other wards. The NICU neonates were primarily premature with low birth weights and respiratory and nutritional issues, while non-NICU neonates were primarily admitted for infections or congenital abnormalities. Neonates in the NICU experienced significantly higher medication error and potential ADE rates (91 and 46 per 100 admissions, respectively) than neonates in other wards (50 and 9 per 100 admissions, respectively) ($P < .001$ for both comparisons).

Error rates were similar across units (5.5 errors per 100 orders for the NICU, 5.7 for pediatric ICUs, 6.0 for medical wards, 6.1 for combined medical/

surgical wards, and 4.7 for the surgical ward; $P = .31$). However, the NICU had a significantly higher rate of potential or preventable ADEs compared with other wards (2.8 per 100 orders vs 0.78 for medical wards, 0.44 for surgical wards, 0.77 for combined medical/surgical wards, and 1.3 for pediatric ICUs; $P < .001$).

Most medication errors were dosing errors (28%), followed by route of administration, MAR transcription and documentation, date, and frequency of administration errors (TABLE 2). Similarly, most potential ADEs were due to dosing errors (34%), followed by frequency and route errors. The most common stage for medication errors and potential ADEs was physician ordering (74% and 79%, respectively), followed by transcription and nurse administration. The most common drugs involved in medication errors and potential ADEs were anti-infective agents, analgesics and sedatives, electrolytes and fluids, and bronchodilators. The drug routes of medication errors and potential ADEs were most commonly intravenous followed by oral and inhalation.

In addition, physician reviewers judged that 93% of the potential ADEs were potentially preventable by physician computer order entry with clinical decision support, 94% by ward-based clinical pharmacists, and none by computerized MAR. Finally, they judged that computerized physician order entry could have prevented 4 of the 5 preventable ADEs and that ward-based clinical pharmacists could have prevented 4 of the 5 preventable ADEs. For these judgments, the role of the clinical pharmacist included full-time participation in work rounds, monitoring the MAR transcription process, communicating with satellite pharmacies, and assisting nurses with medication dose calculation and administration.

During the study period, 26 ADEs were identified, 5 of which resulted from medication errors and thus were judged to be preventable (TABLE 3). The preventable ADEs included excessive sedation, hypothermia, worsening pain, a

rash, and stool impaction. Errors associated with these 5 incidents included 2 overdoses, a missing dose, a drug administration error, and administration

of a medication to a patient with a known allergy. Two events involved narcotics, 1 an analgesic, 1 an antibiotic, and 1 a laxative. The route of 2 medications

Table 2. Types of Medication Errors and Potential Prevention Strategies*

Variable	Medication Errors (n = 616)	Potential Adverse Drug Events (n = 115)
Error type		
Dose	175 (28)	44 (34)
Frequency	58 (9.4)	23 (20)
Route	109 (18)	16 (14)
Medication administration record transcription or documentation	85 (14)	9 (7.8)
Wrong drug	8 (1.3)	6 (5.2)
Wrong patient	1 (0.16)	1 (0.86)
Known allergy	8 (1.3)	5 (4.3)
Illegible order	14 (2.3)	2 (1.7)
Missing or wrong weight	23 (3.7)	1 (0.86)
No or wrong date	74 (12)	0 (0)
Other	61 (9.9)	8 (7)
Stage of error		
Physician ordering	454 (74)	91 (79)
Transcribing	62 (10)	13 (11)
Nurse administering	78 (13)	5 (4.3)
Pharmacy dispensing	6 (0.97)	4 (3.5)
Patient monitoring	4 (0.65)	0 (0)
Missing	12 (1.9)	3 (2.6)
Drug category		
Anti-infective drugs	120 (20)	32 (28)
Analgesics and sedatives	101 (16)	19 (17)
Electrolytes and fluids	162 (26)	17 (15)
Bronchodilators	44 (7.1)	11 (9.6)
Other	166 (27)	36 (31)
Missing	23 (3.7)	0 (0)
Drug route		
Intravenous	337 (55)	62 (54)
Oral	126 (21)	25 (22)
Inhalation	46 (7.5)	14 (12)
Other	82 (13)	14 (12)
Missing	25 (4.1)	0 (0)
Potential prevention strategy		
Ward-based clinical pharmacist	587 (95)	108 (94)
Computerized physician order entry with decision support	419 (68)	107 (93)
Computerized medication administration record	110 (18)	0 (0)

*Values are expressed as number (percentage).

Table 3. Preventability and Severity of Adverse Drug Events (ADEs) and Potential ADEs

Level of Severity	No. (%) of ADEs		No. (%) of Potential ADEs	
	Not Preventable (n = 21)	Preventable (n = 5)	Not Intercepted (n = 47)	Intercepted (n = 68)
Fatal or life-threatening	2 (10)	0 (0)	2 (4)	16 (23)
Serious	5 (24)	4 (80)	24 (51)	28 (41)
Significant	14 (66)	1 (20)	21 (45)	24 (35)

Table 4. Comparison of Medication Errors and Adverse Drug Events (ADEs) in Pediatric and Adult Hospital Settings

	No. (%)		P Value
	Pediatric (n = 10 778)	Adult* (n = 10 070)	
Medication errors	616 (5.7)	530 (5.3)	.15
Potential ADEs	115 (1.1)	35 (0.35)	.001
ADEs	26 (0.24)	25 (0.25)	.92
Preventable ADEs	5 (0.05)	5 (0.05)	.91
Nonpreventable ADEs	21 (0.20)	20 (0.20)	.95

*Prior study carried out at Brigham and Women's Hospital with similar methods in 1992.¹⁵

was intravenous, 1 oral, 1 epidural, and 1 via suppository. Physician reviewers classified 4 of the preventable ADEs as serious and 1 as significant. Of the 21 nonpreventable ADEs, 14 were related to antibiotic use, including *C difficile* infections, rashes, allergic reactions, gastrointestinal tract distress, and a yeast infection. The remaining 7 were narcotic-related, including respiratory depression, sedation, and gastrointestinal tract and allergic reactions. Fifteen of the medications were administered intravenously, 5 orally, and 1 via epidural.

Of the 115 potential ADEs, 68 (59%) were intercepted while 47 (41%) were not (Table 3). The physician reviewers determined that 18 (16%) of the potential ADEs were potentially fatal or life-threatening, 52 (45%) were serious, and 45 (39%) were significant. Examples of potentially fatal or life-threatening intercepted potential ADEs included physician orders for a heparin overdose, a digoxin overdose, and amoxicillin for a patient with a previous anaphylactic reaction to penicillin. Among the most common errors associated with potential ADEs were physicians ordering inappropriately high or low doses of medications, ordering medications despite known allergies, ordering medications without routes, and the pharmacy dispensing incorrect medications.

COMMENT

We found that medication errors were common in the inpatient pediatric setting. Potential ADEs occurred more frequently in neonates, particularly in the NICU. The rate of medication errors was higher in adults cared for in the pediatric hospital setting.

Errors occurred most commonly at the stage of drug ordering. Dosing errors and errors involving the intravenous route were most frequent. The drug classes associated most frequently with errors were anti-infectives, electrolytes and fluids, and analgesics and sedatives. Most errors appeared to be preventable by physician computer order entry with clinical decision support or full-time, ward-based clinical pharmacists.

We compared the results of this study to a 1992 study using similar methods in an adult patient population (TABLE 4).¹⁵ In 1992, physicians at the adult hospital hand-wrote orders, clerks primarily transcribed orders to the MAR, and pharmacists were primarily satellite-based, with some ward-based involvement in the medical ICU. Both studies had similar rates of medication errors, ADEs, and preventable ADEs; however, the rate of potential ADEs was about 3 times higher in this pediatric study (1.1% vs 0.35%; $P < .001$). Inter-institutional comparisons can be difficult to standardize, although in this case 1 physician (D.W.B.) was involved in both studies.

Relatively little research has addressed the problem of medication errors and ADEs in pediatric inpatient settings. Reliable error detection requires intensive, comprehensive, and active ward-based data collection. We used a multidisciplinary approach that examined all aspects of the medication system, from the physician's order through administration of the drug to the patient. Moreover, we encouraged voluntary reporting by emphasizing the role of systems problems in the origin of er-

rors and by nurturing a blame-free environment. In a previous pediatric study by Folli et al,¹⁹ errors were detected solely by pharmacist review of physician orders, and lower error rates of 0.45 to 0.49 per 100 orders were found. Although 74% of errors in our study occurred in drug orders, many of these errors were detected and corrected prior to the order reaching the pharmacy.

As expected, we found that the errors with potential for harm occurred most often in the youngest, most vulnerable patients cared for in the NICU. Neonatal weights change rapidly, making appropriate dosing particularly difficult. Moreover, medication errors in critically ill neonates may have more serious consequences compared with relatively healthy neonates or older children because they have limited ability to buffer errors. Pharmacists also face special challenges with neonatal drugs because medications generally are not supplied in dosages suitable for neonates and must be diluted.

The relatively small number of adult patients also had significantly higher medication error rates. This may be due to the typically high medical complexity of adult patients cared for in pediatric settings, or the lack of familiarity of pediatric house staff with adult dosing.

The high risk of medication errors highlights the importance of developing, testing, and implementing effective error-prevention strategies in pediatrics. Cogent theories regarding the origin of errors (often categorized as human factor research)²¹ have been developed. Most investigators have focused on problems in health care delivery systems that predispose to error, rather than emphasizing the role of individuals.²²⁻²⁶ Human fallibility is magnified substantially by complex and poorly designed systems, poor teamwork, and psychological and environmental stressors such as fatigue, anxiety, poor lighting, and noise. The safest work environments address these issues by designing systems to prevent errors, make errors visible, and mitigate the effects of errors.²² Ongoing multidisciplinary analysis of incidents, also

termed root cause analysis, is important for developing further system improvements.²⁷

While a number of interventions based on these principles have been studied in adults, few data are available in pediatrics. The study by Folli et al¹⁹ demonstrated that pharmacy review of medication orders could prevent erroneous orders from being implemented at a rate of 14 to 18 per 1000 patient-days. Unfortunately, other interventions remain largely untested in children.

Review of preventable and potential ADEs by the physician evaluators in this study suggested that the majority could potentially have been prevented by computerized physician order entry with clinical decision support (eg, drug-allergy checks, drug-dose checks, drug-drug interaction checks). This finding is not surprising since 79% of the potential ADEs occurred at the stage of ordering of medications. Common types of ordering errors included physician omission or incorrect choice of dose, route, or frequency; order illegibility; and physician use of non-standard terminology.

Studies in adult hospitals have demonstrated the impact of computerized physician order entry on error reduction. Computerized physician order entry reduced the rate of nonintercepted serious medication errors by 55% in a large tertiary care adult hospital.¹⁶ In another study of this system, limited decision support decreased the medication error rate by 64%, and with more developed decision support the error rate decreased by 81%.²⁸ Coupling physician order entry with a computerized MAR is likely to reduce transcription errors, a common class of inpatient medication errors (10% in this study).

It is important to recognize, however, that some of the factors making children vulnerable to errors also complicate development of computerized pediatric systems. For example, pharmacokinetics and appropriate drug doses change rapidly as a premature neonate gains weight and renal and

hepatic drug elimination systems mature. A pediatric computer order entry system will have to be sufficiently flexible to respond to these changes.

Review of preventable and potential ADEs by the physician evaluators in this study suggested that full-time, ward-based clinical pharmacists potentially could have prevented the majority of errors. Traditionally, physicians decide on drug therapy, and pharmacists and nurses implement these decisions. The presence of clinical pharmacists on work rounds may lead to more informed clinical decisions by physicians, as well as interception of errors before medication orders are finalized. Their presence on the wards should facilitate communication between clinical staff and the pharmacy. In addition, clinical pharmacists could independently monitor the transcription process, assist nurses with drug preparation and administration, and monitor the drug preparation, storage, and distribution systems. They also could be involved in developing education programs and drug therapy protocols. Although ward-based pharmacists were present in one of the hospitals we studied, they were not involved full time in work rounds, monitoring the transcription process, or other ward-based error prevention activities.

A clinical pharmacist participating in physician rounds in an adult ICU decreased preventable ADEs by 66%.¹⁷ In addition, ward-based interventions may reduce costs of care. During a 3-month study, a clinical pharmacist made 345 interventions in an adult ICU, leading to a \$24 000 cost reduction.²⁹ However, the impact of ward-based clinical pharmacists has not been assessed in pediatrics.

Our study has several limitations. We studied 2 academic institutions, so our results may not be generalizable to nonacademic hospitals in which most children receive care. Despite a comprehensive multidisciplinary approach to data collection, we probably failed to detect some errors, particularly

administration errors detected more reliably by trained observers following nurses during routine patient care activities.³⁰ Also, we did not attempt to detect inappropriate drug choice, which is detected most reliably using explicit criteria based on evidence, rather than implicit criteria based on clinical judgment.³¹ Because nurses and physicians on the study wards were aware of the study, the Hawthorne effect could have affected both the occurrence and detection of errors. In addition, the incidence of errors could have been reduced as the study progressed because we were obliged to take corrective action when we identified serious practice problems. For example, an incorrect preparation of insulin was dispensed to one of the medical floors resulting in mild hypoglycemic events in children with diabetes, and we notified the pharmacy immediately.

Classification bias may have affected our finding that the highest rate of potential ADEs occurred in neonates, since we used expert clinical judgment and consensus to classify incidents. The 2 investigators who made these determinations may have been inclined to consider errors as potentially harmful when they occurred in critically ill neonates. However, the potential ADE rate was so much higher in this group that it is unlikely to be completely attributable to subjectivity. Furthermore, 3 of the 5 preventable ADEs occurred in neonates in the NICU.

The development and testing of medication error reduction interventions is important in pediatrics, especially in the NICU, given the increased medical vulnerability and decreased communication ability of small and critically ill children, the need for weight-based dosing, and the need for pharmacy dilution of stock medications. To reduce the rates of potential and preventable ADEs in pediatrics, the most effective interventions are likely to be computerized physician order entry with integrated clinical decision support and full-time, ward-based clinical pharmacists.

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REFERENCES

1. Brennan TA, Leape LL, Laird N, et al. Incidence of adverse events and negligence in hospitalized patients: results from the Harvard Medical Practice Study I. *N Engl J Med.* 1991;324:370-376.
2. Leape LL, Lawthers AG, Brennan TA, Johnson WG. Preventing medical injury. *Qual Rev Bull.* 1993;19:144-149.
3. Thomas EJ, Studdert DM, Burstin HR, et al. Incidence and types of adverse events and negligent care in Utah and Colorado. *Med Care.* 2000;38:261-271.
4. *To Err is Human: Building a Safer Health System.* Washington, DC: National Academy Press; 1999.
5. Leape LL. Institute of Medicine medical error figures are not exaggerated. *JAMA.* 2000;284:95-97.
6. McDonald CJ, Weiner M, Hui SL. Deaths due to medical errors are exaggerated in Institute of Medicine report. *JAMA.* 2000;284:93-95.
7. Brennan TA. The Institute of Medicine report on medical errors—could it do harm? *N Engl J Med.* 2000;342:1123-1125.
8. Leape LL, Brennan TA, Laird NM, et al. The nature of adverse events in hospitalized patients: results from the Harvard Medical Practice Study II. *N Engl J Med.* 1991;324:377-384.
9. Bates DW, Cullen D, Laird N, et al. Incidence of adverse drug events and potential adverse drug events: implications for prevention. *JAMA.* 1995;274:29-34.
10. Leape LL, Bates DW, Cullen DJ, et al. Systems analysis of adverse drug events. *JAMA.* 1995;274:35-43.
11. Bates DW, Spell N, Cullen DJ, et al. The costs of adverse drug events in hospitalized patients. *JAMA.* 1997;277:307-311.
12. Classen DC, Pestotnik SL, Evans RS, Lloyd JF, Burke JP. Adverse drug events in hospitalized patients: excess length of stay, extra costs, and attributable mortality. *JAMA.* 1997;277:301-306.
13. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA.* 1998;279:1200-1205.
14. Bates DW, Leape LL, Petrycki S. Incidence and preventability of adverse drug events in hospitalized adults. *J Gen Intern Med.* 1993;8:289-294.
15. Bates DW, Boyle DL, Vander Vliet MB, Schneider J, Leape LL. Relationship between medication errors and adverse drug events. *J Gen Intern Med.* 1995;10:199-205.
16. Bates DW, Leape LL, Cullen DJ, et al. Effect of computerized physician order entry and a team intervention on prevention of serious medication errors. *JAMA.* 1998;280:1311-1316.
17. Leape LL, Cullen DJ, Clapp MD, et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. *JAMA.* 1999;282:267-270.
18. Evans RS, Pestotnik SL, Classen DC, et al. A computer-assisted management program for antibiotics and other antiinfective agents. *N Engl J Med.* 1998;338:232-238.
19. Folli HL, Poole RL, Benitz WE, Russo JC. Medication error prevention by clinical pharmacists in two children's hospitals. *Pediatrics.* 1987;79:718-722.
20. Naranjo CA, Busto O, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther.* 1981;30:239-245.
21. Reason J. *Human Error.* Cambridge, England: Cambridge University Press; 1990.
22. Leape LL. Error in medicine. *JAMA.* 1994;272:1851-1857.
23. Perrow C. *Normal Accidents.* New York, NY: Basic Books; 1984.
24. Forrester JW. Counterintuitive behavior of social systems. *MIT Technol Rev.* 1971;73:52-68.
25. Berwick DM. Continuous improvement as an ideal in health care. *N Engl J Med.* 1989;320:53-56.
26. Glauber J, Goldmann DA, Homer CJ, Berwick DM. Reducing medical error through systems improvement: the management of febrile infants. *Pediatrics.* 2000;105:1330-1332.
27. Joint Commission on Accreditation of Healthcare Organizations. *Comprehensive Accreditation Manual for Hospitals: The Official Handbook.* Oakbrook, Ill: Joint Commission on Accreditation of Healthcare Organizations; 1999.
28. Bates DW, Teich J, Lee J, et al. The impact of computerized physician order entry on medication error prevention. *J Am Med Inform Assoc.* 1999;6:313-321.
29. Katona BG, Ayd PR, Walters JK, Caspi M, Finkelshtein BW. Effect of a pharmacist's and a nurse's interventions on cost of drug therapy in a medical intensive-care unit. *Am J Hosp Pharm.* 1989;46:1179-1182.
30. Allan EL, Barker KN. Fundamentals of medication error research. *Am J Hosp Pharm.* 1990;47:555-571.
31. Asthon CM, Kuykendall DH, Johnson ML, et al. An empirical assessment of the validity of explicit and implicit process-of-care criteria for quality assessment. *Med Care.* 1999;37:798-808.