

ERROR MANAGEMENT

Medication errors in paediatric care: a systematic review of epidemiology and an evaluation of evidence supporting reduction strategy recommendations

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Qual Saf Health Care 2007;16:116–126. doi: 10.1136/qshc.2006.019950



Appendices are available on the QSHC website <http://qshc.bmj.com/supplemental>

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Accepted 27 January 2007

Background: Although children are at the greatest risk for medication errors, little is known about the overall epidemiology of these errors, where the gaps are in our knowledge, and to what extent national medication error reduction strategies focus on children.

Objective: To synthesise peer reviewed knowledge on children's medication errors and on recommendations to improve paediatric medication safety by a systematic literature review.

Data sources: PubMed, Embase and Cinahl from 1 January 2000 to 30 April 2005, and 11 national entities that have disseminated recommendations to improve medication safety.

Study selection: Inclusion criteria were peer reviewed original data in English language. Studies that did not separately report paediatric data were excluded.

Data extraction: Two reviewers screened articles for eligibility and for data extraction, and screened all national medication error reduction strategies for relevance to children.

Data synthesis: From 358 articles identified, 31 were included for data extraction. The definition of medication error was non-uniform across the studies. Dispensing and administering errors were the most poorly and non-uniformly evaluated. Overall, the distributional epidemiological estimates of the relative percentages of paediatric error types were: prescribing 3–37%, dispensing 5–58%, administering 72–75%, and documentation 17–21%. 26 unique recommendations for strategies to reduce medication errors were identified; none were based on paediatric evidence.

Conclusions: Medication errors occur across the entire spectrum of prescribing, dispensing, and administering, are common, and have a myriad of non-evidence based potential reduction strategies. Further research in this area needs a firmer standardisation for items such as dose ranges and definitions of medication errors, broader scope beyond inpatient prescribing errors, and prioritisation of implementation of medication error reduction strategies.

The Institute of Medicine report *To Err Is Human* shone a spotlight on preventable medical errors and since the release of the report patient safety has become the pre-eminent issue for health care.¹ With our understanding of the problems and solutions for patient safety growing daily, it has become clear that the prescribing, dispensing, and administration of medications represent a substantial portion of the preventable medical errors that occur with children and that children are more at risk for medication errors than adults.^{2,3}

Despite the awareness that children are at increased risk for medication errors, little is known about the epidemiology of these errors and where the gaps remain in our present knowledge. We conducted a systematic literature review to synthesise all the peer reviewed knowledge on medication errors for children published since the release of the *To Err Is Human* report.¹ Our scope included all care settings and all types of medications. In addition, we synthesised all the recommendations to improve paediatric medication safety from national entities and evaluated the paediatric evidence provided to support these recommendations for effectiveness, efficacy, cost effectiveness, feasibility, appropriateness in different settings and institutional barriers.

METHODS

Study inclusion criteria for systematic literature review on medication errors

Articles eligible for inclusion in our synthesis had to report peer reviewed English language original data on the epidemiology of

medication errors in children published between 1 January 2000 and 30 April 2005. Medication errors were defined as any preventable error in the medication administration process starting from prescribing and including preparing, dispensing, administering, monitoring the patient for effect, and transcribing (eg, medication administration record (MAR)). We only included adverse drug events (ADEs) that were described by the studies as either preventable or having significant potential for harm to the patient (fig 1).²

Search strategy for systematic literature review on medication errors

We completed searches of PubMed, Embase and Cinahl in April 2005. The search strategy combined terms for the population (eg, paediatric) and terms to identify articles dealing with medication errors (eg, medication errors as Medical Subject Heading, preventable adverse event) (Appendix 1, available at <http://qshc.bmj.com/supplemental>). References for all eligible articles were also reviewed. The search results were tracked in a database created in the bibliographic software ProCite (ISI, Berkeley, California, USA).

Two independent non-blinded reviewers screened the title and abstract of each article to determine eligibility. At the full-text level, two non-blinded reviewers screened articles and, if the article was eligible, extracted relevant information in a

Abbreviations: ADEs, adverse drug events; MAR, medication administration record

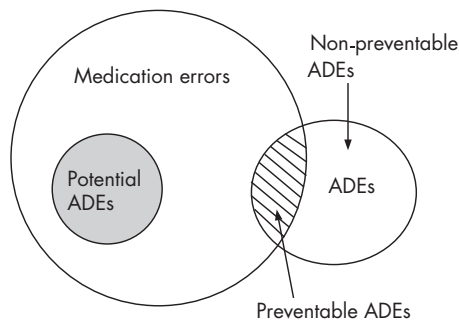


Figure 1 Relationship between medication errors, potential adverse drug events (ADEs), and ADEs.⁴

sequential fashion so that the second reviewer was able to see the extraction results from the first reviewer. All reviewers had either clinical degrees or health services research degrees with experience in systematic reviews. All reviewer pairings at all stages of this effort included at least one clinician, and the reviewer pairings for the abstracts were kept for the full text review. Discrepancies were resolved by consensus between the two reviewers after discussion. We developed and pilot tested forms to extract information such as duration of the study, type of study, the incidence of medication errors and information about the medication errors studied, such as the type and severity (Appendix 2, available at <http://qshc.bmj.com/supplemental>). Evidence tables summarising the information from the articles were created from the spreadsheets and we qualitatively synthesised the literature since no articles included comparable numerators, denominators, or definitions for medication error that would have permitted quantitative synthesis of the articles.

Synthesis of recommendations to reduce medication errors for children

Working in conjunction with the Institute of Medicine, we identified national entities that have created and disseminated recommendations to improve medication safety either specifically for children or more broadly for all patients. These entities were: Institute for Safe Medication Practices, Pediatric Pharmacy Advocacy Group, American Hospital Association, American Academy of Pediatrics/National Initiative for Children's Healthcare Quality, Institute of Medicine, National Quality Forum, Massachusetts Hospital Association/Massachusetts Coalition for the Prevention of Medical Errors, National Coordinating Council for Medication errors Reporting and Prevention, Agency for Healthcare Research and Quality, and Joint Commission on Accreditation of Healthcare Organizations.¹⁻⁴⁻²² We reviewed all the published recommendations from these bodies and any cited literature to support the recommendations to determine whether this literature included, or was specific for, children.

RESULTS

Literature search for systematic review on medication errors

Our search identified 358 articles. Eight-four (23%) of these articles were deemed eligible through the title and abstract screening. The most common reason for excluding an article from further consideration was lack of original data. A further 52 articles were excluded during the full-text review, and we were unable to retrieve one article, leaving 31 articles for full text data extraction.²³⁻⁵³ Figure 2 provides an overview of the search and screening process (Appendix 3 lists the articles excluded, available at <http://qshc.bmj.com/supplemental>).

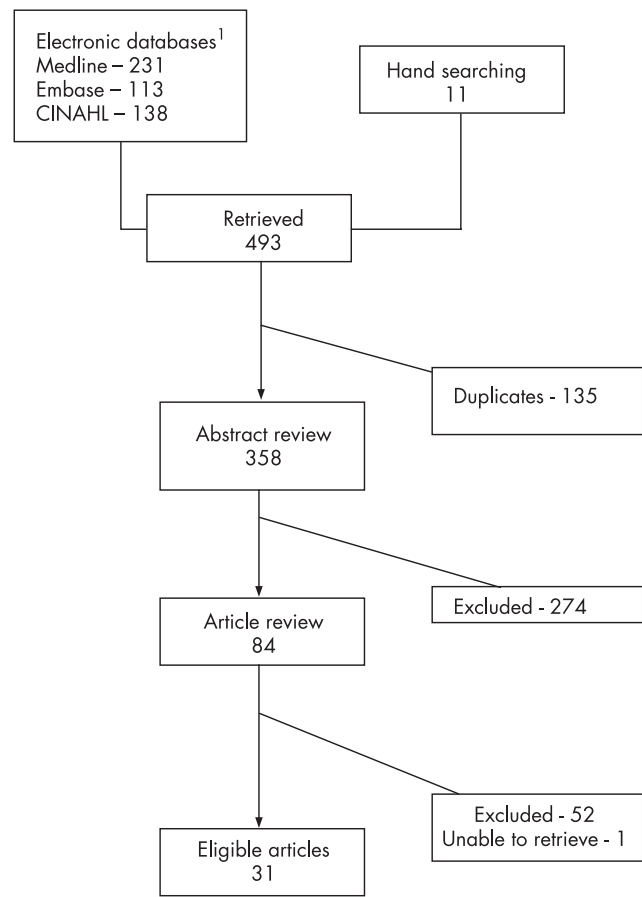


Figure 2 Summary of search and review process.

Systematic literature review on medication errors Study characteristics

Design

Table 1 details the characteristics of the 31 studies. Twenty-three of the 31 studies occurred within single institutions and 21 included data from a ≤ 1 year period, with the minimum time period being 1 week. Twenty-two of the studies evaluated paediatric inpatients, five studies were focused on either ambulatory clinics or emergency departments and three studies evaluated the home setting. Eighteen of the studies evaluated all medications able to be dispensed in that care setting, whereas 13 studies focused on only a subset of medications (table 1).

Overall the numerator data reported was described as or was consistent with "medication errors" in 25 studies, "ADEs" in 1 study, and 5 studies reported both medication errors and ADEs. The types of medication errors reported included prescribing errors ($n = 14$), dispensing errors ($n = 7$), administering errors ($n = 14$), monitoring patient for effects errors ($n = 1$), MAR errors ($n = 7$), and overall lumping of all of these error types ($n = 14$). There was non-uniformity in the definitions used, if they were explicitly stated, for medication errors. For example, one study defined an error as only those orders with a 10-fold dosing error and another defined medication errors as only those with $>10\%$ deviation from recommended dose. These differences are detailed in tables 3-8 under numerator and numerator description columns.

Denominator data

The denominator data were equally non-uniform among the studies. The possible denominators included: manual

Table 1 Summary of article characteristics

Citation	Type of study	Setting	Type of medication studied	Type of numerator	Type of denominator	How were data obtained	Types of errors collected
Simpson <i>et al</i> ²³	Interventional	ICU patients only	All types		Patient days	Incident/error reports	All types
Petridou <i>et al</i> ²⁵	Retrospective review without controls	Clinic or outpatient	Vaccines	Medication errors	Time period (2 years)	Incident/error reports	All types
Cimino <i>et al</i> ²⁸	Interventional	ICU patients only	All types	Adverse drug events and medication errors	Manual medication orders	Chart reviews	All types
Butte <i>et al</i> ³¹	Cohort		Immunisations	Medication errors	Manual medication orders and patients	Chart reviews	All types
Marino <i>et al</i> ³³	Cohort	Inpatient	All types	Medication errors	Manual medication orders and patient days	Chart reviews	All types
Cote <i>et al</i> ³⁵		Inpatient and outpatient	Sedatives for procedures	Medication errors	Manual error reports	Incident/error reports, solicited case reports	All types
Upperman <i>et al</i> ³⁷	Interventional	Inpatient	All types	Adverse drug events	Per 1000 doses dispensed	Incident/error reports	All types
Slonim <i>et al</i> ³⁹	Retrospective review without controls	Inpatient	All types	ICD9 code 995.2!	Admissions	Administrative data (ICD9 codes)	All types
Cowley <i>et al</i> ³⁸	Incident report/case series review	Inpatient	All types	Medication errors	Computerised error reports	Incident/error reports from MER and MedMARx	All types and administering
Potts <i>et al</i> ⁴⁰	Interventional	ICU patients only	All types	Adverse drug events and medication errors	Manual medication orders	Chart reviews	All types and prescribing
Holdsworth <i>et al</i> ⁴⁵	Retrospective chart reviews and staff interviews	Inpatient	All types	Preventable ADEs* as determined by authors and potential ADEs*	Patient days, admissions and medical record evidence of ADE*: excluded errors corrected before medication put into MAR	Chart reviews and interviews	All types, prescribing and dispensing
Sangtawesin <i>et al</i> ⁴¹	Retrospective review without controls	Inpatient	All types	Medication errors	Admissions	Incident/error reports	All types, prescribing, dispensing and administering
Frey <i>et al</i> ⁴⁸	Incident report/case series review	ICU patients only	All types	Medication errors	Manual error reports	Incident/error reports	All types, prescribing, dispensing, administering and MAR/documentation
Kaushal <i>et al</i> ⁴²	Cohort	Inpatient	All types	ADEs and medication errors	Manual medication orders, patient days and admissions	Chart reviews	All types, prescribing, dispensing, administering, monitoring patient for effect and MAR/documentation
Derrough and Kitchin ³⁷	Incident report/case series review	Mix	Vaccines	Inadvertent vaccine administration	Prospective inquiries of inadvertent admission of vaccines: calls by providers to pharmaceutical company information service	Incident/error reports	Administering
Li <i>et al</i> ⁴⁴	Cross sectional	Home	Paracetamol and ibuprofen	Medication errors	Patients ≤ 10 receiving paracetamol or ibuprofen at home in past 24 hours	Survey to parents	Administering
Losek ⁴⁶	Retrospective review without controls	Emergency department	Paracetamol administered by emergency department staff	Medication errors	Patients	Chart reviews	Administering
Feikema <i>et al</i> ⁴¹	Cross sectional	Clinic or outpatient	Vaccines	Extra immunisations	Patients	Chart reviews from National Immunisation Survey screenings	Administering
Goldman and Scolnik ⁵²	Cross sectional parental interview	Home	Paracetamol administered by parents at home	Medication errors	Patients	Interviews	Administering
McErlean <i>et al</i> ⁴³	Cross sectional parental interview	Home	Antipyretic drugs administered by parent at home	Medication errors	Patients	Interviews	Administering
Parshuram <i>et al</i> ⁴²	Prospective observational	ICU patients only	Morphine infusion	Discrepancies between ordered and measured concentrations	Number of infusions	Liquid chromatography	Dispensing
Cable and Craft ²⁶	Retrospective review without controls	Inpatient	All types	Disagreement of Cardex with order	Manual medication orders	Chart reviews	MAR/documentation
Lehmann <i>et al</i> ⁴⁷	Interventional	ICU patients only	TPN	Medication errors	Manual medication orders (TPN)	Order review	Prescribing

Table 1 Continued

Citation	Type of study	Setting	Type of medication studied	Type of numerator	Type of denominator	How were data obtained	Types of errors collected
Cordero <i>et al</i> ⁶⁹	Interventional	ICU patients only	Gentamicin	Medication errors	VLBW infants born consecutively 6 months before CPOE receiving drug	Chart reviews and medical records	Prescribing
Lesar ³⁶	Incident report/case series review	Inpatient	All types	Medication errors	Computerised error reports, patient days and admissions identified by pharmacists and entered into relational database	Incident/error reports	Prescribing
Farrar <i>et al</i> ⁶⁹	Interventional study	Inpatient	All types	Medication errors	Computerised medication orders	Chart reviews	Prescribing
Fontan <i>et al</i> ⁶⁴	Cohort	Inpatient	All types	Medication errors	Manual medication orders and computerised medication orders	Chart reviews	Prescribing and administering
Kozer <i>et al</i> ⁶⁹	Retrospective review without controls	Emergency department	All types	Medication errors	Manual medication orders	Chart reviews	Prescribing and administering
Pichon <i>et al</i> ⁶⁰	Retrospective review with controls	Inpatient	All types	Medication errors	Manual medication orders	Chart reviews	Prescribing and MAR/Documentation
France <i>et al</i> ⁶⁴	Incident report/case series review	Inpatient	Chemotherapy only	Medication errors	Computerised error reports	Incident/error reports	Prescribing, dispensing, administering and MAR/documentation
King <i>et al</i> ⁴³	Interventional	Inpatient	All types	Adverse drug events and medication errors	Manual error reports	Incident/error reports	Prescribing, dispensing, administering and MAR/documentation

ADE, adverse drug event; CPOE, computerised physician order entry; ICU, Intensive care unit; MAR, medication administration record; MedMARx, United States Pharmacopeia database designed to reduce medication errors in hospitals; MER: medication errors reporting programme submitted to United States Pharmacopeia; TPN, total parenteral nutrition; VLBW, very low birth weight.

*ADEs are defined as having the potential to produce significant injury, includes errors detected before drug administration as well as errors that did not produce significant adverse consequences, excludes errors that were identified and corrected before the medication was entered into MAR.

†ICD9, International Classification of Disease, 9th edition. Public Health Service and Health Care Financing Administration. International classification of diseases, 9th revision, clinical modification. Vols 1, 2, and 3; eighth edition. Washington, DC: Public Health Service; 1997.

‡Code 995.2: adverse effect/allergic reaction/hypersensitivity/idiosyncrasy of drug, medicinal and biological substance (due) to correct medicinal substance properly administered.

(paper-based) error reports, computerised error reports, manual medication orders, computerised medication orders, patient days, number of admissions, and time periods. Furthermore, many studies had very narrowly defined denominators, such as number of total parenteral nutrition orders or patients <10 years of age who received paracetamol or ibuprofen in the past 24 hours.

Source of data collection

The majority of the overall data was collected by either chart reviews ($n = 14$) or incident/error reports ($n = 11$). Although studies that used incident/error reports cannot be used to assess overall epidemiology of medication errors in children, we included them in order to provide insight into the distributional epidemiology of types of medication errors seen in children.

Overall medication error results from systematic literature review

Fourteen of 31 studies reported overall medication error data that included the entire spectrum from prescribing through to monitoring patient for effect. Table 2 gives the results of these studies. Of these, seven reported broad estimates of overall medication error rates in all children based on actual or estimated data using denominators such as patient days, admissions, or orders as opposed to evaluating only medication error reports (Simpson 2004²³; Cimino 2004²⁸; Potts 2004³⁰; Sangtawesin 2003³¹; Holdsworth 2003³⁵; Kaushal 2001⁴²; Marino 2000⁴³). Using the studies, the results showed a range of estimated medication errors per medication orders from 5%

to 27% based on three studies with similar numerators and denominators that allow consideration together (Cimino 2004²⁸; Kaushal 2001⁴²; Marino 2000⁴³).

Prescribing error results from systematic literature review on medication errors

Fourteen studies reported medication prescribing errors (table 3). These summarised an estimated prescribing error rate per medication orders of 30%, 20%, and 4% from the three studies that used similar numerators and denominators (Potts 2004³⁰; Fontan 2003³⁴; Kaushal 2001⁴²). The first two studies in this estimate appeared to have broader definitions of medication errors, which may explain the higher error rate estimates. For example, both included all types of omissions as a medication error, such as omissions of weight and prescriber's name. Three of the studies reported overall prescribing errors as rates per patient. The estimates from these studies are prescribing errors for each patient of 4–400 per 1000 patients (Sangtawesin 2003³¹; Kozer 2002³⁹; Kaushal 2001⁴²).

Dispensing error results from systematic literature review on medication errors

Seven studies reported dispensing errors, although the design of the studies was very different (table 4). Looking at the greatest commonality between these studies—namely, those studies based on error reports, the estimates of the percentage of reported errors that are related to dispensing vary widely from 5% to 58% (France 2004²⁴; King 2003³³; Frey 2002³⁸).

Table 2 Summary of studies with overall medication error results

Citation	Numerator and numerator description	Denominator and denominator description
Simpson <i>et al</i> ²³	24.1 Mean monthly medication errors, includes prescribing and administration errors	Per 1000 neonatal activity days, recorded over 3 months
Petridou <i>et al</i> ²⁵	11 Estimated incidence of errors in prescribing, dispensing, administering immunisations based on assumption of 100 000 children born in Greece each year and each child gets 10 immunisations: from National Poison Control Registry with estimated 47 000 calls a year over 2 year period 40 Immunisation errors reported from National Poison Control Registry 12 Wrong route (eg OPV given IM*) errors reported from National Poison Control Registry 13 Overdose errors reported from National Poison Control Registry 6 DTP instead of DT administered errors reported from National Poison Control Registry 3 Expired vaccine errors reported from National Poison Control Registry 7 Extra dose errors reported from National Poison Control Registry	Per 1 000 000 immunisation doses, recorded over 2 years 47 000 Estimated calls a year, recorded over 2 years
Cimino <i>et al</i> ²⁸	3259 Orders with errors 1335 Orders with errors excluding missing date/time only 1924 Orders with only time/date errors 16 Preventable ADEs 2249 Low ADE potential (missing information only)	12 026 Manual PICU orders in 2 weeks
Potts <i>et al</i> ²⁰	147 Potential ADEs*: includes duplicate treatment, inappropriate dose/interval/route, wrong drug, allergy, drug interaction, wrong units 466 Rule violations: includes trailing zeros, abbreviations 2662 Potential ADEs*, medication prescribing errors and rule violations	6803 Manual PICU orders in 2 months
Sangtawesin <i>et al</i> ³¹	322 Medication errors	32 105 Admissions in 14 months
Holdsworth <i>et al</i> ²⁵	46 Preventable ADEs: preventable as determined by authors 94 Potential ADEs* 46 Preventable ADEs as defined above 94 Potential ADEs* as defined above	1197 Admissions in 8 months 10 164 Patient days in 8 months
Frey <i>et al</i> ²⁸	253 Prescription, dispensing and administering errors 93 Dose too high errors, either prescribed, dispensed or administered 55 Drug omitted errors, either prescribed, dispensed or administered 39 Dose too low errors, either prescribed, dispensed or administered 34 Wrong route errors, either prescribed, dispensed or administered 32 Wrong drug errors, either prescribed, dispensed or administered	275 Error reports in 2001
Butte <i>et al</i> ⁴¹	206 Patients with at least one invalid immunisation 289 Invalid doses: dose given before minimum recommended age, doses given within the recommended spacing from previous dose, dose given unnecessarily (this means 1 year earlier than required age), live virus vaccine given too close to previous live virus vaccine 98 Invalid doses because given before recommended age 2 Invalid doses because given too close to live virus dose 96 Invalid doses because unnecessary extra dose 105 Invalid doses because too close to previous dose 12 Invalid doses because too young and too close to previous dose	580 Charts reviewed in 3 months 6983 Immunisation doses given in 3 months
Kaushal <i>et al</i> ⁴²	616 Medication errors defined as errors in drug ordering, transcribing, dispensing, administering or monitoring 115 Potential ADEs* defined as errors with significant potential for injuring patient 5 Preventable ADEs* defined as ADE* associated with medication error 337 IV medication errors 126 Oral medication errors 46 Inhalation medication errors	10 778 Orders, 1120 admissions and 3932 patient days in 6 weeks
Marino <i>et al</i> ²³	784 Medication errors	3312 Orders in summer 1995 11 978 Doses in summer 1995 669 Patient days in summer 1995 95 ADE reports for sedations from 1969 to March, 1996 as described in numerator
Cote <i>et al</i> ²⁵	38 Drug overdoses or local anaesthetic overdoses submitted to the FDA's incident reporting system, cases from USP and case reports from paediatric anaesthesiologists, intensivists, and paediatric emergency medicine specialists 9 Prescribing/transcribing errors as described above	Per 1000 doses, recorded over 9 months 2003 Paediatric errors submitted in 2 years
Upperman <i>et al</i> ⁴⁷	0.3 ADEs	
Cowley <i>et al</i> ²⁸	543 Omission reports submitted to MedMARx database 494 Wrong dose/quantity reports submitted to MedMARx database 253 Wrong time reports submitted to MedMARx database	
Slonim <i>et al</i> ²⁰	0.13 1988 drug errors based on reported ICD9† code 995.2‡. All results are national estimates, no real numerator and denominator stated 0.09 1991 drug errors as described above 0.07 1994 drug errors as described above 0.03 1997 drug errors as described above	Per 100 paediatric admissions reported nationally

ADE, adverse drug event; DT, diphtheria and tetanus toxoids vaccine; DTP, diphtheria and tetanus toxoids and cellular pertussis vaccine; FDA, Food and Drug Administration; IM, intramuscularly; MAR, medication administration record; MedMARx, United States Pharmacopeia database designed to reduce medication errors in hospitals; OPV, oral polio vaccine given; PICU, paediatric intensive care unit; USP, United States Pharmacopeia.

*Potential ADE defined as having the potential to produce significant injury, includes errors detected before drug administration as well as errors that did not produce significant adverse consequences, excludes errors that were identified and corrected before the drug was entered into MAR.

†ICD9, International Classification of Disease, 9th edition. Public Health Service and Health Care Financing Administration. International classification of diseases, 9th revision, clinical modification. Vols 1, 2, and 3; eighth edition. Washington, DC: Public Health Service; 1997.

‡Code 995.2: adverse effect/allergic reaction/hypersensitivity/idiosyncrasy of drug, medicinal and biological substance (due) to correct medicinal substance properly administered.

Table 3 Prescribing error results summary

Citation	Numerator and numerator description	Denominator and denominator description
France <i>et al</i> ⁴	71 Chemotherapy ordering errors: includes dosing, omission and wrong date errors	97 Electronically reported chemotherapy errors in 13 months
Lehmann <i>et al</i> ²⁷	60 TPN errors that required pharmacist to contact provider: includes osmolality problems, insufficient fluid, calculation errors, omissions	557 TPN orders in 1.5 months
Cordero <i>et al</i> ²⁹	14 Gentamicin prescription dosage errors: prescribed dose >10% deviation from recommended dose	105 VLBW infants born consecutively 6 months before CPOE receiving drug
Potts <i>et al</i> ³⁰	5 Gentamicin overdoses: >10% overdose	6803 Manual PICU orders in 2 months
Sangtawesin <i>et al</i> ³¹	9 Gentamicin underdoses: >10% underdose	32105 Admissions in 14 months
King <i>et al</i> ³³	2049 Medication prescribing errors: includes weight not available, missing information	416 Medication errors in 3 years
Fontan <i>et al</i> ³⁴	114 Prescribing errors: includes wrong dose, wrong choice, known allergy and others	4532 Prescribed drugs in 2 months
	13 Prescribing medication errors	
	937 Prescribing errors: includes any error in the prescription of drug's name, form, dosage, route, any omission of these prescribing items including prescriber's name and any drug interaction.	
	419 Computerised prescribing errors as defined above	3943 Computerised prescribed drugs in 2 months
	518 Hand written prescribing errors	589 Hand written prescribed drugs in 2 months
	44 Wrong form errors	4532 Prescribed drugs in 2 months
	19 Wrong route errors	
	47 Wrong dosage errors	
	34 Wrong dosage form errors	
	587 Omission errors	
	152 "Caution" drug interactions	
	0 "Contraindicated" and "not advised" drug interactions	
Holdsworth <i>et al</i> ³⁵	35 Preventable ADEs that were underdose, wrong dose and overdose: preventable was determined by authors	46 Preventable ADEs in 8 months
	39 Potential ADEs* that were underdose and overdose	
Lesar ³⁶	39 Prescribing errors occurring in paediatric patients: all errors were prevented before reaching patient	94 Potential ADEs* in 8 months as defined above
	0.53 10-Fold error rate in paediatric patients	200 Error reports identified by pharmacists and entered into a relational database in 6 months
	0.98 10-Fold error rate in paediatric patients	Per 100 admissions, recorded over 6 months
Frey <i>et al</i> ³⁸	102 Overall prescribing errors	275 Error reports in 2001
	9 Illegible errors	
	37 Calculation errors	
	22 Wrong unit errors (eg ml instead of mg)	
Kozer <i>et al</i> ³⁹	154 Prescribing errors	1532 Charts reviewed in 12 randomly selected days in summer
	117 Wrong frequency errors	
	133 Wrong dose errors	
	5 Wrong drug errors	
	7 Wrong route errors	
Pichon <i>et al</i> ⁴⁰	76 Incomplete non-chemotherapy orders defined as omissions: number of doses missing, route missing, dose missing	198 Non-chemotherapy orders
	89 Non-chemotherapy order omissions: more than one omission possible in a single order	
	19 Omissions on non-chemotherapy PRN orders	
Kaushal <i>et al</i> ⁴²	454 Physician ordering medication errors	22 Non-chemotherapy PRN orders
	91 Physician ordering potential ADEs*: defined as errors with significant potential for injuring patient	10 778 Orders, 1120 admissions and 3932 patient days in 6 weeks
Farrar <i>et al</i> ⁴⁹	29 Prescribing errors for non-paediatricians for orders reviewed	38 Non-paediatricians' orders reviewed
	17 Prescribing errors for paediatricians for orders reviewed	65 Paediatricians' orders reviewed

ADE, adverse drug event; CPOE, computerised physician order entry; MAR, medication administration record; PICU, paediatric intensive care unit; PRN, drug administered as required; TPN, total parenteral nutrition; VLBW, very low birth weight.

*Potential ADE defined as having the potential to produce significant injury, includes errors detected before drug administration as well as errors that did not produce significant adverse consequences, excludes errors that were identified and corrected before the drug was entered into MAR.

Table 4 Dispensing error results summary

Citation	Numerator and numerator description	Denominator and denominator description
France <i>et al</i> ⁴	9 Preparation chemotherapy errors	97 Electronically reported chemotherapy errors in 13 months
Sangtawesin <i>et al</i> ³¹	112 Dispensing errors	32 105 Admissions in 14 months
Parshuram <i>et al</i> ³²	150 Discrepancies of >10% between ordered and measured infusions of morphine	232 Infusions in 7 months
	13 Twofold or greater discrepancy between ordered and measured infusions of morphine	
King <i>et al</i> ³³	19 Dispensing errors	416 Medication errors in 3 years
Holdsworth <i>et al</i> ³⁵	39 Number of dispensing potential ADEs*	94 Potential ADEs* in 8 months
Frey <i>et al</i> ³⁸	162 Dispensing errors	275 Error reports in 2001
Kaushal <i>et al</i> ⁴²	6 Pharmacy dispensing medication errors	10 778 Orders, or 1120 admissions, or 3932 patient days in 6 weeks
	4 Pharmacy dispensing potential ADEs*: defined as errors with significant potential for injuring patient	

ADE, adverse drug event; MAR, medication administration record.

*Potential ADE defined as having the potential to produce significant injury, includes errors detected before drug administration as well as errors that did not produce significant adverse consequences, excludes errors that were identified and corrected before the drug was entered into MAR.

Table 5 Administering error results summary

Citation	Numerator and numerator description	Denominator and denominator description
France <i>et al</i> ⁴⁴	13 Administering chemotherapy errors	97 Electronically reported chemotherapy errors in 13 months
Sangtawesin <i>et al</i> ¹	49 Administering errors: includes wrong time, omission error, wrong strength, unauthorised drug, wrong patient, extra dose, wrong route, wrong dosage form	32105 Admissions in 14 months
King <i>et al</i> ³³	314 Administering errors	416 Medication errors in 3 years
Fontan <i>et al</i> ⁴⁴	1077 Administering errors defined as any deviation between prescribed and administered drugs: includes extra/omitted dose, wrong route, wrong time and patient non-compliant 57 Extra dose errors 454 Dose omission errors 17 Wrong dose errors 2 Wrong route errors 8 Patient non-compliant errors 539 Wrong time errors	4589 Opportunities for administering errors: the sum of administered drugs and omitted drugs in 2 months
Derrough and Kitchin ⁵⁷	161 Inadvertent administration of vaccine to children: includes out of schedule according to the national recommendations, error in reconstitution of vaccine or diluent used, vaccine given at inappropriate age, inappropriate interval between vaccines, wrong vaccine (eg DTP for DT), expired vaccine, vaccine contraindicated. From pharmaceutical company telephone-based vaccine information service	302 Inadvertent vaccine administrations (all age groups) in 1 year
Frey <i>et al</i> ⁸⁸	200 Administering errors	275 Error reports in 2001
Kozer <i>et al</i> ⁹⁹	59 Administering errors	1532 Charts reviewed in 12 randomly selected days in summer
Kaushal <i>et al</i> ⁴²	78 Nurse administering medication errors 5 Nurse administering potential ADEs*: defined as errors with significant potential for injuring patient	10 788 Orders, 1120 admissions and 3932 patient days in 6 weeks
Li <i>et al</i> ⁴⁴	87 Incorrect paracetamol doses at home 66 Paracetamol underdoses at home 21 Paracetamol overdoses at home 6 Paracetamol doses given more frequently than 4 hours at home 19 Incorrect ibuprofen doses at home 9 Ibuprofen underdoses at home 10 Ibuprofen overdoses at home 28 Ibuprofen doses given more frequently than 6 hours at home	140 Patients who received home administrations of paracetamol in past 24 hours, recorded over 3 months 74 Patients who received home administrations of ibuprofen in past 24 hours, recorded over 3 months
Losek ⁴⁶	34 Paracetamol doses outside standing orders of 10–15 mg/kg	156 Emergency department patients receiving paracetamol in 1 week
Cowley <i>et al</i> ⁴⁸	1007 Administering errors submitted to MedMARx database	1956 Paediatric errors with phase of error indicated submitted to MedMARx in 2 years 22806 Paediatric patients in 1997
Feikema <i>et al</i> ⁵¹	4789 Patients overimmunised for at least one vaccine	213 Patients who received home administrations of paracetamol recorded over 3 months
Goldman and Scolnik ⁵²	26 Paracetamol overdoses at home: defined as >10–15 mg/kg	118 Patients who received home administration of antipyretic drugs
McErlean <i>et al</i> ⁵³	87 Paracetamol underdoses at home: defined as <10–15 mg/kg 53 Incorrect doses of antipyretic drug at home compared with recommended dose	

ADE, adverse drug event; DT, diphtheria and tetanus toxoids vaccine; DTP, diphtheria and tetanus toxoids and cellular pertussis vaccine; MedMARx: United States Pharmacopoeia database designed to reduce medication errors in hospitals.

Administration error results from systematic literature review on medication errors

Fourteen studies reported administration errors for children (table 5). Six of these studies were medication-specific with two focused on vaccines and four focused on paracetamol and/or ibuprofen only. Of the three studies which were global in scope, nevertheless, variation among the studies in numerator

and denominator definitions and methods of data collection made comparisons difficult. Using the one study that defined “total opportunities for administering errors” as the global denominator, the distributional epidemiology of administration errors shows that the majority of these errors involved either dose omissions (42%) or wrong time of administration (50%) (Fontan 2003³⁴).

Table 6 MAR documentation error results summary

Citation	Numerator and numerator description	Denominator and denominator description
France <i>et al</i> ⁴⁴	3 Chemotherapy transcription errors	97 Electronically reported chemotherapy errors in 13 months
Cable and Craft ²⁶	109 Disagreement with Cardex 49 Major causes of disagreement: different dose, wrong medication, wrong frequency or duration, missing route 39 Orders not on Cardex	540 Randomly selected paediatric medication orders drawn from over 2 years
Sangtawesin <i>et al</i> ¹	46 “Order processing” errors	32 105 Admissions in 14 months
King <i>et al</i> ³³	70 Transcription errors	416 Reported medication errors in 3 years
Frey <i>et al</i> ⁸⁸	58 Errors in transcription of physicians order onto medication chart	275 Error reports in 2001
Pichon <i>et al</i> ⁴⁰	41 Non-chemotherapy transcription errors 16 Chemotherapy transcription errors	198 Non-chemotherapy orders 135 Chemotherapy orders
Kaushal <i>et al</i> ⁴²	85 Documentation medication errors 9 Documentation potential ADEs: defined as errors with significant potential for injuring patient	10 778 Orders, or 1120 admissions, or 3932 patient days in 6 weeks

ADE, adverse drug event.

Table 7 Monitoring for effect error results summary

Citation	Numerator and numerator description	Denominator and denominator description
Kaushal <i>et al</i> ⁴²	4 Monitoring medication errors; 0 Monitoring potential ADEs defined as errors with significant potential for injuring patient	10 778 Orders, or 1120 admissions, or 3932 patient days in 6 weeks

ADE, adverse drug event.

MAR/documentation error results from systematic literature review on medication errors

Seven studies evaluated documentation errors among children (table 6). The estimate of transcription errors from these studies varies from <1% of orders to 20% of orders having a transcription error.

Monitoring the patient for effect error results from systematic literature review on medication errors

Only one study, listed in table 7, reported monitoring a patient for effect errors and estimated, via chart review, that the incidence was four errors per 1000 patients (Kaushal 2001⁴²).

Distributional epidemiology of medication error from error reports

Four studies provided data that can be synthesised to understand the distributional epidemiology of medication errors in paediatrics based on error reports (France 2004²⁴; King 2003³³; Lesar 2002³⁶; Frey 2002³⁸). Such syntheses are difficult because each study location undoubtedly has different safety culture climates. The safety culture will clearly influence who completes error reports, how often they complete error reports, and what types of event are reported. Little is known about how bias in reporting influences the distributional epidemiology of medication errors. Two of these studies provided data on all medications relative to prescribing, dispensing, administering, and documentation errors (King 2003³³; Frey 2002³⁸). Between these two studies, the distributional epidemiological estimates of the relative percentages of error types are: prescribing 3–37%, dispensing 5–58%, administering 72–75%, and documentation 17–21%.

Estimates of the severity of medication errors for patients

Only 11 studies categorised medication errors by severity of outcome for the patient (Simpson 2004²³; France 2004²⁴; Cimino 2004²⁸; Sangtawesin 2003³¹; Holdsworth 2003³⁵; Frey 2002³⁸; Kozer 2002³⁹; Kaushal 2001⁴²; Marino 2000⁴³; Upperman 2005⁴⁷; Cowley 2001⁴⁸). Among these studies, however, at least four different scales were used to rank error severity from scales with two categories to scales with nine categories.

Synthesis of recommendations to reduce medication errors for children

We identified a total of 26 unique recommendations for strategies to reduce medication errors from national entities. The recommendations ranged from equipment/software tools, representation of personnel on groups making decisions on paediatric medications, training and competency of personnel, policies, clear labelling, continuous quality improvement efforts, clear and accurate documentation, standardisation, patient education, and teamwork improvement. Table 8 summarises these recommendations and the paediatric specific evidence behind. In short, none of these recommendations was based on published evidence of effectiveness in children. The vast majority of recommendations were based on expert opinion (n = 22), with the remainder being based on studies in adult populations (n = 4). No recommendation had support-

ing paediatric specific evidence on efficacy, cost effectiveness, feasibility, appropriateness in different settings, and institutional barriers or risks.

CONCLUSIONS

Since the Institute of Medicine *To Err Is Human* report¹ a significant amount of research has been done on medication errors in children, and a significant number of recommendations have been made by various entities on how to make medication administration safer for children. There can be no doubt, based on this evidence, that medication errors are a significant percentage of medical errors in children. Our review estimates that 5–27% of medication orders for children contain an error somewhere along the spectrum of the entire delivery process involving prescribing, dispensing, and administering based on three studies (Cimino 2004²⁸; Kaushal 2001⁴²; Marino 2000⁴³). Our review also estimates that there are 100–400 prescribing errors per 1000 patients and highlights that the majority of research to date has focused on the prescribing step of medication delivery (Kozer 2002³⁹; Kaushal 2001⁴²).

Looking at error reporting systems, it is clear that each step of the medication process is error prone, although the majority of research has focused on prescribing errors. Our evidence based estimates at the overall “share of the pie” that each step contributes to the overall rate of medication errors among children are the following: prescribing 3–37%, dispensing 5–58%, administering 72–75%, and documentation 17–21% (King 2003³³; Frey 2002³⁸).

Overall, our depth of understanding of the epidemiology of paediatric medication errors remains poor. Our systematic literature review on medication errors highlights the fact that estimates of the incidence of medication errors in children are severely hampered by the lack of uniform definitions of medication errors (numerator data) and study population (denominator) among studies and by the different means of data collection used to identify errors.

Also of importance, many studies did not explicitly define medication errors. A recently published report looking only at prescribing errors in children highlighted the great difficulty in defining what a medication error is.⁵⁴ Barriers to defining medication errors in children and to then being able to measure the epidemiology of medication errors include: off-label use of medications with dosage ranges extrapolated from adult literature, different recommendations for dosing ranges for the same medication from different sources, and unclear rules as to when adult doses may be appropriate for children. None of the studies looking at all medications with details on prescribing errors stated what the “correct” dosing range was that guided their definitions and data collection.

Focusing on the source of data, the vast majority of studies evaluated in this report relied on either chart review or error reports, with a handful using administrative or registry data. Although each mode of identifying medication errors has strengths and weaknesses and will produce varying results, it seems likely that an ideal error identification system may involve multiple data sources and potentially include triangulation between administrative data, chart review, and voluntary error reports of critical incidents in order to maximise the

Table 8 Approaches recommended to reduce medication errors in paediatric

Approaches to reduce medication errors	Entities supporting approach (reference citations at end of table)	Based on published effectiveness evidence specific for children?	Alternative processes used to support approach	Efficacy, cost, feasibility, appropriateness in different settings, barriers data available for children?
1. Computerised provider order entry	PPAG, ISMP, AHA	No	Expert opinion	No
	AHRQ report	No	Adult data	No
	AAP/NICHQ	No	Expert opinion	No
	IOM report	No	Adult data	No
	NQF	No	Adult data	No
	MHA	No	Adult data	No
	NCC MERP	No	Expert opinion	No
2. Automated dispensing devices	AAP	No	Expert opinion	No
	ISMP, PPAG, AHA	No	Expert opinion	No
3. Paediatric presence with formulary management	AHRQ report	No	Adult data	No
	ISMP, PPAG, AHA	No	Expert opinion	No
4. Appropriate and competent pharmacy personnel and environment	AAP	No	Expert opinion	No
	ISMP, PPAG, AHA	No	Expert opinion	No
5. Pharmacist available "on call" when pharmacy is closed	NQF	No	Expert opinion	No
	NCC MERP	No	Expert opinion	No
	AAP	No	Expert opinion	No
	ISMP, PPAG	No	Expert opinion	No
6. Policies on verbal orders	AHA	No	Expert opinion	No
	MHA	No	Expert opinion	No
	ISMP, PPAG, AHA	No	Expert opinion	No
7. Clear and accurate labelling of medications	JCAHO	No	Expert opinion	No
	NQF	No	Expert opinion	No
	NCC MERP	No	Expert opinion	No
	AAP	No	Expert opinion	No
8. Quality improvement efforts with drug use evaluation and medication error reporting and review	ISMP, PPAG, AHA	No	Expert opinion	No
	NQF	No	Expert opinion	No
	NCC MERP	No	Expert opinion	No
	AAP	No	Expert opinion	No
9. Healthcare workers have access to current clinical information and references	ISMP, PPAG, AHA	No	Expert opinion	No
	IOM report	No	Expert opinion	No
	MHA	No	Expert opinion	No
	NCC MERP	No	Expert opinion	No
10. Emergency medication dosage calculation tools	AAP	No	Expert opinion	No
	ISMP, PPAG	No	Expert opinion	No
11. Accurate documentation of medication administration	ISMP, PPAG	No	Expert opinion	No
	MHA	No	Expert opinion	No
	NCC MERP	No	Expert opinion	No
12. Medication standardisation and appropriate storage	ISMP, AHA	No	Expert opinion	No
	IOM report	No	Expert opinion	No
	JCAHO	No	Expert opinion	No
	NCC MERP	No	Expert opinion	No
	ISMP, PPAG	No	Expert opinion	No
	IOM report	No	Expert opinion	No
	JCAHO	No	Expert opinion	No
	NQF	No	Expert opinion	No
	MHA	No	Expert opinion	No
	NCC MERP	No	Expert opinion	No
13. Training of all healthcare providers in appropriate medication prescribing, labelling, dispensing, monitoring, and administration	AAP	No	Expert opinion	No
	ISMP, AHA	No	Expert opinion	No
	IOM report	No	Expert opinion	No
	MHA	No	Expert opinion	No
14. Patient education on drugs	NCC MERP	No	Expert opinion	No
	AAP	No	Expert opinion	No
	ISMP, AHA	No	Expert opinion	No
	IOM report	No	Expert opinion	No
15. Direct participation of pharmacists in clinical care	MHA	No	Expert opinion	No
	NCC MERP	No	Expert opinion	No
	AAP	No	Expert opinion	No
16. Computer detection/alert systems for adverse drug events	AHRQ report	No	Some studies	No
	IOM report	No	Expert opinion	No
17. Reducing adverse drug events related to anticoagulants	NQF	No	Expert opinion	No
	AHRQ report	No	Some studies	No
18. Unit dose drug distribution systems	AHRQ report	No	Some studies	No
	AHA	No	Expert opinion	No
	NQF	No	Expert opinion	No
	MHA	No	Expert opinion	No
19. Special procedures and written protocols for high alert drugs	AHA	No	Expert opinion	No
	IOM report	No	Expert opinion	No
	NQF	No	Expert opinion	No
	JCAHO	No	Expert opinion	No
	MHA	No	Expert opinion	No
20. Use pharmaceutical software	IOM report	No	Expert opinion	No
	MHA	No	Expert opinion	No
21. Pharmacy-based IV admixture systems	MHA	No	Expert opinion	No
22. Use of bar coding for medication administration	MHA	No	Expert opinion	No
	NCC MERP	No	Expert opinion	No
23. Standardise equipment (e.g., pumps, weight scales)	AAP	No	Expert opinion	No
24. Standardise measurement systems (kilograms)	AAP	No	Expert opinion	No
25. Standardise order sheets to include areas for weight and allergies	AAP	No	Expert opinion	No
26. Encourage team environment for review of orders among nurses, pharmacists, prescribers	AAP	No	Expert opinion	No

PPAG, Pediatric Pharmacy Advocacy Group⁴⁻⁶; ISMP, Institute for Safe Medication Practices⁴⁻⁶; AHA, American Hospital Association⁷; AAP/NICHQ, American Academy of Pediatrics/National Initiative for Children's Healthcare Quality⁹⁻¹²; IOM, Institute of Medicine¹; NQF, National Quality Forum¹³⁻¹⁴; MHA, Massachusetts Hospital Association/Massachusetts Coalition for the Prevention of Medical Errors¹⁵⁻¹⁶; NCC MERP, National Coordinating Council for Medication errors Reporting and Prevention¹⁷⁻¹⁸; AHRQ, Agency for Healthcare Research and Quality¹⁹⁻²²; JCAHO, Joint Commission on Accreditation of Healthcare Organizations.²¹⁻²²

ability to identify events at each step of the process. Taken alone, each data source has significant limitations for defining the epidemiology of medication errors. Administrative data, as analysed here, are inexpensive, nearly universal, and permit unsolicited identification of potential events, although the depth of clinical information is limited. Chart review, on the other hand, provides in-depth clinical information but is fairly expensive to implement on a large scale and is limited by what is documented in the chart. Lastly, voluntary critical incident reporting depends completely on the compliance of providers with reporting but does provide real time in-depth clinical insights. Interdigitated use of these types of data collection would create a system less likely to produce a biased estimate of the epidemiology.

These significant limitations of the examined studies—namely, differing definitions of the numerators and denominators, lack of consistent definition of medication error, less robust and/or narrowly focused methodologies, and the aforementioned short time frames of data collection and single institutional experiences in these studies, make it very difficult, if not impossible, to generalise easily the findings to all healthcare settings. Indeed the vast ranges on some of the results for estimates of different types of medication errors bear testament to this difficulty.

Despite the limitations of the available literature, several key findings warrant discussion and suggest a further national agenda for medication errors in children.

First, standardisation of recommended doses for children is an essential step to enable providers, researchers, and developers of technological solutions for prescribing to speak a common and uniform language on what doses are acceptable and what doses are in error for children. For example, a recent review exploring the limitations of recommended doses for children found a nearly twofold difference in recommended doses of oxycodone, a narcotic, among three widely used references while a fourth reference simply listed no weight-based dose recommendation.⁵⁴ In a recently published study on paediatric ambulatory medication errors, one key finding was that no fewer error rates occurred at the one of three sites evaluated that used an electronic prescription writer.⁵⁵ This last finding was probably due to the absence of paediatric-specific dosing logic in the electronic prescription writer. Despite the push for computerised order entry and prescribing, the lack of uniform agreement on standard paediatric doses is at least part of the reason for the usual absence of paediatric-specific dosing tables powering most commercially available computerised order entry tools. Without standard paediatric doses, and requirements that these dosage rules are built into computerised prescribing tools, children will fail to reap the benefit of information technology in the medication delivery process.

Second, standardisation of definitions of medication errors is a clear need at hand. As examples of this problem based on the studies examined here, the range of definitions of medication errors included medications prescribed at >10% of the recommended dose all the way up to medications prescribed at 10-fold the recommended dose. The vast majority of the articles simply did not describe the details of the definition of a medication error that was used. Comparably, looking at the entire medication delivery system, some articles did not include errors that were detected before they reached the patient, whereas other articles counted these events as errors. This ambiguity about what exactly is a medication error also permits a wide range of severity of errors to be lumped together. For example, some of the studies counted as medication errors orders that were lacking a prescriber's signature. Although this is clearly an error, the magnitude of potential harm to patients is substantially different from that of orders with dosage errors.

Without standardised guidance, all these vastly different interpretations of medication errors are lumped together and make elucidation of high priority areas difficult.

Third, despite much work on medication errors in the inpatient setting, our review identified only a handful of research on medication errors in the emergency department, ambulatory care, and home environments. All of these are critical targets for future research.

Fourth, most of the research to date has been skewed on prescribing errors. Our review of error reporting systems' data clearly shows that the medication process steps of dispensing and administering are as error-prone, if not more so, than prescribing. Understanding the unique risks for children in these two steps is critical in order to understand better which interventions will remedy the risks. Unlike the medication process for adults, these steps for children rely much more heavily on manual compounding of liquid medications and administration to patients who are unable to perform their own medication safety checks. These facts may well make the dispensing and administering of medications more error prone for children than adult patients.

Last, our synthesis of the various medication error reduction strategies recommended by national bodies resoundingly illustrated the lack of paediatric-specific evidence. However, it is inarguable that many items on the list of reduction strategies do not need multiple clinical trials to prove their impact. High cost or high resource problems such as computerised order entry, automated dispensing devices, and use of bar coding for medication administration clearly do need high quality evidence in order to foster use and, perhaps more importantly, need to have paediatric-specific evidence. Many other items, on the other hand, are relatively inexpensive, and many even broach on commonsense based on knowledge of human factors. Strategies in this latter category include: paediatric presence on Formulary committees, appropriate and competent pharmacy personnel and environment, policies on verbal orders, and clear and accurate medication labelling. The lack of paediatric-specific data on these types of recommendations is non-troubling. Perhaps more troubling is the enormous scope of recommendations coming from numerous official bodies. Such a piecemeal recommendation path leaves most providers unclear about which of the recommendations has a greater priority should they be faced with human or monetary resource limitations. National research and efforts to summarise and endorse recommendations could help care givers prioritise safety efforts and ensure that the most promising strategies of those recommended are broadly implemented first.

In summary, our review of the literature on medication errors in children and on medication error reduction strategies highlights without question that we know medication errors occur across the entire spectrum of prescribing, dispensing and administering and are a significant source of concern for paediatric patients. Furthermore, the research also confirms that medication errors are a significant concern across all settings of care, including within the home. There can be no doubt of the need for greater understanding of all the aspects of medication errors discussed here so that effective interventions and policy can be crafted. This desired understanding, however, needs a firm foundation of standardisation for issues such as dose ranges, definitions of medication errors, and even for prioritisation of implementation of medication error reduction strategies.

ACKNOWLEDGEMENTS

This research was supported by contract M-150-IOM-2005-001 from the Institute of Medicine. The Institute of Medicine helped design the study and has given approval for publication.

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