

Interventions to Reduce Dosing Errors in Children

A Systematic Review of the Literature

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Abstract

Children are a particularly challenging group of patients when trying to ensure the safe use of medicines. The increased need for calculations, dilutions and manipulations of paediatric medicines, together with a need to dose on an individual patient basis using age, gestational age, weight and surface area, means that they are more prone to medication errors at each stage of the medicines management process. It is already known that dose calculation errors are the most common type of medication error in neonatal and paediatric patients. Interventions to reduce the risk of dose calculation errors are therefore urgently needed. A systematic literature review was conducted to identify published articles reporting interventions; 28 studies were found to be relevant. The main interventions found were computerised physician order entry (CPOE) and computer-aided prescribing. Most CPOE and computer-aided prescribing studies showed some degree of reduction in medication errors, with some claiming no errors occurring after implementation of the intervention. However, one study showed a significant increase in mortality after the implementation of CPOE. Further research is

needed to investigate outcomes such as mortality and economics. Unit dose dispensing systems and educational/risk management programmes were also shown to reduce medication errors in children. Although it is suggested that 'smart' intravenous pumps can potentially reduce infusion errors in children, there is insufficient information to draw a conclusion because of a lack of research. Most interventions identified were US based, and since medicine management processes are currently different in different countries, there is a need to interpret the information carefully when considering implementing interventions elsewhere.

Medication errors have been defined as "any preventable event that may cause or lead to inappropriate medication use or patient harm, while the medication is in the control of the healthcare professional, patient, or consumer. Such events may be related to professional practice, healthcare products, procedures and systems including: prescribing; order communication; product labelling, packaging and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use".^[1] Medication errors can occur during prescribing, transcribing, dispensing, administering or monitoring of drugs.^[2]

It is recognised that children are a particularly challenging group of patients for safe use of medicines.^[1] Paediatric medicines are more prone to medication errors at each stage of the medicine management process because their prescribing, administration and dispensing typically involve more calculations than adult medicines.^[2] Furthermore, many medicines are only available in adult formulations and concentrations, and must be modified or diluted for use in children. This poses particular challenges in drug ordering and delivery.

Because of the rapid and dynamic changes taking place between birth and adulthood, there is great variability in the pharmacokinetics of the drugs that children are given. In addition, there can be rapid and dramatic differences in a child's weight over time, necessitating frequent dose recalculations. This means that drug dosages must be calculated individually for each patient, leading to an increased risk of errors. In addition, children, especially those who are critically ill, have fewer physiological reserves with which to buffer errors such as overdoses, should they occur.^[3]

There have been many studies investigating medication errors occurring in healthcare and by far the majority of these studies have been carried out in adults; however, potential adverse drug events (where there is a potential for injury but no injury occurred)^[4] in children may be three times more common than in adults, with dosing errors and errors involving the intravenous route of drug delivery the most commonly reported.^[5] A further study by Folli et al.,^[6] also found that the most common type of medication errors in children were dosing errors, with antibacterials being the most commonly involved type of drug.

A 1-week study in UK hospitals (involving >10 000 beds) showed that on paediatric wards the number of prescriptions that had to be changed, following pharmacist intervention, was second only to the number changed in the intensive care unit.^[7] The number was higher than that on geriatric, medical or surgical wards, and most of the interventions were prescribing error related.

A previous systematic review was conducted by Wong et al.^[8] in 2004 to establish the strength of the evidence base that dosage errors are a significant problem in paediatric practice. Sixteen papers^[5,6,9-22] specifically investigated the incidence of medication errors in children and also reported the incidence of dosing errors. Of these 16 studies, 11 found that dosing errors were the most common type.^[5,6,9-11,13-17,22] Three of the remaining five studies found it to be the second most common type, regardless of variation in study settings, countries, methodology and definitions.^[12,18,19] Additionally, 17 case reports of dosing errors in children were found, most of which had devastating consequences.^[23-26]

The evidence so far clearly indicates that dosing errors are the most common type of paediatric medication error, comprising both potential and actual errors. The compounding factors previously highlighted augment the likelihood of such errors. Therefore, there is an urgent need to identify interventions to reduce such medication errors.

1. Systematic Literature Review

A scoping exercise was commissioned by the UK Patient Safety Research Programme of the Department of Health to identify interventions that have been put into place to reduce errors in the calculation of drug doses in paediatric medicine. The Co-operative of Safety of Medicines in Children (COSMIC) team was formed to conduct this scoping exercise, consisting of members from the School of Pharmacy, University of London; University of Nottingham; the Royal College of Paediatrics and Child Health; and the Neonatal and Paediatric Pharmacists Group.

The first step taken by the COSMIC team was to conduct a systematic literature review to identify interventions to assist in the calculation of drug doses in paediatric practice that have been explored and published. This review was performed in two parts. The initial review was conducted when the COSMIC project was commissioned and identified publications from the earliest years available on the databases to August 2004. Since completing the first review, further relevant reports have been published; therefore, the COSMIC team conducted an update review of recent publications (between September 2004 and October 2006). The results of both reviews are reported in this article.

2. Literature Search Methodology

The following databases were searched for relevant articles published up to October 2006: MEDLINE, EMBASE, International Pharmaceutical Abstracts (IPA), Pharmline, British Nursing Index, Allied & Complementary Medicine and Cochrane Library (CENTRAL, CDSR, DARE). In addition, Cumulative Index to Nursing and Allied Health Literature (CINAHL) was searched for articles published up to November 2006.

The search engine Dialog was used to facilitate simultaneous searching of MEDLINE, EMBASE, IPA and CINAHL. The search included studies published in all languages

The search strategy used consisted of the following keywords: 'prescribing error' OR 'prescribing mishap' OR 'administration error' OR 'error reduction' OR 'error rate' OR 'prescribing mistake' OR 'medication error' OR 'administration mistake' OR 'medication mistake' OR 'medication mishap' OR 'dispensing error' OR 'medical error' OR 'prescribing errors' OR 'administration mistakes' OR 'medication mistakes' OR 'dispensing errors' OR 'medical errors' OR 'calculation error' OR 'calculation mistake' AND 'adolescents' OR 'baby' OR 'infants' OR 'paediatric' OR 'child' OR 'pediatric' OR 'paediatrics' OR 'pediatrics'.

After reviewing the results, the reference lists of the final selection of papers were also reviewed in order to identify additional relevant studies. In addition, volumes from the last 10 years (1995–2006) of three journals relevant to drug safety were hand searched: *Drug Safety*, *Quality and Safety in Health Care* and *British Journal of Healthcare Computing*. An expert researcher in the field of medication error research was also consulted.

The criteria for selection were:

- an intervention must be carried out or reported;
- an intervention must be related to dose calculations;
- any non-specific interventions, such as computerised physician order entry (CPOE), that reduce all types of medications errors were included.

A search of all the databases cited using all keywords produced a total of 3302 articles: 2774 articles from the initial review and 528 from the updated review. The abstracts of these articles were analysed independently by two reviewers. Articles that were found to be irrelevant were removed, leaving a final list of 28 relevant articles. A categorisation of irrelevant citations can be found in table I.

Reviewer 1 identified 26 relevant articles,^[3,21,27-50] and reviewer 2 identified 31 articles.^[21,27-31,34-36,38-40,43-61] The reviewers compared their final lists, and articles that were not found on both were read by a third reviewer who made the final decision regarding relevan-

Table I. Reasons for exclusion from review

Category	No. of Citations
Intoxication and poisoning	89
Interventions on the effects of overdoses	50
Total parenteral nutrition	11
Evaluation of treatment complications	159
Legal implications	83
Review, letter, comments	311
Case reports	248
Educational reports	32
Non-calculation intervention	64
Medication error causes/rate	124
Duplication	421
Medical error	573
Irrelevant or wrong indexing	1109
Total	3274

cy.^[21,27-32,34-40,42-50,56,57,59-61] Thus, three articles were excluded from reviewer 1's selection^[3,33,41] and six articles were excluded from reviewer 2's selection.^[51-55,58] Studies that met the inclusion criteria are listed in table II.

Based on our experience in paediatric medication error research, we had correctly anticipated that the studies would be heterogeneous because of a lack of standardised methodology and outcome measures; therefore, we did not attempt to summarise the data statistically. Instead, the outcomes and characteristics of each study were summarised using a table (table II).

3. Results

The majority of the final papers selected had formal outcome measures, usually reported as error rate reduction (table III). However, none of the articles had follow-up evaluation, although some interventions were ongoing at the time. Five of the reports are >10 years old and may have been superseded by now.

The interventions had been assessed in studies lasting 8 weeks to 5 years, with most studies including a pre-intervention and a post-intervention period. The outcomes for most interventions were

positive. Although this review aimed to report all clinical, humanistic and economic outcomes, most articles only discussed clinical outcomes.

Electronic prescribing systems, also known as CPOE and computer-assisted prescribing, were the most commonly reported interventions. CPOE is a computer system that allows prescription entry directly by physicians. The purpose of CPOE design is to reduce prescribing errors, minimise ambiguity and remove the problem of illegible hand-written prescriptions. Of the 28 articles identified, 14 institutions had introduced at least one intervention involving a form of electronic prescribing. A further two hospitals had introduced computerised protocols, three had introduced electronic calculators and one had updated its electronic information system. When considering outcomes of interventions related to CPOE and computerised-assisted prescribing, most studies revealed a large reduction in total errors when pre-intervention error rates were compared with post-intervention error rates. One hospital evaluating CPOE found that they had had no prescribing or calculation errors since its introduction.^[28] Several other studies revealed similarly high reductions in error rates when CPOE was introduced.^[28,31,35-38,57] However, recent studies have not demonstrated the same effects.^[47,50]

Four hospitals described the introduction of a unit dose dispensing system (UDDS).^[21,30,32,39] In UDDS, each drug dose is dispensed in a package ready to administer to the patient. This system was developed to assist nurses in medication administration. It has been found to lead to a great reduction in medication errors, with one study claiming that dose calculation errors decreased from five per month to zero per month after introduction of this system.^[32] It should be noted that the remaining hospitals claimed a reduction in general medication errors, not specifically in dose calculation errors.

Other reported interventions included education/risk management programmes^[37,49,59] and smart pumps.^[46] All these studies showed positive effects on error reduction.

Table II. Details of intervention studies included in this review

Study	Country	Setting	Duration	Nature of intervention	Personnel involved	Reason for implementing intervention
Kelly et al., ^[34] 1984	USA	Children's hospital (PICU)	Two examinations of a maximum of 30 minutes each	Programmed calculator for constant infusion medication calculations	Nurses, pharmacists, paediatric residents	To improve the accuracy and speed of personnel handling constant-infusion vasoactive medications
O'Brodovich and Rappaport, ^[39] 1991	Canada	Children's hospital; two paediatric medical wards	Pre: 1 month Intervention: 7 weeks Post: 1 month	UDDS	Pharmacist and nurses	The hospital was in the process of converting wards from traditional system of drug distribution to the unit dose system
Enderlin and Summerfield, ^[30] 1992	USA	Children's hospital	Pre: 6 months Post: 6 months	UDDS for controlled drugs	Nurse, pharmacist	Hospital discovered that reported error rate with controlled drugs was twice the overall medication error rate
Gard et al., ^[32] 1995	USA	NICU	2 years	Computer-generated antimicrobial dosing protocol consisting of programmed spreadsheet for antimicrobial dosing plus UDDS	Doctors, nurses, pharmacists	To avoid dosing error problems
Olsen et al., ^[40] 1997	Denmark	Children's hospital and satellite pharmacy at a regional hospital	Pre: 2 months Post: 2 months	Unit dose pharmacy satellite service	Pharmacists, prescribers and nurses	Not specified
Myers et al., ^[38] 1998	USA	NICU	4 years	Computer-assisted prescribing system; neonatal medication ordering pathway	Not specified	Not specified
Mullett et al., ^[56] 2001	USA	PICU	Pre: 6 months Post: 6 months	Anti-infective decision support tool	Resident physicians, nurse practitioners and pharmacists	Tool was already being used successfully in adults and was modified for use in paediatrics
Cox et al., ^[29] 2001	USA	Tertiary care teaching hospital	4 years	Recording weights into MIS. Limitation of verbal orders. MIS initiatives (update screens, make system more user-friendly). Pharmacy intervention reporting. Incident report modification (anonymisation of reports)	Doctors pharmacists, secretaries, nurses	To increase the use of CPOE and decrease medication errors

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Table II. Contd

Study	Country	Setting	Duration	Nature of intervention	Personnel involved	Reason for implementing intervention
Koren, ^[36] 2002	Canada	Children's hospital	Pre: 1992–3 Post: 1998–9	CPOE; double calculation check for hazardous drugs; review errors and implement changes; removal of hazardous drugs; participation of medical trainees in calculation of drug doses; computerised system in PICU to calculate drug doses and stock solution volume	Pharmacists, pharmacologists, nurses, physicians, paediatricians, administration	Hospital recognised that medication errors are iatrogenic and preventable source of morbidity and mortality
Bizovi et al., ^[27] 2002	USA	Emergency department at Oregon Health and Science University	Pre: May–Jun 1999 Post: May–Jun 2000	Computer-assisted prescription writing	Doctor, pharmacist	To reduce prescribing errors
Farrar et al., ^[31] 2003	UK	District general hospital	Not available	Electronic-order pathways for paediatric medicines	Physicians, pharmacists, paediatricians, IT analysts	To reduce potential error in prescription of medicines for children
Fontan et al., ^[21] 2003	France	Nephrology ward at a paediatric and maternity hospital	8 weeks (1 Feb 1999–31 Mar 1999)	Computerised prescribing and computerised UDDS	Physicians, pharmacist, nurses, pharmacy technicians, 5th-year pharmacy students	Not specified
King et al., ^[35] 2003	Canada	Tertiary care paediatric teaching hospital. Two medical wards (intervention). One medical and two surgical wards (control)	Pre: 3 years (Apr 1993–Apr 1996) Post: 3 years (Jan 1997–Dec 1999)	CPOE	Physicians and nurses	To reduce serious medication error rate
Cordero et al., ^[28] 2004	USA	NICU at a state university medical centre	Pre: 6 months Post: 6 months	CPOE, electronic prescribing, drug administration, inventory management	Doctors, nurses and pharmacists	Not specified

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Table II. Contd

Study	Country	Setting	Duration	Nature of intervention	Personnel involved	Reason for implementing intervention
Lykowski and Mahoney, ^[37] 2004	USA	370-bed tertiary care children's hospital	5 years (1998–2003)	ICIS: CPOE, clinical documentation, web-based portal, medication/IV charting, rules engine, longitudinal clinical repository	Doctors, nurses and pharmacists	Participated in a Child Health Accountability Initiative on Medication Errors, where a paediatric multi-site consortium identified significant opportunities for improvement and reduction in medication errors related to prescribing practices
Wong and Tam, ^[42] 2004	Hong Kong	District Teaching hospital	9 years (since 1996)	Computer-aided prescribing	Not specified	Overhaul of clinical management system
Potts et al., ^[37] 2004	USA	20-bed paediatric critical care unit in a children's hospital	Pre: 2 months Post: 2 months	CPOE	Clinical pharmacists, physician, reviewer	To prevent medication errors that occur during the medication ordering process
Cimino et al., ^[38] 2004	USA	PICUs in nine freestanding, collaborating tertiary care children's hospitals	Pre: 2 weeks data collection 3 months site-specific error reduction interventions Post: 2 weeks data collection	Communication/educational; dosing 'assist'; floor stocks	Not specified	Prescription errors deemed to be underestimated A need for a methodology to identify, document and report prescribing errors
Simpson et al., ^[46] 2004	UK	Tertiary referral NICU	Jan 2002–Jan 2003	Risk management/clinical pharmacy-led education programme	Risk management, pharmacy	Limited information on the impact of interventions introduced in NICU has been reported
Kirk et al., ^[46] 2005	Singapore	The National University Hospital	Mar 2003–Aug 2003	A computer-calculated dose program	Physicians	Limited research on the effect of computer calculated doses in general paediatric settings
Han et al., ^[43] 2005	USA	Tertiary, acute care paediatric facility	1 Oct 2001–31 Mar 2003	CPOE	Physicians	To reduce medical errors and mortality
Upperman et al., ^[60] 2005	USA	Tertiary care paediatric hospital	Pre: Jan 2002–Oct 2002 Post: started in Nov 2003	CPOE	All layers of management and personnel	Hospital began a transformation process focused on moving from written orders to paperless

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Table II. Contd

Study	Country	Setting	Duration	Nature of intervention	Personnel involved	Reason for implementing intervention
Larsen et al., ^[46] 2005	USA	242-bed university-affiliated tertiary paediatric hospital	Pre: 1 year Post: 1 year	Standard concentrations; 'smart' syringe pumps; pharmacy-generated medication labels	Nurses, pharmacists, clinical engineering, physicians (neonatologist, paediatric intensivist, cardiothoracic surgeon, anaesthesiologist), hospital safety manager	Consensus on how to limit errors with continuous medication infusion has not been reached in paediatric practice
White et al., ^[44] 2005	USA	16-bed tertiary care PICU	Not available	DRF for ordering IV potassium chloride	Multiple disciplines: pharmacy, nursing, paediatric nephrology, PICU medicine (PICU residents, fellows and attending), senior staff members and administrators	The PCEs can be identified prospectively in order to prevent adverse events
Kim et al., ^[50] 2006	USA	Paediatric oncology in an academic medical centre	2001–4	CPOE	Not specified	The complexity of paediatric chemotherapy makes it vulnerable to errors. The CPOE was introduced to investigate error reduction
Blackledge et al., ^[61] 2006	USA	Tertiary, acute care paediatric facility	Mar–May 2003 to assess accuracy of manual calculations prior to 8-week trial period. Dates of follow-up studies not provided	A web-based paediatric arrest medication calculator that calculates medication dosage requirements during emergency situations	Domain experts included a paediatrician, a paediatric nurse and a paediatric pharmacist	To prevent ADEs for paediatric patients, increase care provider efficiency and reduce stress for care providers
Lehmann et al., ^[46] 2006	USA	Children's hospital at an academic medical centre	Pre: Feb–Mar 2003 Post: Feb–Apr 2004	Web-based calculator and decision support system (vs handwritten orders)	Pharmacists	IT systems have been recognised as a tool to reduce and prevent medication errors
Abboud et al., ^[47] 2006	USA	A 423-bed tertiary care children's hospital	Pre: 3 months Post: 3 months	CPOE and clinical decision support: aminoglycoside corollary order screen	Physicians, pharmacists, nurses, information services analyst	To improve the safety of aminoglycoside medication use in children

ADE = adverse drug event; **CPOE** = computerised physician order entry; **DRF** = drug request form; **ICIS** = integrating clinical information system; **IT** = information technology; **IV** = intravenous; **MIS** = medical information system; **NICU** = neonatal intensive care unit; **PCEs** = proximal causes of errors; **PICU** = paediatric intensive care unit; **post** = post-intervention; **pre** = pre-intervention; **UDDS** = unit dose dispensing system.

4. Discussion

4.1 Electronic Prescribing (Computerised Physician Order Entry and Computer-Assisted Prescribing)

Table III shows that the rate of error reduction varied. This is likely to be due to the different outcome measures used by different investigators. Cordero et al.^[28] for example, measured the reduction of calculation errors, which were completely eliminated after the introduction of CPOE. Alternatively, Lykowski and Mahoney^[37] described a 50% reduction in all medication errors. Another difference is the population in which the intervention was studied. In contrast to the Lykowski and Mahoney study, Potts et al.^[57] described a very high reduction in all medication errors. It may be that studies, like the study by Potts et al.^[57] conducted in small specialised settings, such as the neonatal intensive care unit (NICU) or paediatric intensive care unit (PICU), have a greater reduction in errors than those conducted in large hospitals, such as the studies by Lykowski and Mahoney^[37] and King et al.^[35] Finally, many of these studies measured the rate of error reduction after implementation of a number of changes; therefore, the outcome measured would not be solely a result of the CPOE system.

Several studies described the benefits of computer-assisted prescribing; however, it is difficult to determine how similar this form of electronic prescribing is to the CPOE discussed earlier.^[21,27,42] It is unclear from the literature whether these computer-assisted prescribing systems have any decision support functions and, secondly, whether they are 'homegrown' programmes developed specifically for each hospital.

In all of these cases, it was assumed that a decrease in medication error rates alone was sufficient to determine CPOE efficacy. Although this seems to be a logical assumption, there is evidence that such endpoints do not necessarily imply improved patient outcomes. King et al.^[35] first noted this in their analysis of CPOE introduction into their hospital, finding a 40% decrease in medication error rates on the wards, yet a lack of evidence to demonstrate any effect on actual or potential patient harm. Han et

al.^[43] have recently shown that the mortality rate was significantly increased (from 2.8% to 6.6%) after the introduction of CPOE. This study also found that there were delays in medication administration when using CPOE, as more time was needed to enter orders than for written forms, with potentially significant patient care consequences. Nurses were required to spend more time at a computer terminal, and less time at the bedside, reducing staff-to-patient ratios during critical periods, such as when the patient was first admitted. However, Del Beccaro et al.^[62] investigated the effect of CPOE on mortality rates in a PICU and found no association. The studies by Han et al.^[43] and Del Beccaro et al.^[62] have demonstrated how evaluation and interpretation of research in CPOE can be complex; further research should focus on the effect of CPOE on patient and economic outcomes rather than purely on incidence of error.

4.2 Dose Calculators

Three studies^[45,48,61] have demonstrated that web-based or computer dose calculators can significantly reduce calculation errors. However, these calculators were developed to manage a very small number of medications and usually in a specific setting; therefore, the generalisability is unknown. Furthermore, electronic prescribing is likely to be widely adopted in the future and this may make these types of dose calculators redundant.

4.3 Unit Dose Dispensing Systems

Four hospitals described the use of a UDDS. One study described application of this system only for controlled drugs^[30] while another used it only for antimicrobials.^[32] Both Fontan et al.^[21] and O'Brodovich and Rappaport^[39] described using a UDDS on general wards for all medicines. While three studies described fully integrated UDDS,^[21,32,39] Enderlin and Summerfield^[30] used a modification of UDDS; although some of the advantages of UDDS were still apparent. In spite of these differences, all studies found that the use of UDDS greatly reduced the rate of medication errors in their hospitals.

Table III. Intervention articles: pre- and post-intervention outcomes

Study	Outcome measured	Results
Kelly et al. ^[34]	Calculation error test score	Pre: 61.9%; post: 100%. Significant reduction in time required for calculations for all except pharmacists. All pharmacists felt the calculator would help their computation and felt reassured by the calculator as a second check of their own figures
O'Brodovich and Rappaport ^[39]	Total error rate	Pre: 10.3%; post: 2.9%
	Wrong dose errors	Pre: 6.4%; post: 1.2%
	Wrong time errors	Pre: 27%; post: 18%
	Time that pharmacists spent on drug distribution	Pre: 33%; post: 35%
	Nurses' time spent on medication-related activities	Post: decreased by 2.1%
	Pharmacist clinical activities	Post: increased by 8%
	Average medication cost per patient day	Post: decreased by 4%
Enderlin and Summerfield ^[30]	Number of controlled substance doses	Pre: 8.6% total; post: 5.7% total
	Number of controlled substance errors	Pre: 19% total; post: 5.8% total
	Controlled substance errors (error rate)	Pre: 31 (0.22%); post: 15 (0.12%)
	Non-controlled substance errors (error rate)	Pre: 130 (0.086%); post: 242 (0.12%)
Gard et al. ^[32]	Dose calculation errors	Pre: 5 per month; post: 0 per month
Olsen et al. ^[40]	Wrong doses	Pre: 7.7% (66/856); post: 0% (0/544)
Myers et al. ^[38]	Error rate (including transcription, dosage, formulation, preparation and administration errors for 1993–4)	Pre: 3.2/1000 patient days; post: 0.6/1000 patient days. All types of errors were reduced. Substantial decrease in average total hospital cost per infant and decrease in average length of stay during 1993–6
Mullett et al. ^[56]	Rate of pharmacy interventions for incorrect drug doses	Post: reduced by 59%
	Rate of anti-infective subtherapeutic patient days	Post: reduced by 36%
	Excessive dose days	Post: reduced by 28%
	Impact reported by paediatricians and nurses	Post: beneficial
	Estimate of the cost of anti-infectives used	Post: decreased by 9%
Cox et al. ^[29]	Weight interventions by pharmacists	Post: eliminated
	Unsigned orders at discharge	Post: decreased to almost 0
	Use of MIS system by residents	Post: increased by 86%
	Overall direct-order entry	Post: increased by 61%
	Number of interventions reported by pharmacists	Post: tripled and continued to increase
	Reporting of drug errors	Post: increased
Koren ^[36]	Total errors by nurses and physicians	Post: reduced by 50%
	Total errors by pharmacists	Post: reduced by 75%
	Errors by nurses	Pre: 1190 (0.11%); post: 650 (0.06%)
	Errors by pharmacists	Pre: 0.04%; post: 0.01%
	Total number of actual incidents	Post: reduced by 50%
	Severity of errors	Post: reduced by 72% (minor), 69% (moderate), 73% (severe)
Bizovi et al. ^[27]	Overall error	Pre: 2.32%; post: 0.69%
	Incorrect dose	Pre: 0.13%; post: 0.06%

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Table III. Contd

Study	Outcome measured	Results
Farrar et al. ^[31]	Clarification rate	Pre: 3.9%; post: 0.8%
	Error rate by non-paediatricians	Pre: 76%; post: 12%
	Error rate by paediatricians	Pre: 26%; post: 4%
Fontan et al. ^[21]	Prescription error rate	Pre: 87.9%; post: 10.6%
	Potentially clinically significant errors	Pre: 4.8%; post: 2.9%
	Administration error rate (including administration time errors)	Pre: 29.3%; post: 22.5%
	Administration error rate (excluding administration time errors)	Pre: 24.3%; post: 9.7%
King et al. ^[35]	Error rate	Post: decreased by 40%. CPOE would prevent one medication error for every 490 patient days. Large decrease in potential ADEs on the control as compared with intervention wards
Cordero et al. ^[28]	Medication turn-around times	Pre: 10.5 ± 9.8 hours; post: 2.8 ± 3.3 hours
	Prescription medication errors	Pre: 13%; post: 0%
	Calculation errors	Pre: 6%; post: 0%
	Radiology turn-around times	Pre: 42 ± 12 minutes; post: 32 ± 16 minutes
Lykowski and Mahoney ^[37]	Pain assessment documentation requirements	Post: 100% compliance
	Medication turnaround times	Post: improved by 52%
	All medication errors	Post: reduced by 50%
	Verbal orders for controlled substances	Post: reduced by 24%
	Care consistency	Post: increased by 20%
	Clinician/service provider pages/phone calls to clarify orders.	Post: reduced
	Medication transcription errors	Post: eliminated
Wong and Tam ^[42]	Error rate	Pre: >100 per year; post: 40 per year. Reduction of 60%
Potts et al. ^[57]	Potential ADEs	Post: reduced by 40.9%
	MPEs	Pre: 30.1/100 orders; post: 0.2/100 orders
	RVs	Pre: 6.8/100 orders; post: 0.1/100 orders
	Total errors	Pre: 39.1/100 orders; post: 1.6/100 orders
	All types of medication ordering errors	Post: reduced by 95.9%
	MPEs	Post: reduced by 99.4%
	RVs	Post: reduced by 97.9%
Cimino et al. ^[59]	Error rate	Pre: 11.1%; post: 7.6%. Z = 10.5; p < 0.001. However, site results varied considerably
Kirk et al. ^[48]	Error rate	Pre: 28.2% (534/1893); post: 12.6% (299/2381). Computer calculated dose was a significant variable influencing the error rate (RR 0.436; 95% CI 0.336, 0.520; p < 0.001)
Han et al. ^[43]	Mortality rate	Pre: 2.80%; post: 6.57%. Multivariate analysis revealed that CPOE remained independently associated with increased odds of mortality (OR 3.28; 95% CI 1.94, 5.5)
Upperman et al. ^[60]	ADEs	Pre: 0.3 ± 0.04 per 1000 doses; post: 0.37 ± 0.05 per 1000 doses (p = 0.3)
	Harmful ADEs	Pre: 0.05 ± 0.017 per 1000 doses; post: 0.03 ± 0.003 per 1000 doses (p = 0.05)

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Table III. Contd

Study	Outcome measured	Results
Larsen et al. ^[46]	Error rate	Pre: 3.1/1000 doses; post: 0.8/1000 doses. Absolute risk reduction of 2.3 errors per 1000 doses (95% CI 1.1, 3.4; $p < 0.001$)
White et al. ^[44]	Preparation errors in pharmacy	Pre: 0.66/1000 doses; post: 0.16/1000 doses
	Incidence rate of post-infusion elevation in serum potassium levels	Pre: 7.7%; post: 0%. The rate of PCEs was significantly decreased ($p < 0.001$)
Kim et al. ^[50]	Improper dosing	Post: reduced. RR 0.26 (95% CI 0.11, 0.61)
	Incorrect dosing calculations	Post: reduced. RR 0.09 (95% CI 0.03, 0.34)
	Missing cumulative dose calculations	Post: reduced. RR 0.32 (95% CI 0.14, 0.77)
	Incomplete nursing checklists	Post: reduced. RR 0.51 (95% CI 0.33, 0.80)
	Improper dosing on treatment plans	Post: no difference
Blackledge et al. ^[61]	Not matching medication orders to treatment plans	Post: increased. RR 5.4 (95% CI 3.1, 9.5)
	Error rate on the emergency card	Post: 0%. Anecdotal evidence suggests a significant decrease in the level of stress among team members during an emergency because they are no longer checking and double checking calculations
	Legibility of the emergency card	Post: 100%
Simpson et al. ^[49]	Need to perform manual calculations during emergency situations	Post: almost totally eliminated
	Monthly medication errors mean (SD)	Pre: 24.1 (1.7) per 1000 neonatal activity days; post: 5.1 (3.6) per 1000 neonatal activity days ($p < 0.001$)
Lehmann et al. ^[45]	Errors	Pre: 27%; post: 13.6% ($p < 0.01$)
	High-risk errors (incorrect decimal, dose or unit of measure)	Pre: 26%; post: 0% ($p < 0.00001$)
Abboud et al. ^[47]	Frequency of therapeutic, toxic or subtherapeutic values	Post: no significant difference

ADE = adverse drug event; **CPOE** = computerised physician order entry; **MIS** = medical information system; **MPE** = medication prescribing errors; **OR** = odds ratio; **PCEs** = proximal causes of errors; **post** = post-intervention; **pre** = pre-intervention; **RR** = relative risk; **RV** = rule violation.

4.4 Intelligent Infusion Pump Systems (Smart Pumps)

Recently, 'smart-pump' technology has become available. Smart pumps incorporate sophisticated computer technologies for storing drug information (e.g. drug library with doses, pre-programmed concentrations), automating calculations and checking information entered against administration parameters (i.e. a safety net). Theoretically, they should reduce medication errors in the infusion of critical care drugs. This has particular relevance in the high-risk area of neonatal and paediatric drug therapy, where 10-fold overdoses are far more common than in adult settings.

Larsen et al.^[46] reported that 'smart syringe pumps' together with other measures reduced the number of reported errors by 73%, suggesting that smart pumps could be an effective intervention to

reduce medication errors in children. Unfortunately, the study used critical incident reports to evaluate effectiveness, a method notorious for grossly underestimating the incidence of medication errors.^[8] Conversely, a controlled trial of smart infusion pumps in critically ill adult patients in the US reported that they had no impact on serious medication error rates but this was likely to be due in part to poor user compliance.^[63] Therefore, the true effect of smart-pump technology is still unclear.

4.5 Education and Feedback of Errors

According to Reason's 'human error theory', poor education and training create 'latent conditions' for medication errors.^[64] Latent conditions, as the term suggests, may lie dormant within the system before they combine with other conditions to create an accident opportunity. Therefore, there is a

strong theoretical basis for education and training in medication errors reduction. Furthermore, based on human error theory or root cause analysis, if corrective actions can be identified and implemented, future errors could be avoided. Potentially this approach is a very powerful tool in preventing medication errors. Simpson et al.,^[49] Cimino et al.^[59] and Lykowski and Mahoney^[37] have demonstrated that educational/risk management programmes were able to reduce medication errors in children.

4.6 Limitations

4.6.1 Reporting Biases

It is important to bear in mind that this literature review has mainly identified published articles reporting interventions that have successfully reduced errors. It is likely that interventions that were not beneficial or statistics from unfavourable interventions were not mentioned in the literature. Publication bias has been demonstrated in several studies approved by research ethics committees, showing that researchers are more likely to submit reports with positive results.^[65] It cannot be overlooked that positive-outcome bias is evident when studies are submitted for publication.^[66]

4.6.2 Methodological Challenges

Traditional patient-based randomised clinical trials are almost impossible to conduct in medication errors prevention research, because of the complex interactions between patients, health professionals, healthcare systems and medications. Although, it is possible to conduct a randomised clinical trial using a ward or hospital as a randomised unit (cluster), it is challenging to recruit sufficient 'units', and the cost would certainly be prohibitive in such a large scale study. Consequently, most of the studies are examples of pre- and post-intervention assessment. Furthermore, the literature needs to be evaluated carefully, as there are several methodological issues that can markedly affect the interpretation of findings. These issues, summarised by Wong et al.^[8] and Ghaleb et al.,^[67] include the definition of medication errors used, the method by which errors are detected and the setting studied.

Owing to the aforementioned challenges and the objective of the COSMIC project being to conduct a

scoping exercise to identify interventions being used to assist in the calculation of drug doses in paediatric medicine, we have presented the results of the identified studies purely as they were reported by the authors. We have not attempted to critically analyse or compare them. Readers should therefore interpret the results with caution in light of the reported limitations.

5. Conclusions

There have been a number of interventions described in the literature that aimed to reduce medication errors in children, particularly dosing and calculation errors. The main interventions described in the published studies were CPOE and computer-aided prescribing. Most CPOE and computer-assisted prescribing studies showed some degree of reduction in medication errors, with some claiming no errors occurring after implementation of the intervention. One study,^[43] however, showed a significant increase in mortality after the implementation of CPOE. Further research is needed to investigate clinical outcomes, such as mortality and economics. UDDS systems and educational/risk management programmes were also shown to reduce medication errors in children. Although, smart pumps can potentially reduce infusion errors in children, there is insufficient information to draw a firm conclusion, because of a lack of research. Most interventions identified were US-based. Since medicine management processes are currently different in different countries, there is a need to interpret the information carefully when considering implementing such interventions in other countries.

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