REVIEW ARTICLE

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# 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<br>Intervention: 7 weeks<br>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<br>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<br>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<br>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<br>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<br>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)<br>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<br>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.,[57] 2004 | USA | 20-bed paediatric critical care unit in a children's hospital | Pre: 2 months<br>Post: 2 months | CPOE | Clinical pharmacists, physician, reviewer | To prevent medication errors that occur during the medication ordering process |
| Cimino et al.,[59] 2004 | USA | PICUs in nine freestanding, collaborating tertiary care children's hospitals | Pre: 2 weeks data collection<br>3 months site-specific error reduction interventions<br>Post: 2 weeks data collection | Communication/educational; dosing 'assists'; floor stocks | Not specified | Prescription errors deemed to be underestimated<br>A need for a methodology to identify, document and report prescribing errors |
| Simpson et al.,[49] 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.,[48] 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<br>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<br>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.,[45] 2006 | USA | Children's hospital at an academic medical centre | Pre: Feb–Mar 2003<br>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<br>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 |
|---|---|---|
| | Clarification rate | Pre: 3.9%; post: 0.8% |
| Farrar et al.[31] | 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) |
| | Preparation errors in pharmacy | Pre: 0.66/1000 doses; post: 0.16/1000 doses |
| White et al.[44] | 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 |
| | Not matching medication orders to treatment plans | Post: increased. RR 5.4 (95% CI 3.1, 9.5) |
| Blackledge et al.[61] | 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% |
| | Need to perform manual calculations during emergency situations | Post: almost totally eliminated |
| Simpson et al.[49] | 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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