REVIEW ARTICLE

Medication Errors in Pediatric Emergencies

A Systematic Analysis

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SUMMARY

Background: Errors in drug administration are among the commonest medical errors. Children are particularly at risk for such errors because of the need to calculate doses individually. Doses that are ten times the correct amount (1000% of the correct dose) are occasionally given and can be life-threatening. In a simulated resuscitation in a pediatric emergency room, an error of this type occurred for one of the 32 medications that were ordered. The highest error rates are to be expected in prehospital emergency medicine. In this review, we analyze the process of ordering medications and describe the potential interventions for lowering error rates that have been evaluated to date.

Method: Systematic literature review

Results: We found 32 original publications that concerned the evaluation of interventions for lowering error rates in the ordering of medications for children. Error rates can be lowered by interventions that improve prescribers' knowledge of pediatric pharmacotherapy (courses, immediately accessible sources of information) and by aids to the cognitive process of ordering medication (calculators, computer programs, tables of doses by weight). They can also be lowered by raising awareness of the problem of erroneous medication ordering and by monitoring medication orders, as well as by structured communication and standardized, unambiguously labeled drug preparations. In the hospital setting, computer programs for medication orders with a built-in pediatric pharmacological database are highly recommended. In the prehospital setting, the "pediatric emergency ruler" enables accurate estimation of the patient's weight, provides age-appropriate dosage recommendations, and directly indicates the steps needed for calculation of the correct dose.

Conclusion: Children in medical emergency situations are at significant risk for medication errors. The measures described here can markedly lower the rate of dangerous errors.

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The American Institute of Medicine estimates that 7000 people die every year in the USA as a result of medication errors, including self-medication and doctors' prescriptions in patients of all ages (1). In hospitals, drug administration errors are also some of the most common medical errors (e1). Because of age group–specific contraindications and the need for personalized dose calculation, children can be expected to be particularly at risk of medication errors (e2–e4). For example, in one pediatric hospital the observed rate of potentially dangerous prescribing errors was three times higher (e5) than the rate observed in an identically designed study in adults (e6). The error rate increases in any care situation that requires speed and large numbers of prescriptions (e7). As part of a risk audit in a pediatric emergency department, a tenfold deviation, corresponding to 1000% of the recommended dose, was observed in one in every 766 prescriptions on average, although measures to improve this had already been put in place (electronic prescription system, standardized drug preparation) (2). In a prospective study, as many as one in every 32 prescriptions in a pediatric emergency department contained a tenfold error during simulated resuscitation by pediatric emergency physicians (3). It is important to remember that errors of this scale can cause serious harm and in many cases even prove fatal (4, e8, e9).

Because neither exclusively pediatric staff nor treatment procedures optimized for pediatric patients can be provided for the prehospital emergency care of children (e10), a particularly high error rate is to be expected in this field (e11). A retrospective analysis of 360 prehospital prescriptions in the USA showed medication errors in 35% of all cases. Excessively high doses of intravenous epinephrine were an average of 808% of the recommended dose (5). No specific incidence rates from larger populations are available for emergency medicine (e12), but it is likely that a considerable number of prehospital medication errors are not reported (e13). This means that the likely frequency and the consequences of medication errors in prehospital pediatric emergency care give rise to a substantial danger, which must be reduced.

Method

This article is based on a systematic review of the literature, using a search of PubMed *(Table 1)*.

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TABLE 1

PubMed research (database existing since 1963, last accessed in May 2012)

Search terms: “medication errors, pediatrics” AND “emergency” OR “prevention”			
Total:	219 publications, 32 studies		
of which:	Outpatient or elective care, self-medication		149
	of which:	Review articles, expert opinions, editorials	52
		Case reports, readers’ letters	11
		Other related subjects	39
		Methodical works, error detection, surveys	39
		Observation of use, cohort studies	7
		Randomized controlled trials	1
of which:	Prehospital and/or hospital emergency care, intensive care units		70
	of which:	Review articles, expert opinions, editorials	24
		Case reports, readers’ letters	10
		Other related subjects	12
		Methodical works, error detection, surveys	10
		Observation of use, cohort studies	12
		Randomized controlled trials	2

Results

The authors identified 22 clinical studies on the prevention of medication errors in pediatric care. A further search, using each of the studied interventions as keywords, allowed us to add a further 10 pediatric articles. The scientific quality of all 32 original articles retrieved in this way was assessed *(Table 2)*. To date no meta-analyses on which treatment recommendations or guidelines might be based are available, and none can be produced from the currently available data. This is because there are many factors involved, because individual approaches cannot be compared with each other, and also simply because the definitions used are heterogeneous (6). This article aims to analyze the prescribing process and its sources of errors and so to indicate approaches that might contribute to a reduction in errors.

Analysis of the drug prescribing process and sources of error

Determining the indication

Prescription always begins with examination of the indication and consideration of any promising alternatives to drug therapy. In some situations, a child’s proximity to his/her mother may make pharmacological sedation unnecessary. Age group–specific contraindications must also be observed in pediatric care *(Table 3)*.

Determining recommended dose

Weight-based recommended doses form the basis of prescription. These can vary significantly according to age group. For example, substantial circulatory depression was observed when 1 mg/kg propofol was administered to preterm infants to induce narcosis (e14). However, no hypotension was described following administration of 3 mg/kg propofol and 2 or 3 µg/kg remifentanil in children between 5 and 10 years of age (e15).

Determining weight

Often, little importance is attached to a child’s actual weight in medical care. In one pediatric emergency department, for instance, only 2% of children were weighed and the weight of all other children was estimated in various ways (e16). Age-related formulae were the most common method used; these are known to be of poor quality (9). For example, the weights of the six-year-old children in the study mentioned above ranged from 19 to 30 kg (e16). In prehospital emergency care too, sufficient importance is not always attached to children’s weight. This is also evident from the fact that the standardized emergency care protocol based on the recommendations of the German Interdisciplinary Association for Intensive and Emergency Care (*Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin,* DIVI), which contains 203 parameters, has no field to indicate weight (e17, e18). In everyday clinical practice, it can also be observed that in individual cases drug doses are even established in the form of a proportion of an adult dose, with no specific estimate of weight.

Dose calculation, preparation

The very need for individual calculation of the required dose entails the possibility of calculation errors (e2). For example, infants’ body weight generally doubles between birth and the age of six months. This means that familiarity with the usual dose cannot be assumed, and even tenfold dosing errors do not seem suspect and occur regularly (2). Determining the correct dose seems to be the most significant step, as this is where the highest error rate is observed (38, e19, e20). A further source of errors is the choice of preparation. As a result of the considerable variation in doses, many drugs are available in various package sizes and concentrations, and diluted forms are produced so that usable volumes can be administered.

Compiling and issuing prescriptions

Communication problems are also responsible for many medication errors (e21). A complete prescription contains both a dosing formula (e.g. in mg/kg) and the absolute dose according to the patient’s body weight (e.g. in mg). It must also state the concentration used (e.g. in mg/mL) and the resulting absolute quantity of the solution to be administered (e.g. in mL). Care must also be taken with similar-sounding names (e.g. esmeron and esmolol) (e22). If a diluted form is to be used, its exact name and preferably also instructions for producing it must be given. In simulated resuscitation events in a pediatric hospital’s emergency department, 17% of prescriptions were incomplete according to this definition (3).

TABLE 2

Measures to improve the quality of drug prescriptions for children and evidence of their effects

Level of evidence according to EBM[*1], author, year	Study design	Intervention	Effect
Source of error: age group–specific knowledge (indication, contraindications, dosing recommendations)			
III, Mullett 2001 (7)	Prospective cohort study	Database	Significant reduction in error rate
IV, Sard 2008 (8)	Retrospective cohort study	Dosing table	Significant reduction in error rate
Source of error: determining weight			
III, Krieser 2007 (9)	Prospective observational study	Comparison of methods used to estimate weight	Length-related estimates proved superior
Source of error: dose calculation			
II, Shah 2003 (10)	Prospective randomized controlled cross-over study, comparison of drug doses, use of a pediatric emergency ruler	Simulated resuscitation events in groups of children, every 4 resuscitation events by 28 physicians 1) Not using 2) Using the pediatric emergency ruler	Deviation of doses from recommended dose, % 1) 36.3% (CI: 29.3 to 51.2) 2) 7.6% (CI: 4.5 to 9.1)
III, Cordero 2004 (11)	Prospective cohort study	Electronic calculation aid	Reduction in error rate
III, Kirk 2005 (12)	Prospective cohort study	Electronic calculation aid	Significant reduction in error rate
II, Bernius 2008 (13)	Randomized controlled trial, correct prescriptions on a prescription form, table used for reference	Pediatric prescription form, 523 emergency physicians 1) Using 2) Not using table for reference	Correct pediatric questionnaire forms 1) 65% 2) 94%
III, Wong 2009 (14)	Prospective observational study	Introduction of handbook/dosing table	Higher rate of correct prescriptions
Source of error: issuing prescription			
II, Kozer 2005 (15)	Randomized controlled trial, comparison of error rates on structured prescription form	787 drug prescriptions, pediatric emergency department 1) Written on blank paper 2) Written on form	Rate of medication errors 1) 16.6% 2) 9.8% (OR: 0.55; CI: 0.21 to 0.77)
IV, Larose 2008 (16)	Retrospective cohort study	Prescription written on form	Significant reduction in error rate
IV, Broussard 2009 (17)	Retrospective observational study	Prescription written on form	Significant reduction in error rate
Comprehensive or multiple measures			
III, Morriss 2009 (18)	Prospective cohort study	Introduction of barcodes & inspection system	Significant reduction in medication errors
III, Davey 2007 (19)	Prospective cohort study	Training in pediatric prescriptions	Significant reduction in rate of prescription errors
II, Gordon 2011 (20)	Randomized controlled trial, comparison of results of a test on pediatric prescriptions, e-learning on pediatric prescriptions	Written test, 86 doctors did not receive training, 76 did 1) Before e-learning 2) One month after e-learning 3) Three months after e-learning	Correct results in written tests 1) 67% vs. 67% (p = 0.56) 2) 79% vs. 63% (p <0.0001) 3) 79% vs. 69% (p <0.0001)
III, Taylor 2008 (21)	Prospective observational study	Electronic prescription system	Reduction in deviations from recommended dose
III, Walsh 2008 (22)	Prospective observational study	Electronic prescription system	Reduction in dangerous errors & harm
III, King 2003 (23)	Prospective observational study	Electronic prescription system	Significant reduction in rate of prescription errors
III, Campino 2009 (24)	Prospective cohort study	Training	Significant reduction in rate of prescription errors
III, Potts 2004 (25)	Prospective cohort study	Electronic prescription system	Reduction in errors/dangerous errors
III, Kazemi 2011 (26)	Prospective cohort study	Electronic prescription system & database	Significant reduction in dangerous errors
III, Kidd 2010 (27)	Prospective cohort study	Training, handbook, pocket calculator	Better results in written tests
IV, Kadmon 2009 (28)	Retrospective cohort study	Electronic prescription system & database	Significant reduction in errors/dangerous errors
III, Campino 2008 (29)	Prospective controlled cohort study	Inspection of prescriptions	Significant reduction in rate of dosing errors
IV, Costello 2007 (30)	Controlled cohort study	Inspection, training, CIRS	Reduction in errors/dangerous errors
III, Larsen 2005 (31)	Prospective cohort study	Multiple interventions	Reduction in errors/tenfold errors

Level of evidence according to EBM[*1], author, year	Study design	Intervention	Effect
III, Stewart 2010 (32)	Prospective comparative study	Seminar participation	Improvement
IV, Otero 2008 (4)	Retrospective comparative study	Multiple interventions	Significant reduction in rate of medication errors
III, Leonard 2006 (33)	Prospective cohort study	Multiple interventions	Significant reduction in rate of dangerous errors
III, Kaji 2006 (34)	Prospective observational study	Use of emergency ruler	Improved rate of correct dosing
III, Ligi 2010 (35)	Prospective cohort study	CIRS plus multiple strategies	Significant reduction in rate of tenfold errors
IV, Koren 2002 (36)	Retrospective cohort study	Multiple interventions	Significant reduction in rate of tenfold errors
IV, Sharek 2008 (37)	Prospective/retrospective control group	Multiple interventions	Significant reduction in rate of tenfold errors

[*1]Level of evidence according to the Centre for Evidence-Based Medicine, 2011 (e37):
I: Meta-analysis of randomized controlled trials; II: Randomized controlled trial; III: High-quality (prospective) controlled trial (nonrandomized);
IV: Case series, case-control study, or historically controlled trial; V: Case reports, expert opinions. CIRS: Critical Incident Reporting System; CI: Confidence interval;
OR: Odds ratio. For a detailed summary of trials with levels of evidence III and IV please confer to the *eTable*

Preparing and administering prescribed drugs

In most clinical situations preparing a drug solution of the required concentration and administering the necessary dose in the form of the indicated quantity is the task of a emergency medical technician. In the prospective observational study mentioned above involving simulated resuscitation events in a pediatric emergency department, the prepared syringes were collected. A concentration that deviated from the stated concentration by more than 50% was found in 7% of the syringes (3).

The effect of care context on error rate

All the sources of error described above become even more significant when urgency is greater and the number of prescriptions is higher. This has been demonstrated in intensive care units for adults (e23) and neonates (e5), for example. In a retrospective cohort study in a pediatric emergency department, 10% of prescriptions were rated as erroneous (38). In prehospital emergency care, even higher rates of dosing errors are to be expected. In addition to the emotional pressure experienced by many emergency physicians (e24), prehospital care structures have neither specialized pediatric staff nor treatment procedures optimized for pediatric patients. In hospitals, control mechanisms involving several persons with comparable skills provide a significant gain in safety; these are also absent in prehospital care. These problems were clearly shown in a prospective study in which correct doses were used in only 34% of prehospital administrations of epinephrine for resuscitation (34). It has also been shown that excessive fatigue among prescribing staff and nighttime hours contribute to higher error rates (38, e25–e26).

Interventions for improving drug prescriptions

Below is an outline of strategies to prevent such errors, and where possible an evaluation of their effectiveness on the basis of a comparison of the literature.

Determining indication and dosing recommendations

All staff should have a basic knowledge of age group–specific properties of emergency drugs. Several summaries of pediatric drug therapy are available, and it seems useful to be able to refer to one of these during prehospital care *(Table 4)*. Access to pediatric pharmacological information has been shown to increase the rate of correct dosing (7), even if the information in question is merely a summary table (8). In specific situations it may also be useful to consult the nearest pediatric intensive care unit by telephone.

Determining weight

Various authors insist that a child must be weighed before a drug is prescribed (39), but this is often impossible in emergency care. It would be a useful initial step simply to attach sufficient importance to weight. In many cases, a child's parents are available and can be asked the child's weight, and this should be done. In a comparison of weight estimates for 410 children, parents were able to estimate weight correctly to within 10% accuracy in 78% of cases (9), and this was far superior to age-related formulae. The next best method is length-related estimating, which determines an average weight (i.e. ideal weight) on the basis of percentiles. This is therefore the method that should be used if it is impossible to weigh a child (percentile curves or pediatric emergency ruler). Dosing according to ideal weight is beneficial even for obese children, as they have a lower proportional extracellular volume by weight, and this is the decisive distribution volume for the dosing of emergency drugs, analgesics, and sedatives (e27).

Dose calculation, preparation

Once dosing recommendations and weight have been determined, the required dose can be calculated. Electronic aids (e.g. a pocket calculator) are useful for this, because they have been shown to minimize calculation errors (11). For example, in one pediatric hospital the use of a computer program to calculate doses halved dosing errors in prescriptions (12). However, any other measure that can reduce the number of steps required in calculation can also reduce the error rate (e28). For example, in a prospective study in the USA 500 prehospital emergency physicians were asked to calculate pediatric prescriptions in a questionnaire, in a quiet, stress-free situation. All the necessary information was always given, and only whole numbers were used. Following randomization, approximately half of the participants were allowed to consult a table for reference *(Table 5)*. Of those without the table, only 65% of the emergency physicians completed the whole questionnaire with no errors, compared to 94% with the table (13).

Issuing prescriptions

It is preferable to issue prescriptions in writing whenever possible. This can hardly be guaranteed in acute emergencies. However, at least orally, detailed and comprehensive information as well as all steps of calculation must be communicated. The recipient of the prescription should repeat these in full, as confirmation. It is expected that establishing this type of communication structure will reduce the rate of drug errors (e11, e12), although this has not yet been researched for oral instructions. However, a lower error rate has been recorded following introduction of a written prescription form *(Table 6)* (15–17).

Preparing and administering prescribed drugs

Wherever possible, the number of concentrations used should be kept to the minimum required. If drug administration is followed by flushing, in many cases the undiluted drug solution can be used, with small syringes (1 mL syringes calibrated in 0.01 mL increments). Syringes containing various concentrations of the same active substance should be avoided. The necessary solution concentrations must be observed precisely. Commercially preprepared, labeled syringes achieve higher levels of safety, as quality control is incorporated into the manufacturing process (39). A disadvantage of these preprepared syringes is their limited shelf life and high cost. Every preprepared syringe should be labeled clearly; this is an effective check in itself (e29). The use of color-coded stickers, as established in international standard ISO 26825, seems to be beneficial (e30). It has been shown that this type of labeling system can reduce at least mix-ups between drug groups (39). In addition, syringe barcodes that can be read by smart syringe pumps seem to be particularly advisable (18). However, it seems that this measure cannot yet be implemented in prehospital care.

Additional interventions for improving drug prescriptions

Below is a description of possible ways to achieve improvements in drug prescription. These could either not be assigned to any of the points outlined above or represent groups of several subpoints.

TABLE 3

Examples of age group–specific contraindications for drugs that are unproblematic in adults

Drug	Age group–specific property
Acetylsalicylic acid	In those under 12 years old, only to be used with the strictest indication, Reye syndrome (e34)
Metoclopramide	May cause extrapyramidal disorders in those under 12 years old (e35)
Promethazine	May increase the risk of sudden infant death (promethazine or other antihistamines with sedative effect) (e36)

TABLE 4

Examples of short summaries on pediatric drug therapy (in German)

Author, year	Title, publisher
Wigger et al., 2001	Lightfaden Medikamente in der Pädiatrie, Urban & Fischer
Ege et al., 2009	PÄD i.v., W. Zuckschwerdt Verlag
Renner, 2006	Arzneimittel in der Pädiatrie, Thieme Verlag

TABLE 5

Reference adaptation of Bernius emergency dosing card (13)

	3.5 kg	5 kg	10 kg	…
Adenosine (0.1 mg/kg initial dose) (6 mg/2 mL) (0.2 mg/kg second dose) Rapid IV/IO push	0.35 mg 0.1 mL 0.7 mg 0.2 mL	0.5 mg 0.17 mL 1 mg 0.3 mL	1 mg 0.3 mL 2 mg 0.7 mL	…
…	…	…	…	…
Epinephrine: bradycardia/arrest 1:1000 (ETT) 1:10 000 (IV/IO route)	0.35 mL	0.5 mL	1 mL	…
…	…	…	…	…

Staff training, observation and reporting systems

It is certainly impossible to guarantee comprehensive prehospital emergency care provided by pediatricians and pediatric nursing staff. However, it has been shown more than once that experience and training can reduce error rates. For example, training in both knowledge of pediatric drug therapy and the causes of drug errors and how to resolve them can reduce the rate of prescribing errors (4, 19, 20, 24, 32). Error reporting systems (critical incident reporting system, CIRS) increase the number of errors that are reported and are the subject of constructive discussion in hospitals (e20), and although as yet there is no evidence, this can be expected to reduce errors. However, the introduction of inspections

TABLE 6

Presciption form after Kozer (15)

Date	Time	Patient Weight (kg)	Dose (mg/kg)	Total Daily Dose	Dose to Administer (mg/kg)	Frequency	Dosing Route	Physician´s signature

Figure 1: The German pediatric emergency ruler (PädNFL), placed with one end by the heels of a child lying with legs outstretched. Weight, age-appropriate normal values, sizes of equipment, and weight-related doses of emergency drugs can be read off the section that lies by the child's head

by hospital pharmacists has been shown in itself to reduce the error rate in a neonatal intensive care unit (29). This step was announced to staff and has clearly led to an increase in their levels of vigilance.

Electronic prescription systems

When computer-based prescription systems are used, required doses, routes of administration, and frequencies are entered into a program, and the computer performs the calculation. A system of this kind has been shown to reduce the rate of incomplete prescriptions (21), although in isolation it cannot reduce the rate of dangerous dosing errors (23, e31). The incorporation of a database on pediatric drug therapy that includes information on dosing recommendations and a control mechanism has successfully reduced the number of dangerous dosing errors significantly (23, 25, 26).

The pediatric emergency ruler

The German pediatric emergency ruler (PädNFL, *Pädiatrisches Notfalllineal*) provides support at all the stages of drug prescription outlined above. In prehospital care in particular, in which some of the measures indicated above to increase prescription safety cannot be implemented due to structural factors, the pediatric emergency ruler may be useful. It makes it possible to estimate patients' weight accurately, avoiding excessively high dosing as a result of obesity, and provides age group–specific dosing recommendations. Based on standardized drug preparation, the volumes to be administered according to the concentrations used are directly indicated on the pediatric emergency ruler. A majority of the cognitive effort involved in drug prescription is therefore covered by the pediatric emergency ruler, so it is not surprising that the use of a similar tool (the Broselow tape) has already repeatedly been shown to be beneficial in simulated resuscitation events (10). In prehospital pediatric emergency care too, the rate of correct epinephrine doses increased almost twofold when this aid was introduced in a prospective cohort study (34). In addition, length-related tracheal tube selection is superior to age-related selection methods (40). Physiological normal values can also be consulted at a glance, and compliance with these values is essential to an optimum neurological outcome (e32). The demonstrated benefit of this length-based calculation method has led to its use being recommended in the American Heart Association (AHA) Guidelines for

Cardiopulmonary Resuscitation and Emergency Cardiovascular Care (e33) *(Figure 1)*.

Conclusion

Medication errors pose a substantial danger to all patients, and children in emergencies are exposed to a particularly high risk. It would be desirable and probably also beneficial for there to be intensive, coordinated research on this subject. In general, raising staff's awareness of this issue and relevant continuing education alone result in lower numbers of dosing errors. The same is true of all measures that lead to a reduction in the cognitive effort required for drug prescription.

KEY MESSAGES

- Staff should receive regular training in the causes and prevention of medication errors and knowledge of pediatric drug therapy. Regular inspection of prescriptions also significantly improves their quality.
- Children's weight plays an essential role in drug therapy. Appropriate methods should be used to estimate weight. Doses should be calculated using electronic aids (e.g. pocket calculators) or weight tables.
- Access to data on pediatric drug therapy (age group–specific doses, drug preparation, and contraindications) must be guaranteed at all times. They may be provided electronically, or in the form of tables or booklets that can be carried in staff's pockets.
- The lowest possible number of drug concentrations should be used; wherever possible, dilution should be avoided (e.g. using 1 mL syringes calibrated in 0.01 mL increments). Syringes must be labeled as systematically as possible (e.g. according to standard ISO 26825).
- Wherever possible, prescriptions should be written on structured prescription forms. If prescriptions are issued orally, a communication structure must be established whereby a structured, complete request is made and repeated in full by its recipient as confirmation.

Conflict of interest statement
Dr. Kaufmann possesses a utility patent and receives royalties for the German pediatric emergency ruler (PädNFL).
The other authors declare that no conflict of interest exists.

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REVIEW ARTICLE

Medication Errors in Pediatric Emergencies

A systematic analysis

Jost Kaufmann, Michael Laschat, Frank Wappler

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eTABLE

Measures to improve the quality of drug prescriptions for children and evidence of their effects

Level of evidence according to EBM[*1], author, year	Study design, target criterion, intervention	Methods, groups	Effect
Source of error: age group–specific knowledge (indication, contraindications, dosing recommendations)			
III, Mullett 2001 (7)	Prospective cohort study, comparison of error rate in antibiotics prescriptions, introduction of electronic database for treatment decisions	1758 patients admitted over one year, pediatric intensive care unit 1) Before 2) After introduction of database	Risk of inappropriately high or low doses (of clinical relevance) 1) 16 per 100 patient days 2) 11 per 100 patient days (p <0.0001)
IV, Sard 2008 (8)	Retrospective cohort study, comparison of error rate in drug prescriptions, introduction of table summarizing pediatric drug therapy	724 prescriptions, pediatric emergency department 1) Before 2) After introduction of dosing table	Comparison of error rate 1) 18% 2) 2% (RR: 0.10, CI: 0.02 to 0.42)
Source of error: determining weight			
III, Krieser 2007 (9)	Prospective observational study, comparison of estimated/measured weight, various methods of estimating	410 children aged 0 to 10 years, pediatric emergency department 1) Estimated by parents 2) Length-related estimates 3) Three age-related formulae	Comparison of estimated & measured weight 1) 78% of cases within 10% 2) 61% of cases within 10% 3) 34% to 42% of cases within 10%
Source of error: dose calculation			
II, Shah 2003 (10)	Prospective, randomized, controlled crossover study, comparison of deviation of drug doses from recommended dose, use of a pediatric emergency ruler	Simulated resuscitation on pediatric manikins, each 4 events by 28 physicians 1) Not using 2) Using pediatric emergency ruler	Deviation of doses from recommended dose, % 1) 36.3% (CI: 29.3 to 51.2%) 2) 7.6% (CI: 4.5 to 9.1%)
III, Cordero 2004 (11)	Prospective cohort study, comparison of error rate in prescriptions of gentamicin, introduction of electronic calculation aid	211 preterm infants, neonatal intensive care unit 1) Before 2) After introduction of electronic calculation aid	Comparison of error rate 1) 13% 2) 0%
III, Kirk 2005 (12)	Prospective cohort study, comparison of error rate in drug prescriptions, introduction of electronic calculation aid (dose calculated by computer)	4274 drug prescriptions, pediatric hospital 1) Before 2) After introduction of electronic calculation aid	Comparison of error rate 1) 28.2% 2) 12.6% (RR: 0.44; p <0.001)
II, Bernius 2008 (13)	Randomized controlled trial, correct prescriptions in a prescription form, table used for reference	Pediatric prescription form, 523 emergency physicians 1) Using 2) Not using table for reference	Correct pediatric prescription forms 1) 65% 2) 94%
III, Wong 2009 (14)	Prospective observational study, correct prescriptions of gentamicin in a prescription form, using a handbook or dosing table	Four prescriptions (2 neonatal, 2 pediatric) in a test, 51 nurses, pediatric hospital 1) Using handbook 2) Using dosing table	Correct answers, pediatric prescription 1) 80% 2) 100% Correct answers, neonatal prescription 1) 35% 2) 55% (only errors of prescription frequency)
Source of error: issuing prescription			
II, Kozer 2005 (15)	Randomized controlled trial, comparison of error rates in a structured prescription form	787 drug prescriptions, pediatric emergency department 1) Written on blank paper 2) Written on form	Rate of medication errors 1) 16.6% 2) 9.8% (OR: 0.55; CI: 0.21 to 0.77)
IV, Larose 2008 (16)	Retrospective cohort study, comparison of error rates in a structured prescription form	719 drug prescriptions, pediatric emergency department 1) Written on blank paper 2) Written on form	Rate of medication errors 1) 15% 2) 6% (Δ 9%; CI: 5 to 13)
IV, Broussard 2009 (17)	Retrospective observational study, comparison of error rates in a structured sedative prescription form	84 prescription forms, pediatric hospital 1) Written in patients' records 2) Written on form	Rate of medication errors 1) 25% 2) 9% (p <0.001)

Level of evidence according to EBM[*1], author, year	Study design, target criterion, intervention	Methods, groups	Effect
Comprehensive or multiple measures			
III, Morriss 2009 (18)	Prospective cohort study, risk rate of medication errors, barcodes on syringes & electronic control system	92 398 prescriptions, neonatal intensive care unit After introduction of barcodes & control system	Relative risk of medication errors RR: 0.53 (CI: 0.29 to 0.91; p = 0.04)
III, Davey 2007 (19)	Prospective cohort study, comparison of prescription errors, training in pediatric prescriptions	Total of 515 prescriptions, pediatric hospital 1) Before 2) After training	Rate of prescription errors 1) 31% 2) 17% (p <0.001)
II, Gordon 2011 (20)	Randomized controlled trial, comparison of results of a test on pediatric prescriptions, e-learning on pediatric prescriptions	Written test, 86 doctors did not receive training, 76 did 1) Before e-learning 2) One month after e-learning 3) Three months after e-learning	Correct results in written tests 1) 67% vs. 67% (p = 0.56) 2) 79% vs. 63%) (p <0.0001) 3) 79% vs. 63% (p <0.0001)
III, Taylor 2008 (21)	Prospective observational study, comparison of deviations from recommended doses, introduction of electronic prescription system	Total of 526 prescriptions, neonatal intensive care unit 1) Before 2) After introduction of electronic prescription system	Deviation from recommended doses 1) 20% of prescriptions 2) 11% of prescriptions (RR: 0.53)
III, Walsh 2008 (22)	Prospective observational study, comparison of error rate, introduction of electronic prescription system (inspection of prescription had already been implemented)	12 672 prescriptions, neonatal & pediatric intensive care units, normal ward 1) Before 2) After introduction of electronic prescription system	Dangerous prescription errors 1) 22 per 1000 patient days 2) 7% reduction in harm caused by prescription errors 1) 7 per 1000 patient days 2) No reduction
III, King 2003 (23)	Prospective observational study, comparison of prescription errors & potentially dangerous errors, introduction of electronic prescription system (without pediatric drug database)	Rate of prescription errors & potentially dangerous errors 1) Units with 2) Units without electronic prescription system	Comparison of rate of prescription errors 2) RR: 0.6 (CI: 0.48 to 0.74), i.e. an improvement Comparison of rate of dangerous errors 2) RR: 1.3 (CI: 0.47 to 3.52), i.e. a deterioration
III, Campino 2009 (24)	Prospective cohort study, rate of dosing errors, training	Total of 5694 prescriptions, neonatal intensive care unit 1) Before 2) After introduction of training	Rate of prescription errors 1) 5% 2) 0.2% (p <0.001)
III, Potts 2004 (25)	Prospective cohort study, comparison of rate of prescription errors, introduction of electronic prescription system with incorporated pediatric drug database	Total of 13 828 prescriptions, pediatric intensive care unit 1) Before 2) After introduction of prescription system	Comparison of rate of prescription errors 1) 30.1 per 100 prescriptions 2) 0.2 per 100 prescriptions (p <0.001) Comparison of rate of dangerous errors 1) 2.2 per 100 prescriptions 2) 1.3 per 100 prescriptions (p <0.001)
III, Kazemi 2011 (26)	Prospective cohort study, comparison of rate of dangerous prescription errors, introduction of electronic prescription system with incorporated database	Total of 3206 prescriptions, neonatal unit 1) Before 2) After introduction of electronic prescription system 3) With the addition of incorporated database	Rate of dangerous prescription errors 1) 2.5% 2) 2.4% 3) 0.8% (p <0.005)
III, Kidd 2010 (27)	Prospective cohort study, comparison of results of a test on pediatric prescriptions, introduction of training, specialist information & pocket calculator available	32 vs. 30 young physicians, pediatric hospital 1) Before 2) After training, handbook, pocket calculator	Correct answers 1) 58% of answers correct 2) 93% (Δ 36%; CI: 24 to 47)
IV, Kadmon 2009 (28)	Retrospective cohort study, rate of prescription errors & potentially dangerous errors, introduction of electronic prescription system/incorporation of database into such system/prescriptions issued by physicians only (previously also issued by nurses)	3750 prescriptions (antibiotics & anticonvulsives), pediatric hospital 1) Before 2) After introduction of electronic prescription system 3) Incorporation of database 4) Prescriptions can only be issued by physicians	Prescription errors/potentially dangerous errors 1) 5.5%/2.5% 2) 5.3%/2.4% 3) 3.8% (p <0.05)/0.8% (p <0.001) 4) 0.7% (p <0.005)/0.7% (p <0.001)
III, Campino 2008 (29)	Prospective, controlled cohort study, rate of dosing errors, introduction of inspection of prescriptions by hospital pharmacists	4304 prescriptions, neonatal intensive care unit 1) Before 2) After introduction of inspection	Rate of dosing errors 1) 14% 2) 5% (p <0.001)

Level of evidence according to EBM[*1], author, year	Study design, target criterion, intervention	Methods, groups	Effect
IV, Costello 2007 (30)	Controlled cohort study (retrospective control group, prospective intervention groups), rate of medication errors causing potential or actual harm, introduction of inspection of prescriptions by hospital pharmacists/CIRS/training	Pediatric intensive care unit 1) Before (2 months observation period) 2) After introduction of inspection (4 months observation period) 3) Inspection, training, CIRS (4 months observation period)	Rate of medication errors causing potential of actual harm 1) 46% 2) 8% 3) 0%
III, Larsen 2005 (31)	Prospective cohort study, rate of reported medication errors & tenfold errors in continuous intravenous administration, introduction of standard concentrations/computer-generated syringe barcodes/smart syringe pumps	12 399 prescriptions, pediatric hospital 1) Before 2) After interventions	Medication errors per 1000 prescriptions 1) 3.1 2) 0.8 (Δ 2.3; CI: 1.1 to 3.4; p <0.001) Tenfold errors per 1000 prescriptions 1) 0.41 2) 0.08
III, Stewart 2010 (32)	Prospective comparative study, results of a test on pediatric prescriptions, seminars on pediatric drug therapy, communication, & teamwork	Comparison of test results of 68 participants 1) Before 2) After seminar participation	Improved knowledge of - Awareness of drug safety - Causes of drug errors - Communication & teamwork
IV, Otero 2008 (4)	Retrospective comparative study, rate of medication errors, development of training program with multiple components (standardized prescriptions, supervision, interdisciplinary discussions, pharmacist ward round, checklists, CIRS, database)	1734 prescriptions, pediatric units 1) Before 2) After multiple interventions	Medication errors per 1000 prescriptions 1) 11% 2) 7% (OR: 0.61; CI: 0.5 to 0.75)
III, Leonard 2006 (33)	Prospective cohort study, rate of medication errors, e-learning/inspection of prescriptions with feedback/monthly discussions	8718 prescriptions, pediatric hospital 1) Before 2) After multiple interventions	Rate of potentially dangerous prescription errors 1) 78 per 100 prescriptions 2) 40 per 100 prescriptions (p = 0.01)
III, Kaji 2006 (34)	Prospective observational study, comparison of epinephrine dosing accuracy within 20% of the recommended dose, introduction of a pediatric emergency ruler (the Broselow tape)	141 children, prehospital resuscitations 1) Not using 2) Using emergency ruler	Accurate dose recommended/administered to within 20% 1) 34% 2) 67%
III, Ligi 2010 (35)	Prospective cohort study, rate of tenfold medication errors, introduction of a CIRS system & error prevention strategies based on it	1033 patients, neonatal intensive care unit 1) Before 2) After introduction of CIRS plus derived strategies	Rate of tenfold dosing errors 1) 2.3 per 100 patients 2) 0.6 per 100 patients (p = 0.02)
IV, Koren 2002 (36)	Retrospective cohort study, rate of medication errors, computer-based prescription system/sorting of available drugs/training	1.8 million drug administrations annually, 2-year observation period, pediatric hospital 1) Before 2) After intervention	Rate of medication errors made by physicians 1) 0.04% 2) 0.02% (p <0.001)
IV, Sharek 2008 (37)	Prospective observational study with retrospective control group, rate of potentially dangerous medication errors, participation in risk analysis & multifactor process optimization	Anesthesiology departments in 14 pediatric hospitals Before/after intervention	Frequency of drug errors 67% reduction (p <0.001)

[*1]Level of evidence according to the Centre for Evidence-Based Medicine, 2011 (e37): I: Meta-analysis of randomized controlled trials; II: Randomized controlled trial; III: High-quality (prospective) controlled trial (nonrandomized); IV: Case series, case-control study, or historically controlled trial; V: Case reports, expert opinions.
CIRS: Critical Incident Reporting System; CI: Confidence interval; RR, Relative risk; OR: Odds ratio; Δ: Difference