BJA

British Journal of Anaesthesia, 118 (5): 670–9 (2017)

doi: 10.1093/bja/aex072
Review Article

Drug safety in paediatric anaesthesia

J. Kaufmann[1,2,*], A. R. Wolf[3], K. Becke[4], M. Laschat[1], F. Wappler[1,2] and T. Engelhardt[5]

[1]Department for Paediatric Anaesthesia, Children's Hospital Cologne, Cologne, Germany, [2]Faculty for Health, University of Witten/Herdecke, Witten, Germany, [3]Department of Paediatric Intensive Care, Bristol Royal Children's Hospital, Bristol, UK, [4]Department for Anaesthesiology and Intensive Care Medicine, Cnopf Children's Hospital, Nürnberg, Germany and [5]Department for Anaesthesia, Royal Aberdeen Children's Hospital, Aberdeen, UK

*Corresponding author. E-mail: jost.kaufmann@uni-wh.de

Abstract

Life-threatening drug errors are more common in children than in adults. This is likely to be because of their variations in age and weight, combined with the occasional exposure of most anaesthetists to paediatric patients. Drug administration in anaesthesia is mostly undertaken by a single operator and thus represents a potentially greater risk compared with other areas of medicine. This increased risk is believed to be offset by anaesthetists working with only a limited number of drugs on a very frequent and repetitive basis. However, high rates of errors continue to be reported. Paediatric anaesthesia practice requires individual age- and weight-specific drug dose calculations and is therefore without a 'familiar' or 'usual' dose. The aim of this narrative systematic review of existing recommendations and current evidence of preventive strategies is to identify measures to enhance the safety and quality of drug administration in paediatric anaesthesia. This review collates and grades the evidence of such interventions and recommendations and assesses their feasibility. Most highly effective available measures require low or limited costs and labour. The presented solutions should, therefore, achieve a high level of acceptance and contribute significantly to safety and quality of care in paediatric anaesthesia.

Key words: anaesthesia; child; medication errors; paediatrics; patient safety

'Medication errors are perhaps the most common threat to patient safety.'[1] The incidence of self-reported medication errors in adult anaesthesia is estimated to be 1 in every 133 patients.[2] However, self-report is likely to underestimate the real incidence because of non-recognition, forgetfulness, or intentional omission of errors. The potential magnitude of this problem was highlighted in a recent study reporting a medication error of 1 in every 20 drug administrations and every second anaesthesia procedure. One-third of these errors led to real harm of the patient.[3] Although this study used wide definitions of errors and harm, these data confirm that drug administration errors are more common than generally assumed.

Children are at a particular risk because of age- and size-related individual drug dose calculations.[4] Large medication errors (factor of 10) frequently occur if small volumes are taken from a 'stock' solution.[5] In addition, such errors also occur easily by placing the decimal point in the wrong position, with potentially fatal consequences.[6–8] Anaesthesia drug administration represents a potentially greater risk because the entire process is often conducted by a single person,[9] in contrast to other areas of medicine.[10] Several recommendations addressing this issue already exist, but none offers a systematic analysis of key measures. Therefore, the aim of this narrative review was systematically to identify known measures to reduce errors according to

their level of evidence and feasibility with paediatric practice. This review could form the basis for a guideline supported by different paediatric anaesthetic societies and, possibly, by other organizations and medical specialties.

Methods

The search strategy for this narrative systematic review is illustrated in Fig. 1. The databases of the 'Guidelines International Network (GIN)' and the websites of international medical societies related to guidelines, anaesthesia, or paediatrics (American Academy of Pediatrics (AAP), Australian and New Zealand College of Anaesthetists (ANZCA), Association of Paediatric Anaesthetists of Great Britain and Ireland (APA), Anesthesia Patient Safety Foundation (APSF), American Society of Anesthesiologists (ASA), Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF), Berufsverband Deutscher Anästhesisten (BDA), Deutsche Gesellschaft für Anästhesiologie &

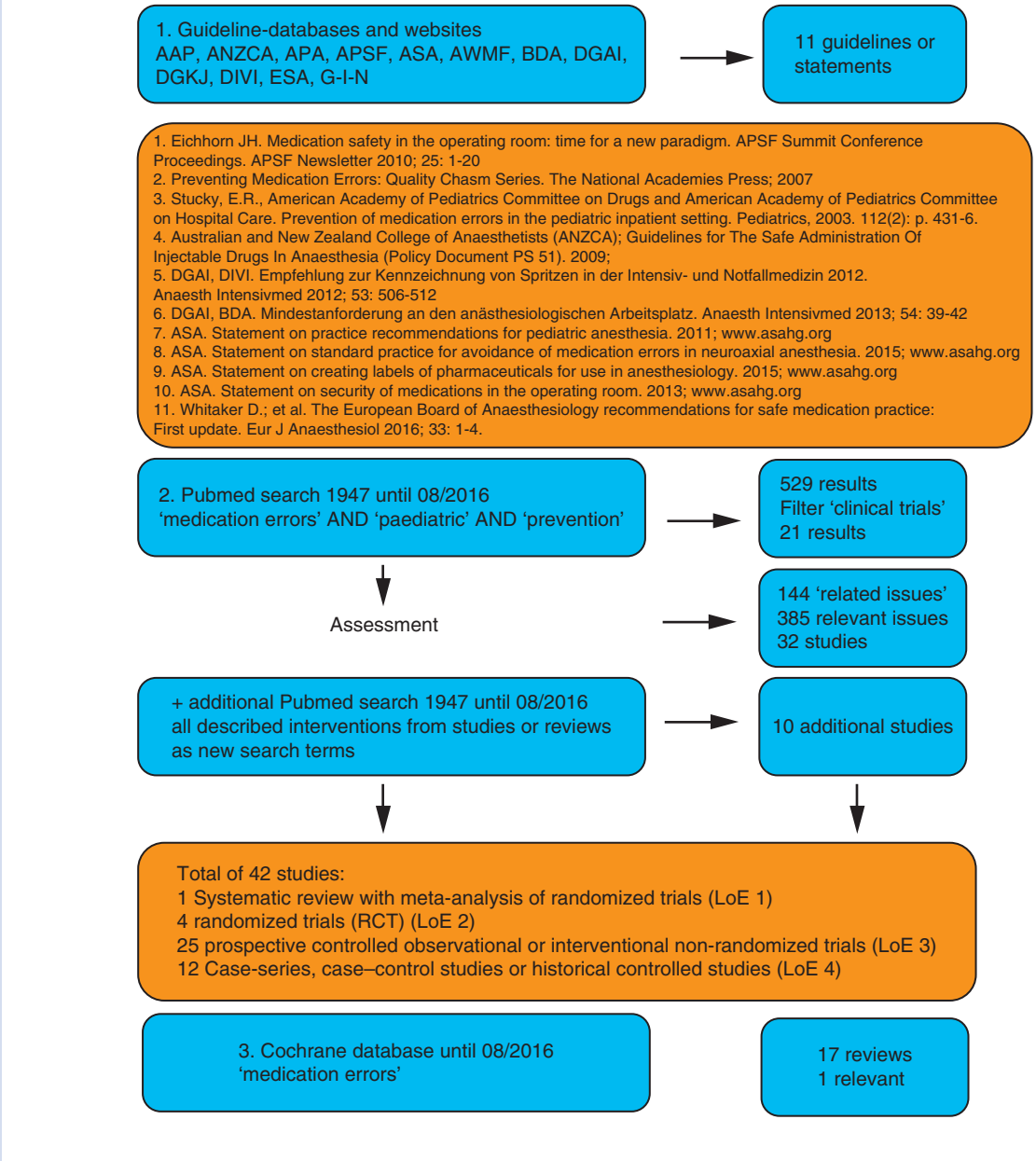

Fig 1 Flow chart of systematic literature review. AAP, American Academy of Pediatrics; ANZCA, Australian and New Zealand College of Anaesthetists; APA, Association of Paediatric Anaesthetists of Great Britain and Ireland; APSF, Anesthesia Patient Safety Foundation; ASA, American Society of Anesthesiologists; AWMF, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften; BDA, Berufsverband Deutscher Anästhesisten; DGAI, Deutsche Gesellschaft für Anästhesiologie & Intensivmedizin; DGKJ, Deutsche Gesellschaft für Kinder- und Jugendmedizin; DIVI, Deutsche Interdisziplinäre Vereinigung für Intensiv und Notfallmedizin; ESA, European Society of Anaesthesiology; G-I-N, Guidelines International Network; LoE, level of evidence; RCT randomized controlled trial.

Intensivmedizin (DGAI), Deutsche Gesellschaft fär Kinder- und Jugendmedizin (DGKJ), Deutsche Interdisziplinäre Vereinigung für Intensiv und Notfallmedizin (DIVI), European Society of Anaesthesiology (ESA) were searched. A total of 11 guidelines that included the phrase 'medication AND/OR safety' were identified and included.[11–21] Reports and statements from national or international authorities available on webpages were also included.[22–25]

A search of Medline (Pubmed) and the Cochrane Library, using the search terms 'medication errors' AND 'paediatric' AND 'prevention', was conducted and their level of evidence (LoE) assessed based on the recommendations of the Oxford Centre for Evidence-Based Medicine.[26] In addition to the LoE, the feasibility of the analysed interventions was assessed separately by estimating associated costs for consumables and labour. The feasibility was classified as good (negligible costs), limited (sizeable costs), or poor (high costs). The assessed evidence and feasibility is provided as Appendix 1. Essential interventions that have a high LoE (1 or 2) and a good feasibility are marked with a Grade of Recommendation (GoR) 'A1' and with limited or poor feasibility as 'A2' (Fig. 2). Desirable interventions with limited LoE (3) and good feasibility are classified as GoR 'B1' and with limited or poor feasibility as 'B2'. Possible interventions with low LoE (4) but good feasibility are labelled with GoR 'C1' or if the feasibility is limited or poor with 'C2'. The highest grade of recommendation achieved by each measure is provided after each statement that is based on evidence in the manuscript and Table 1 (which also contains the LoE and assessments of feasibility). For some statements, no published evidence could be found. If these statements are meaningful and reasonable, they are included and marked as 'good practice (GP)' in the summary Table 1, but no additional GoR is provided within the document. The structure of this narrative review follows the time course of drug administration.

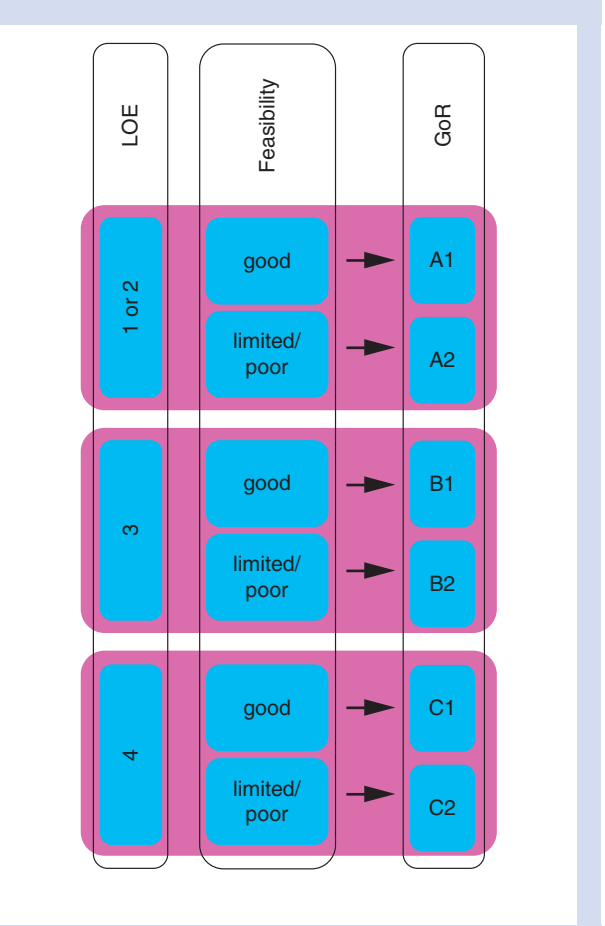

Fig 2 Graphical presentation of the method to classify the grade of recommendation (GoR). The level of evidence (LoE) follows the classification of the Oxford Centre for Evidence-Based Medicine. Levels are defined as follows: 1, systematic review of randomized trials or n-of-1 trials; 2, randomized trial or observational study with dramatic effect; 3, non-randomized controlled cohort/follow-up study; and 4, case series, case–control studies, or historically controlled studies. Feasibility is classed as good (negligible costs and consumption of working time), limited (relevant costs, consumption of working time, or both), or poor (high costs, consumption of working time, or both).

Results and recommendations

Personal and institutional competency

Challenges of competency

Human factors are the most frequent causes for threatening events during anaesthesia.[27 28] Education and individual experience are contributing factors in avoiding complications in paediatric anaesthesia[29] and drug errors.[30 31] For example, in Germany every anaesthetic must adhere to the standards set out by the German Society of Anaesthesiology and Intensive Care Medicine (DGAI)[16] and competently provided, as follows:[32] 'The conduct of anaesthesia requires (…) adequate practical and clinical experience in order to provide the medically and legally accepted specialist standard'. The American Academy of Pediatrics (AAP), Section on Anesthesiology,[33] requires an anaesthetist with paediatric expertise and special competence capable of handling any complications and emergencies always to be immediately available. It is recommended that specially trained and experienced assistants should be employed for paediatric patients.[16] Inexperienced staff must be guided, supported, and monitored by consultant paediatric anaesthetists during induction and recovery from anaesthesia as a minimal requirement.

Solutions for improving competency

Teaching courses on paediatric pharmacology and causes of medication errors enhance quality of drug treatment and reduce prescription errors (GoR A2).[7 34–39] Besides an enhancement of the pharmacological knowledge, such courses can contribute to an improvement of the vigilance of the participants for the relevance of drug safety issues. Other resources of pharmacological knowledge, such as tabular or electronic references, are also able to improve drug prescription quality (GoR A2).[34 36 39–43] Essential paediatric pharmacological knowledge (age-group-specific indications, contraindications, and dose recommendations) are critical. Such information should be established as 'institutional knowledge' in the form of a standard operating protocol and made immediately available at every workplace (GoR A2). Several Web-based programs and smartphone applications are available, but none is currently licenced or evaluated, and no firm recommendation can be made.[44]

Operator vigilance

Challenges of operator vigilance

Constant awareness of the threat of medication errors affects vigilance. Awareness that someone cross-checks medical drug prescriptions significantly reduces errors when compared with when

Table 1 Summarized recommendations for avoidance of drug errors. GoR, grade of recommendation (see Methods section and Fig. 2); CIRS, Critical Incident Reporting System; GP, good practice; ISO, International Organization for Standardization; LoE, level of evidence

Grade of recommendation	Recommendation
Solutions for improving competency	
GP	Specialist standard with additional expertise in paediatric anaesthesia
GP	Assistants experienced in paediatric anaesthesia
A2	Lectures and courses in paediatric drug therapy [LoE 2–4, feasibility limited, GoR A2–C2]
A2	Standard operating protocols for age/group-specific indications, contraindications, and dosage recommendations [LoE 2–4, feasibility good–limited, GoR A2–C2]
A2	(Electronic) reference sources for paediatric drug therapy [LoE 2–4, feasibility good to limited, GoR A2–C2]
Solutions for improving vigilance and safety culture	
GP	Lectures and courses addressing awareness of drug safety
B2	External quality controls [LoE 3–4, feasibility limited, GoR B2–C2]
B2	Establishment and maintenance of a CIRS [LoE 3–4, feasibility limited, GoR B2–C2]
GP	Establishment and maintenance of safety and error culture
Solutions to avoid confusions of drugs	
GP	Avoidance of 'look-alike' or 'sound-alike' drugs if possible
GP	Notification of responsible authorities of potential confusions because of naming, labelling, or packaging of drugs
GP	Avoidance of different preparations (concentrations and additives) if possible (if unavoidable, choose different storage places)
GP	Clearly defined and distinct storage place for each drug
GP	Uniform storage place for each drug at every working place within the same facility; notify and display clear visible warning if drug storage place has changed
GP	Drugs with high potential for harm and frequent use: store at the workplace but separate from other drugs
GP	Drugs with high potential for harm and infrequent use: do not store at the workplace
GP	Clear and distinct labelling of syringes (ISO-norm)
Solutions to improve drug prescribing	
GP	Measure and document weight
B1	If weight is unknown, use weight provided by parents [LoE 3, feasibility good, GoR B1]
B1	Length-based estimation methods are an alternative if weight is unknown [LoE 3, feasibility good, GoR B1]
GP	Careful documentation of allergies and underlying conditions
A1	Tabular references [LoE 2, feasibility good, GoR A1]
A2	Length-based references [LoE 2–3, feasibility limited, GoR A2–B2]
B1	Electronic support for calculating drug dose (calculators or spreadsheet programs) [LoE 3, feasibility good-limited, GoR B1–B2]
B2	Computerized physician order entry systems [LoE 3, feasibility poor, GoR B2]
B2	Computerized physician order entry systems with integrated pharmacological database [LoE 3–4, feasibility poor, GoR B2–C2]
GP	Exact naming and repeating of entire relevant information (closed-loop communication)
GP	The whole team checks each other regardless of existing hierarchies
A1	Written prescriptions for drugs with high potential for harm, complex calculations, or continuing therapies [LoE 2–4, feasibility good, GoR A1–C1]
GP	Repeatedly independent check by a second person ('double-check')
Solutions for the avoidance of drug preparation failures	
GP	Avoid dilution whenever possible (use of 1 ml syringes)
GP	Select drug concentration that allows easy calculations
GP	Avoid distractions during drug preparation
GP	Standardized instructions for drug preparation at the workplace
GP	First draw the dilution agent and then drug into separate syringes; inject the drug into the syringe with the diluting agent (use appropriate filling/drawing needles)
GP	Use only compatible diluting agents according to the recommendations of the manufacturer
GP	Avoid contamination or pollution
B2	Ready-prepared syringes [LoE 3, feasibility poor, GoR B2]
Solutions for the avoidance of drug administration errors	
GP	Flushing of drugs
GP	Follow manufacturer's instructions (speed of administration, compatibility of diluting agents, drug incompatibility)
GP	Dead space of catheters must be known
GP	Discard the dead space of catheters if primed with drug solution (e.g. to protect line patency)
GP	Labelling of syringes in pumps and the lines near to the patient (ISO-norm)
B2	Smart syringe pumps with label reader, pharmacological database, or both [LoE 3, feasibility poor, GoR B2]
GP	Double-check of every syringe pump
GP	Kinking-free lines of syringe pumps
GP	Avoidance of vertical repositioning of syringe pumps
GP	Usage of non-return valves at the confluence of lines
GP	Usage of gastric tubes with connectors incompatible to Luer; for gastric medications, use colour-marked syringes with compatible connectors
GP	Clearly define, mark, and hand over a port where injection on bolus medications are immediately possible

this control is not known. The knowledge that a pharmacist will cross-check the drug prescription significantly reduced errors, most probably because of increased prescriber vigilance.[45]

Solutions for improving vigilance and safety culture

Regular random checks of anaesthetic protocols (by an experienced paediatric anaesthetist or a pharmacist) should be performed and staff be made aware and results audited (GoR B2).[46] This analysis then forms the basis of a continuing quality assurance programme. Critical incident reporting systems (CIRS) increase the rate of reported errors[47] and must be present in every medical facility. There are no studies available to suggest that CIRS on their own improve drug safety. However, a number of studies combine several different drug safety measures, including CIRS, with beneficial results (GoR B2).[7 48–50] In order to establish and improve a safety culture, feedback and involvement of health-care providers is essential in addition to a suitable CIRS. However, CIRS do not automatically improve safety, but depend on voluntary contributions and use. Therefore, a successful CIRS requires a safety and error-reporting culture without apportioning blame for the reporting staff.[9] The report must be acknowledged as an essential contribution to a systematic improvement. A constructive processing of all reports, timely implementation of meaningful changes, and subsequent re-evaluation are the conditions that enable improvements through CIRS.[11 37]

Confusion of drugs

Challenges to avoid confusions of drugs

The causes for the mix-up of original packaged drugs are as follows: (i) similar-looking ampules or packaging ('look alike'); (ii) similar sounding names ('sound alike'); (iii) falsely anticipated or confounded storage location; and (iv) falsely anticipated or confounded course of action.[11 51] Confusion can also occur referring to the preparation, the concentration, and the route of administration. In addition, drug preparations with additives (for example, local anaesthetics or analgesic suppositories) may be confused with the equivalent preparation without additives. Once a drug has been drawn into a syringe, a reliable detection of the contained drug and its concentration by appearance only is impossible.

Solutions to avoid confusions of drugs

Drugs or preparations likely to be confused because of their appearance or names should be separated or not stocked if possible. Preparations with or without additives should be clearly labelled and stored in different places. Only the same concentrations of the same drug must be kept at the immediate workplace. If an additional concentration of the same drug is essential, the concentration used less frequently should be stored away from the immediate working place to avoid unintentional use.

Drugs used regularly must be stored at the workplace. Every drug requires a clearly defined and distinct storage place assigned and labelled (e.g. ampoule bag, drawer with dividers). This storage should be chosen uniformly at all anaesthesia workstations throughout the department. All staff must be notified of any changes to its location, and changes must be accompanied by a clearly visible warning. Drugs with high potential for harm and frequent use (e.g. epinephrine, bupivacaine) should be well separated from other drugs at the workplace.[52] Drugs with high potential for harm and infrequent use (e.g. potassium, insulin) should be held in a storage area away from the operating room.

The pharmaceutical industry has to take responsibility for the appearance and labelling of drugs. Manufacturers who have optimized their product range (e.g. various concentrations of local anaesthetics clearly distinguishable) and are meeting the requirements defined by the national authorities[22] should be preferred. Every user should report concerns regarding not clearly distinguishable labelling of the original packing of drugs to all colleagues and should notify the responsible authority about the concern. Every prepared syringe must be clearly and distinctly labelled. The labelling process itself is a potential source for error but also allows control and error detection.[53] The labelling should include a colour as defined by international norm ISO 26825 and recommended by several medical societies, institutions, or authorities.[22–24 53–55] The main principle of colour-coded drug groups (e.g. opioids = light blue) is supplemented by tall-man-lettering and additional colour features.[15] Such labels may be placed lengthwise on the syringe to ease the reading of all information provided without covering the scaling. Such labelling is able to reduce confusions between medication groups.[53]

Prescription and dispensing of drugs

Challenges of dose finding and drug calculations

Age-related pharmacokinetic and -dynamic parameters must be considered when prescribing and administering drugs to children. Knowledge of body weight is mandatory and required for calculating drug doses. Drug dose calculations based on lean body weight are generally preferred, although the measured weight is the most practicable. An erroneous body weight will inevitably lead to drug dosing errors. Arithmetic calculating errors are possible, and cross-checking is advisable.[56] No 'routine' or 'familiar' dose can be expected when anaesthetizing children, which is in stark contrast to adult anaesthetic practice. Even factor-of-10 errors occur frequently and are likely not to be noticed because they still represent only an unsuspiciously small volume of a stock solution.[57] Determination of the correct dose is the most important step, where the highest rate of (life)-threatening errors are observed.[5 47 58] This is particularly true for complex calculations required, for example, in syringe pumps.[59]

Solutions for dose finding and drug calculations

The weight of the child is of central importance and must be documented reliably in the medical record and on the anaesthesia chart. This must be guaranteed in all elective patients.[52] If this is not possible during emergency procedures, parental reporting is acceptable (GoR B1).[60] Age-related formulas for weight estimation are less suitable.[61] The most reliable estimation of the weight is provided by a length-based method (GoR B1),[62] which provides the lean body weight and is better correlated with the extracellular volume than the measured weight. This is crucial for the distribution of emergency drugs, analgesics, and anaesthetics,[63] and advantageous in obese children. Prescription errors also occur when allergies, paradoxical reactions, interactions with other drugs, or preconditions that influence the indication, contraindication, or correct dispensing of a drug are ignored. Due diligence must be provided for information about allergies and other conditions affecting drug therapy.

Calculation of drug doses should be supported by electronic means (e.g. calculators or spreadsheet programs), which have been shown to minimize drug dosing errors (GoR B1).[64 65] This is essential for drugs with a high potential for harm or complex calculations (syringe pumps). It can be assumed that all other measures reducing the cognitive demands on the prescriber improve safety;[66] for instance, the use of a simple tabular reference providing emergency drug doses related to weight groups (GoR A1)[67] or length-related dose recommendations (GoR A2)[68–70]

reduced error rates during simulated paediatric emergencies. A positive impact is observed if computerized physician order entry systems are used (GoR B2),[71 72] particularly those that use an integrated database of paediatric (e.g. age-related) pharmacological recommendations (GoR B2).[73 74] Such systems can actively warn if relevant interactions occur between the intended medication and the patient's individual conditions (e.g. allergies, renal impairment, cholinesterase deficiency) if used within a patient information system. This is successfully used in paediatric intensive care and paediatric oncology.[71–73 75] The high investment costs can be offset by the avoidance of expensive complications and claims.[28]

Challenges of drug prescribing

Communication deficits are a significant cause for medication prescription errors.[76] Most of the prescriptions in anaesthesia are given as verbal prescriptions. However, an entirely written or verbal prescription must always contain a dose (e.g. milligrams per kilogram) and the total amount according to body weight (e.g. milligrams). The concentration (e.g. milligrams per millilitre) and the amount of the solution (e.g. millilitres) are also necessary. In paediatric simulation scenarios, up to 17% of all verbal prescriptions did not contain a distinct dose.[10] Additional deficits frequently occur at the handover (change of the anaesthesia team or change of the care area).[12 77] Communication deficits are also a result of hierarchical structures. Real harm to a patient still occurs despite at least one person being aware of the error and not being able to contradict more senior staff. In a paediatric emergency department, a life-threatening error confusing adenosine and amiodarone occurred because nobody dared to contradict an experienced consultant. Although several participants knew that this was a life-threatening error, they did not intervene. This was reproduced in five identically simulated scenarios after the event.[78]

Solutions to improve drug prescribing

The introduction of a structured sheet or computer-based forms for written prescriptions on paediatric intensive care units significantly reduces the number of errors (GoR A1).[1 79–82] However, this is neither feasible nor necessary for the vast majority of drugs used in paediatric anaesthesia. The prescriber should always verbally communicate all important information and calculation steps. With familiar medications, this can be done by simply naming the dose and the amount of drug to be administered. An exact communication of relevant information (weight of the patient, dose, total amount, concentration of solution, and volume of solution to be administered) is essential with less commonly or potentially more dangerous drugs or the use in complex situations (e.g. epinephrine during resuscitation). The recipient of this prescription must repeat this prescription ('closed-loop' communication) and verify this through recalculation. Only when everybody is in agreement that the right amount of the right drug is about to be given may it be administered. There must be no barrier for any member of staff to voice concerns about a prescription. Therefore, the only issue during drug prescription and administration is in relationship to the (clinical) facts and not to any existing hierarchy. This communication structure reduces error frequency and aids staff satisfaction through identification.[76 83] Written prescriptions should always be provided for complex or potentially dangerous drugs. These should be 'double-checked' by a second person.[84] This may particularly apply after transfer to paediatric intensive care or high-dependency units and for specialist pain treatments.[12 85 86]

Preparation of medications

Challenges of drug preparation

The preparation of drugs (drawing of the drug into a syringe and subsequent dilution) is another important source of drug errors. A systematic analysis of a Critical Incidence Reporting System (CIRS) register demonstrated that 44% of reported drug errors were attributable to the errors in drug preparation.[87]

The wide range of drug doses in paediatric anaesthesia necessitates the provision of anaesthetic and analgesic drugs in different concentrations and packages. Dilution regularly results in failure to achieve the desired concentration.[10 88]

Solutions for the avoidance of drug preparation failures

The person responsible in the preparation of medications must be free of other duties and not be distracted. A separate workplace and specific signage (warning vest) may be helpful. The dilution of drugs should be avoided wherever possible. In the most instances, this can be achieved for most drugs by using 1 ml syringes with 0.01 ml markings, permitting an accurate amount to 0.05 ml after flushing to be administered. Some drugs, such as epinephrine, require clear and easy-to-follow instructions for dilutions and should be standardized and hygiene standards followed. Dilutions should be chosen that enable simple further calculations (e.g. 1 mg ml^{-1} or 100 μg ml^{-1}) and dilutions. The diluting agent should be drawn into a syringe first and verified. Then the predetermined amount of the drug should be drawn into an appropriate separate syringe (using a suitable filling or drawing needle). After verification, the drug should then be injected into the target syringe or perfusion syringe with a new filling needle. If possible, the preparation of critical medications should be observed and confirmed by a second person. Pre-prepared, labelled, and sealed syringes (commercial or hospital pharmacy) are more accurate because of quality controls during the manufacturing process[53] and can contribute to a reduction of error rates and time required until administration (GoR B2).[89 90] However, limited shelf life and higher costs are a disadvantage and should be considered for rarely used emergency drugs.

Administration of medications

Challenges of drug administration

Very small volumes of drug solutions are commonly administered in paediatric anaesthesia. Drugs may remain in the i.v. line and be administered inadvertently at a later stage. The dead space of large catheters (haemodialysis or chemotherapy) is particularly prone to drug flushing errors. If this dead space was primed with a drug solution (e.g. heparin lock to protect the line patency) or a previous administration was not adequately flushed, an unintended bolus from this dead space occurs.

Pharmaceutical drug incompatibilities at peripheral and central i.v. lines are possible. Multiple line connectors may lead to back flow and unintentional boluses if unidirectional (non-return) valves are not used. Kinking of i.v. lines, incorrect syringe position within the pump, (vertical) changes of pump position, and failure to use anti-siphon valves may substantially change the rate of drug administration, resulting in potentially life-threatening situations.[91]

Solutions for the avoidance of drug administration errors

Drug administration requires the following five steps ('5-R-rule'). (i) Right patient? (ii) Right drug? (iii) Right dosage? (iv) Right moment? (v) Right route?

High-risk drugs must be double-checked. High-risk drugs are defined as medications that contain a high potential for severe harm when used erroneously. Errors do not necessarily occur more frequently, but consequences to the patient might be life-threatening. They include potassium, blood and blood products, continuous opioid infusions Patient controlled analgesia (PCA), heparin, insulin, and catecholamines (bolus and infusions).

Every administered drug should be given according to the manufacturer's instructions and flushed with a sufficient amount of an appropriate solution. The dead space of large catheters should be known and must be discarded before use, if it was primed with a drug solution. Non-return valves reduce in-line incompatibilities, and suitable i.v. giving sets and lines (filter, compliance, diameter, and length) should be considered. Syringe pump settings need to be carefully and regularly checked, especially at handover. Syringe pumps with an integrated drug database are preferable, provided the entered weight is correct. Double-checking for syringe pumps is essential; i.v. lines must be secured (no kinks), and vertical position change should be avoided whenever possible. Recommended labels for syringes in pumps must be used, containing clear and easy-to-read essential information (drug name, concentration, date and time of preparation, in addition to name of patient, route of administration, dilution agent, flow of infusion if fixed, and duration of administration). Information of drugs added to existing syringes or infusion/bottle/bag must be clearly visible, with a label with printed tall letters 'PLUS' attached. Near-patient labelling of infusions should be established.[55] The whole process of prescribing, preparation, and delivery of high-risk drugs should be observed and confirmed by a second person, whenever possible. The port used for bolus injections must be clearly labelled in order to allow safe and immediate drug administration, especially when multiple i.v. lines are in use.

The use of 'smart' syringe pumps that are connected to patient information systems, use integrated pharmacological databases that are able to scan drug labels, and patient identity tags are available and would be highly desirable (GoR B2).[92] A two-dimensional data matrix has been developed with industry and can be used to create machine-readable labels.[15]

Syringe and tube connectors must not be compatible for drugs intended for enteral and for i.v. administration. 'Foolproof' syringes are colour marked for enteral drug administration. At the handover of patients to another anaesthesia team or another care area, a port where injection boluses of i.v. medications is immediately possible must be labelled and clearly defined.

Beyond evidence and recommendations

No single intervention or range of interventions can provide complete safety without errors. Most measures used to enhance drug safety that were investigated in studies and are presented in this review significantly reduced error rates, but none of them could eliminate them. Even the strictest code of conduct for every drug, person, and institution relies on constant and never-failing vigilance. It may, therefore, appear pragmatic to prioritize high-risk drugs and procedures most likely to result in significant harm. A complete procedural separation and restricted access may be required, with a limited number of staff familiar with the risks involved permitted to administer the drug. Examples are the administration of chemotherapy or high-dose heparin.

Another limiting feature of medication safety is the range of human factors. Even very simple tasks, such as reading a drug or dose, may result in erroneous action. Consequently, the reduction of human factors should be maximized as much as possible while maintaining enthusiasm for safety on every occasion and every activity. If this is not further possible, a fundamental understanding of the drug and its risk ('know what you are giving') may further reduce but not eliminate drug errors.

Off-label medication use remains a significant concern in paediatric anaesthesia. Anaesthetists must be aware of the licensed paediatric indications and the knowledge deficiencies in pharmacokinetics and pharmacodynamics. Legislation and licensing is a complex and long process. Practitioners providing anaesthetic care for children must remain vigilant of any new developments and be up to date with any new evidence regarding drug safety.

Recommendations for daily practice

A high level of acceptance and implementation of the recommendations in everyday practice can be realized only if recommendations do not overburden health-care providers. All initiatives to improve drug safety must focus on the safety culture and competency of the team. This requires multiple interventions and a dynamic adoption using team feedback. The following recommendations represent a pragmatic approach for implementation in a busy paediatric anaesthesia operating room service.

There are essential, basic rules and regulations that must be followed whenever drugs are used. A precise amount and concentration of any given drug is prescribed, prepared, and labelled with an ISO-normative label. Any additional safety measures must be correlated with the gravity of the threat of the individual situation. This primarily depends on the familiarity and frequency of the drug administered by a team known to each other and results in a familiarity for recurring situations. For example, it is sufficient for paediatric trained staff working with children in a paediatric anaesthetic department and knowing each other to name the drug and the dose intended. The administering person repeats the drug and the amount to be given. If the prescriber agrees, the drug can be given. This takes only seconds and incurs no costs but improves safety. However, even such a small intervention will be opposed by some members of staff. The authors' experience is to convince a few staff members initially to implement this change in order to convince others. This small but essential step before each drug administration reminds everyone of the importance of drug safety and, therefore, contributes to vigilance fundamental to any drug safety initiative.

Such a routinely performed short check for every drug administration makes it much easier to introduce a formal double-check at a later time. It is much more plausible, and staff members will thoroughly embrace this double-checking for high-risk medications.

A final important recommendation with significant impact on safety is to analyse all existing medications and their departmental storage (see 'Solutions to avoid confusions of drugs'). Which drugs have the highest potential to cause harm and can be stored separately in a meaningful manner? Which drugs can be confused most easily by name, concentrations, or additives? Every department should thoroughly analyse these aspects and

develop a clearly defined, optimized approach. This must be known by all staff members.

Complementing these three above minimal additional measures with regular teaching on drug safety issues and a CIRS system can achieve the most efficient, feasible, and important safety measures.

Authors' contributions

Concept of the manuscript and methods: all authors
Literature research and judgement: all authors
Writing paper: J.K., T.E.
Revising paper: all authors

Declaration of interest

J.K. holds a Europe-wide registered design patent for a device for length-dependent dose recommendation in paediatric emergencies (OHIM no. 002909382-001). This device is not mentioned within this review. He currently has no licensing arrangements and receives no royalties from this patent. A.R.W., K.B., M.L., F.W., and T.E.: none declared.

Funding

This review was funded by internal sources only.

References

1. Taylor JA, Loan LA, Kamara J, Blackburn S, Whitney D. Medication administration variances before and after implementation of computerized physician order entry in a neonatal intensive care unit. *Pediatrics* 2008; **121**: 123–8
2. Webster CS, Merry AF, Larsson L, McGrath KA, Weller J. The frequency and nature of drug administration error during anaesthesia. *Anaesth Intensive Care* 2001; **29**: 494–500
3. Nanji KC, Patel A, Shaikh S, Seger DL, Bates DW. Evaluation of perioperative medication errors and adverse drug events. *Anesthesiology* 2016; **124**: 25–34
4. Kaushal R, Bates DW, Landrigan C, *et al*. Medication errors and adverse drug events in pediatric inpatients. *JAMA* 2001; **285**: 2114–20
5. Kozer E, Scolnik D, Keays T, Shi K, Luk T, Koren G. Large errors in the dosing of medications for children. *N Engl J Med* 2002; **346**: 1175–6
6. Kozer E, Berkovitch M, Koren G. Medication errors in children. *Pediatr Clin North Am* 2006; **53**: 1155–68
7. Otero P, Leyton A, Mariani G, Ceriani Cernadas JM; Patient Safety Committee. Medication errors in pediatric inpatients: prevalence and results of a prevention program. *Pediatrics* 2008; **122**: e737–43
8. Perondi MB, Reis AG, Paiva EF, Nadkarni VM, Berg RA. A comparison of high-dose and standard-dose epinephrine in children with cardiac arrest. *N Engl J Med* 2004; **350**: 1722–30
9. Cooper L, Nossaman B. Medication errors in anesthesia: a review. *Int Anesthesiol Clin* 2013; **51**: 1–12
10. Kozer E, Seto W, Verjee Z, *et al*. Prospective observational study on the incidence of medication errors during simulated resuscitation in a paediatric emergency department. *Br Med J* 2004; **329**: 1321
11. Eichhorn JH. Medication safety in the operating room: time for a new paradigm. APSF Summit Conference Proceedings. *APSF Newslett* 2010; **25**: 1–20
12. Aspden P, Wolcott J, Bootman JL, Cronenwett LR. *Preventing Medication Errors: Quality Chasm Series*. Washington, DC: The National Academies Press, 2007
13. Stucky ER; American Academy of Pediatrics Committee on Drugs; American Academy of Pediatrics Committee on Hospital Care. Prevention of medication errors in the pediatric inpatient setting. *Pediatrics* 2003; **112**: 431–6
14. Australian and New Zealand College of Anaesthetists; Guidelines for the Safe Administration of Injectable Drugs in Anaesthesia (Policy Document PS 51). 2009. Available at http://www.anzca.edu.au/documents/ps51-2009-guidelines-for-the-safe-administration-o.pdf
15. Empfehlung zur Kennzeichnung von Spritzen in der Intensiv- und Notfallmedizin 2012. *Anaesth Intensivmed* 2012; **53**: 506–12
16. Beck G, Becke K, Biermann E *et al*. DGAI, BDA. Mindestanforderung an den anästhesiologischen Arbeitsplatz. *Anaesth Intensivmed* 2013; **54**: 39–42
17. American Society of Anesthesiologists. Statement on practice recommendations for pediatric anesthesia 2011. Available from http://www.asahq.org/~/media/sites/asahq/files/public/resources/standards-guidelines/statement-on-practice-recommendations-for-pediatric-anesthesia.pdf (accessed 15 December 2016)
18. American Society of Anesthesiologists. Statement on security of medications in the operating room 2013. Available from http://www.asahq.org/~/media/sites/asahq/files/public/resources/standards-guidelines/statement-of-security-of-medications-in-the-operating-room.pdf (accessed 15 December 2016)
19. American Society of Anesthesiologists. Statement on standard practice for avoidance of medication errors in neuroaxial anesthesia 2015. Available from http://www.asahq.org/~/media/sites/asahq/files/public/resources/standards-guidelines/statement-on-standard-practice-for-avoidance-of-medication-errors-in-neuraxial-anesthesia.pdf (accessed 15 December 2016)
20. American Soceity of Anesthesiologists. Statement on creating labels of pharmaceuticals for use in anesthesiology 2015. Available from http://www.asahq.org/~/media/sites/asahq/files/public/resources/standards-guidelines/statement-on-labeling-of-pharmaceuticals-for-use-in-anesthesiology.pdf (accessed 15 December 2016)
21. Whitaker D, Bratteb G, Trenkler S, *et al*. The European Board of Anaesthesiology recommendations for safe medication practice: first update. *Eur J Anaesthesiol* 2016; **34**: 4–7
22. National Patient Safety Agency. Design for patient safety—A guide to labelling and packaging of injectable medicines. Available from http://www.nrls.npsa.nhs.uk. NHS 2008: Reference Number 0592 (accessed 15 December 2016)
23. Australian Commission on Safety and Quality in Health Care. National Recommendations for User applied Labelling of injectable Medicine, Fluids and Lines 2010. Available from www.safetyandquality.gov.au (accessed 15 December 2016)
24. Council of Europe: Expert Group on Safe Medication Practices. Creation of a better medication safety culture in Europe: building up safe medication practices 2006. Available from www.edqm.eu (accessed 15 December 2016)
25. Institute for Safe Medication Practices (ISMP). Safe Practice Guidelines for Adult IV Push Medications 2015. Available from http://www.ismp.org (accessed 15 December 2016)
26. OCEBM Levels of Evidence Working Group. "The Oxford Levels of Evidence 2". Oxford Centre for Evidence-Based

Medicine. Available from http://www.cebm.net/index.aspx?o=5653 (accessed 15 December 2016)
27. Craig J, Wilson MEA. Survey of anaesthetic misadventures. *Anaesthesia* 1981; **36**: 933–6
28. Pham JC, Aswani MS, Rosen M, *et al*. Reducing medical errors and adverse events. *Annu Rev Med* 2012; **63**: 447–63
29. von Ungern-Sternberg BS, Boda K, Chambers NA, *et al*. Risk assessment for respiratory complications in paediatric anaesthesia: a prospective cohort study. *Lancet* 2010; **376**: 773–83
30. Honey BL, Bray WM, Gomez MR, Condren M. Frequency of prescribing errors by medical residents in various training programs. *J Patient Saf* 2015; **11**: 100–4
31. Kaufmann J, Laschat M, Wappler F. Medication errors in pediatric emergencies: a systematic analysis. *Dtsch Arztebl Int* 2012; **109**: 609–16
32. DGAI. Ärztliche Kernkompetenz und Delegation in der Anästhesie. Entschließung der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin e.V. und des Berufsverbandes Deutscher Anästhesisten e.V. *Anaesth Intensivmed* 2007; **48**: 712–4
33. Hackel A, Badgwell JM, Binding RR, *et al*. Guidelines for the pediatric perioperative anesthesia environment. American Academy of Pediatrics. Section on Anesthesiology. *Pediatrics* 1999; **103**: 512–5
34. Davey AL, Britland A, Naylor RJ. Decreasing paediatric prescribing errors in a district general hospital. *Qual Saf Health Care* 2008; **17**: 146–9
35. Campino A, Lopez-Herrera MC, Lopez-de-Heredia I, Valls-I-Soler A. Educational strategy to reduce medication errors in a neonatal intensive care unit. *Acta Paediatr* 2009; **98**: 782–5
36. Gordon M, Chandratilake M, Baker P. Improved junior paediatric prescribing skills after a short e-learning intervention: a randomised controlled trial. *Arch Dis Child* 2011; **96**: 1191–4
37. Stewart M, Purdy J, Kennedy N, Burns A. An interprofessional approach to improving paediatric medication safety. *BMC Med Educ* 2010; **10**: 19
38. Sherriff K, Burston S, Wallis M. Effectiveness of a computer based medication calculation education and testing programme for nurses. *Nurse Educ Today* 2012; **32**: 46–51
39. Kidd L, Shand E, Beavis R, Taylor Z, Dunstan F, Tuthill D. Prescribing competence of junior doctors: does it add up? *Arch Dis Child* 2010; **95**: 219–21
40. Mullett CJ, Evans RS, Christenson JC, Dean JM. Development and impact of a computerized pediatric antiinfective decision support program. *Pediatrics* 2001; **108**: E75
41. Sard BE, Walsh KE, Doros G, Hannon M, Moschetti W, Bauchner H. Retrospective evaluation of a computerized physician order entry adaptation to prevent prescribing errors in a pediatric emergency department. *Pediatrics* 2008; **122**: 782–7
42. Wong E, Taylor Z, Thompson J, Tuthill DA. simplified gentamicin dosing chart is quicker and more accurate for nurse verification than the BNFc. *Arch Dis Child* 2009; **94**: 542–5
43. Niemann D, Bertsche A, Meyrath D, *et al*. Drug handling in a paediatric intensive care unit – can errors be prevented by a three-step intervention? *Klin Padiatr* 2014; **226**: 62–7
44. Pramann O, Gärtner A, Albrecht U-V. Medical Apps: Mobile Helfer am Krankenbett. *Dtsch Arztebl* 2012; **109**: A-1201
45. Campino A, Lopez-Herrera MC, Lopez-de-Heredia I, Valls ISA. Medication errors in a neonatal intensive care unit. Influence of observation on the error rate. *Acta Paediatr* 2008; **97**: 1591–4
46. Costello JL, Torowicz DL, Yeh TS. Effects of a pharmacist-led pediatrics medication safety team on medication-error reporting. *Am J Health Syst Pharm* 2007; **64**: 1422–6
47. Neuspiel DR, Stubbs EH, Liggin L. Improving reporting of outpatient pediatric medical errors. *Pediatrics* 2011; **128**: e1608–13
48. Lépée C, Klaber RE, Benn J, *et al*. The use of a consultant-led ward round checklist to improve paediatric prescribing: an interrupted time series study. *Eur J Pediatr* 2012; **171**: 1239–45
49. Ligi I, Millet V, Sartor C, *et al*. Iatrogenic events in neonates: beneficial effects of prevention strategies and continuous monitoring. *Pediatrics* 2010; **126**: e1461–8
50. McClead RE Jr, Catt C, Davis JT, *et al*. An internal quality improvement collaborative significantly reduces hospital-wide medication error related adverse drug events. *J Pediatr* 2014; **165**: 1222–9.e1
51. Basco WT Jr, Ebeling M, Hulsey TC, Simpson K. Using pharmacy data to screen for look-alike, sound-alike substitution errors in pediatric prescriptions. *Acad Pediatr* 2010; **10**: 233–7
52. Merry AF, Anderson BJ. Medication errors – new approaches to prevention. *Paediatr Anaesth* 2011; **21**: 743–53
53. Merry AF, Shipp DH, Lowinger JS. The contribution of labelling to safe medication administration in anaesthetic practice. *Best Pract Res Clin Anaesthesiol* 2011; **25**: 145–59
54. Sybrecht GW, Prien T. Arzneimittelsicherheit: Standard-Spritzenaufkleber in der Akutmedizin. *Dtsch Arztebl* 2010; **107**: A-1031–2
55. Prien T. Farbige Kennzeichnung von Spritzen—Empfehlung der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin. *Anaesth Intensivmed* 2009; **50**: 333–4
56. Davis T. Paediatric prescribing errors. *Arch Dis Child* 2011; **96**: 489–91
57. Kozer E, Scolnik D, Macpherson A, *et al*. Variables associated with medication errors in pediatric emergency medicine. *Pediatrics* 2002; **110**: 737–42
58. Hicks RW, Becker SC, Krenzischeck D, Beyea SC. Medication errors in the PACU: a secondary analysis of MEDMARX findings. *J Perianesth Nurs* 2004; **19**: 18–28
59. Avidan A, Levin PD, Weissman C, Gozal Y. Anesthesiologists' ability in calculating weight-based concentrations for pediatric drug infusions: an observational study. *J Clin Anesth* 2014; **26**: 276–80
60. Krieser D, Nguyen K, Kerr D, Jolley D, Clooney M, Kelly AM. Parental weight estimation of their child's weight is more accurate than other weight estimation methods for determining children's weight in an emergency department? *Emerg Med J* 2007; **24**: 756–9
61. Greig A, Ryan J, Glucksman E. How good are doctors at estimating children's weight? *J Accid Emerg Med* 1997; **14**: 101–3
62. Young KD, Korotzer NC. Weight estimation methods in children: a systematic review. *Ann Emerg Med* 2016; **68**: 441–51.e10
63. Luten RC, Zaritsky A, Wears R, Broselow J. The use of the Broselow tape in pediatric resuscitation. *Acad Emerg Med* 2007; **14**: 500–1
64. Cordero L, Kuehn L, Kumar RR, Mekhjian HS. Impact of computerized physician order entry on clinical practice in a newborn intensive care unit. *J Perinatol* 2004; **24**: 88–93
65. Kirk RC, Li-Meng Goh D, Packia J, Min Kam H, Ong BK. Computer calculated dose in paediatric prescribing. *Drug Saf* 2005; **28**: 817–24

66. Luten R, Wears RL, Broselow J, Croskerry P, Joseph MM, Frush K. Managing the unique size-related issues of pediatric resuscitation: reducing cognitive load with resuscitation aids. *Acad Emerg Med* 2002; **9**: 840–7
67. Bernius M, Thibodeau B, Jones A, Clothier B, Witting M. Prevention of pediatric drug calculation errors by prehospital care providers. *Prehosp Emerg Care* 2008; **12**: 486–94
68. Kaji AH, Gausche-Hill M, Conrad H, *et al*. Emergency medical services system changes reduce pediatric epinephrine dosing errors in the prehospital setting. *Pediatrics* 2006; **118**: 1493–500
69. Shah AN, Frush K, Luo X, Wears RL. Effect of an intervention standardization system on pediatric dosing and equipment size determination: a crossover trial involving simulated resuscitation events. *Arch Pediatr Adolesc Med* 2003; **157**: 229–36
70. Campagne DD, Young M, Wheeler J, Stroh G. Pediatric tape: accuracy and medication delivery in the National Park Service. *West J Emerg Med* 2015; **16**: 665–70
71. King WJ, Paice N, Rangrej J, Forestell GJ, Swartz R. The effect of computerized physician order entry on medication errors and adverse drug events in pediatric inpatients. *Pediatrics* 2003; **112**: 506–9
72. Potts AL, Barr FE, Gregory DF, Wright L, Patel NR. Computerized physician order entry and medication errors in a pediatric critical care unit. *Pediatrics* 2004; **113**: 59–63
73. Kazemi A, Ellenius J, Pourasghar F, *et al*. The effect of Computerized Physician Order Entry and decision support system on medication errors in the neonatal ward: experiences from an Iranian teaching hospital. *J Med Syst* 2011; **35**: 25–37
74. Kadmon G, Bron-Harlev E, Nahum E, Schiller O, Haski G, Shonfeld T. Computerized order entry with limited decision support to prevent prescription errors in a PICU. *Pediatrics* 2009; **124**: 935–40
75. Caldwell NA, Power B. The pros and cons of electronic prescribing for children. *Arch Dis Child* 2012; **97**: 124–8
76. Pruitt CM, Liebelt EL. Enhancing patient safety in the pediatric emergency department: teams, communication, and lessons from crew resource management. *Pediatr Emerg Care* 2010; **26**: 942–8; quiz 949–51
77. Staender SE, Mahajan RP. Anesthesia and patient safety: have we reached our limits? *Curr Opin Anaesthesiol* 2011; **24**: 349–53
78. Calhoun AW, Boone MC, Porter MB, Miller KH. Using simulation to address hierarchy-related errors in medical practice. *Perm J* 2014; **18**: 14–20
79. Larose G, Bailey B, Lebel D. Quality of orders for medication in the resuscitation room of a pediatric emergency department. *Pediatr Emerg Care* 2008; **24**: 609–14
80. Kozer E, Scolnik D, MacPherson A, Rauchwerger D, Koren G. Using a preprinted order sheet to reduce prescription errors in a pediatric emergency department: a randomized, controlled trial. *Pediatrics* 2005; **116**: 1299–302
81. Broussard M, Bass PF 3rd, Arnold CL, McLarty JW, Bocchini JA Jr. Preprinted order sets as a safety intervention in pediatric sedation. *J Pediatr* 2009; **154**: 865–8
82. Walsh KE, Landrigan CP, Adams WG, *et al*. Effect of computer order entry on prevention of serious medication errors in hospitalized children. *Pediatrics* 2008; **121**: e421–7
83. Barata IA, Benjamin LS, Mace SE, Herman MI, Goldman RD. Pediatric patient safety in the prehospital/emergency department setting. *Pediatr Emerg Care* 2007; **23**: 412–8
84. Alsulami Z, Conroy S, Choonara I. Double checking the administration of medicines: what is the evidence? A systematic review. *Arch Dis Child* 2012; **97**: 833–7
85. Bittner EA, George E, Eikermann M, Schmidt U. Evaluation of the association between quality of handover and length of stay in the post anaesthesia care unit: a pilot study. *Anaesthesia* 2012; **67**: 548–9
86. Agarwal HS, Saville BR, Slayton JM, *et al*. Standardized postoperative handover process improves outcomes in the intensive care unit: a model for operational sustainability and improved team performance. *Crit Care Med* 2012; **40**: 2109–15
87. Brinkrolf P, Prien T, van Aken H. Medikationsfehler—Eine systematische Analyse der Berichte im CIRS-AINS. *Anaesth Intensivmed* 2013; **54**: 126–32
88. Adapa RM, Mani V, Murray LJ, *et al*. Errors during the preparation of drug infusions: a randomized controlled trial. *Br J Anaesth* 2012; **109**: 729–34
89. Moreira ME, Hernandez C, Stevens AD, *et al*. Color-coded prefilled medication syringes decrease time to delivery and dosing error in simulated emergency department pediatric resuscitations. *Ann Emerg Med* 2015; **66**: 97–106.e3
90. Stevens AD, Hernandez C, Jones S, *et al*. Color-coded prefilled medication syringes decrease time to delivery and dosing errors in simulated prehospital pediatric resuscitations: a randomized crossover trial. *Resuscitation* 2015; **96**: 85–91
91. Kaufmann J, Fischer JH, Roth B. Periodic catecholamine release by a femoral central venous line in an infant. *Paediatr Anaesth* 2005; **15**: 1020–2
92. Morriss FH Jr, Abramowitz PW, Nelson SP, *et al*. Effectiveness of a barcode medication administration system in reducing preventable adverse drug events in a neonatal intensive care unit: a prospective cohort study. *J Pediatr* 2009; **154**: 363–8, 368.e1
93. Larsen GY, Parker HB, Cash J, O'Connell M, Grant MC. Standard drug concentrations and smart-pump technology reduce continuous-medication-infusion errors in pediatric patients. *Pediatrics* 2005; **116**: e21–5
94. Leonard MS, Cimino M, Shaha S, McDougal S, Pilliod J, Brodsky L. Risk reduction for adverse drug events through sequential implementation of patient safety initiatives in a children's hospital. *Pediatrics* 2006; **118**: e1124–9
95. Condren M, Honey BL, Carter SM, *et al*. Influence of a systems-based approach to prescribing errors in a pediatric resident clinic. *Acad Pediatr* 2014; **14**: 485–90
96. Damhoff HN, Kuhn RJ, Baker-Justice SN. Medication preparation in pediatric emergencies: comparison of a web-based, standard-dose, bar code-enabled system and a traditional approach. *J Pediatr Pharmacol Ther* 2014; **19**: 174–81
97. Koren G. Trends of medication errors in hospitalized children. *J Clin Pharmacol* 2002; **42**: 707–10
98. Manias E, Kinney S, Cranswick N, Williams A, Borrott N. Interventions to reduce medication errors in pediatric intensive care. *Ann Pharmacother* 2014; **48**: 1313–31

Handling editor: Paul Myles