Interventions for reducing medication errors in children in hospital (Review)

Maaskant JM, Vermeulen H, Apampa B, Fernando B, Ghaleb MA, Neubert A, Thayyil S, Soe A

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[Intervention Review]

Interventions for reducing medication errors in children in hospital

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ABSTRACT

Background

Many hospitalised patients are affected by medication errors (MEs) that may cause discomfort, harm and even death. Children are at especially high risk of harm as the result of MEs because such errors are potentially more hazardous to them than to adults. Until now, interventions to reduce MEs have led to only limited improvements.

Objectives

To determine the effectiveness of interventions aimed at reducing MEs and related harm in hospitalised children.

Search methods

The Effective Practice and Organisation of Care Group (EPOC) Trials Search Co-ordinator searched the following sources for primary studies: *The Cochrane Library*, including the Cochrane Central Register of Controlled Trials (CENTRAL), the Economic Evaluation Database (EED) and the Health Technology Assessments (HTA) database; MEDLINE, EMBASE, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO, Proquest Dissertations & Theses, Web of Science (citation indexes and conference proceedings) and the EPOC Register of Studies. Related reviews were identified by searching the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects (DARE). Review authors searched grey literature sources and trial registries. They handsearched selected journals, contacted researchers in the field and scanned reference lists of relevant reviews. They conducted searches in November 2013 and November 2014. They applied neither language nor date limits.

Selection criteria

Randomised controlled trials, controlled before-after studies and interrupted time series investigating interventions to improve medication safety in hospitalised children (≤ 18 years). Participants were healthcare professionals authorised to prescribe, dispense or administer medications. Outcome measures included MEs, (potential) patient harm, resource utilisation and unintended consequences of the interventions.

Data collection and analysis

Two review authors independently selected studies, extracted data and assessed study quality using the EPOC data collection checklist. We evaluated the risk of bias of included studies and used the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach to assess the quality of the body of evidence. We described results narratively and presented them using GRADE tables.

Main results

We included seven studies describing five different interventions: participation of a clinical pharmacist in a clinical team (n = 2), introduction of a computerised physician order entry system (n = 2), implementation of a barcode medication administration system (n = 1), use of a structured prescribing form (n = 1) and implementation of a check and control checklist in combination with feedback (n = 1).

Clinical and methodological heterogeneity between studies precluded meta-analyses. Although some interventions described in this review show a decrease in MEs, the results are not consistent, and none of the studies resulted in a significant reduction in patient harm. Based on the GRADE approach, the overall quality and strengfh of the evidence are low.

Authors' conclusions

Current evidence on effective interventions to prevent MEs in a paediatric population in hospital is limited. Comparative studies with robust study designs are needed to investigate interventions including components that focus on specific paediatric safety issues.

PLAIN LANGUAGE SUMMARY

Interventions for reducing medication errors in children in hospital

Medication safety is important for hospitalised children, as they are at risk of experiencing unintended harm as a result of medication errors. Hospitals implement various interventions to reduce medication errors. This review examines the effectiveness of these interventions. We included seven studies describing five different interventions. The clinical pharmacist, the computerised prescribing system and the barcode medication administration system are interventions at the organisational level. The check and control checklist and a preprinted order sheet are categorised as professional interventions.

The introduction of a clinical pharmacist resulted in a significant decrease in serious medication errors in an intensive care setting, but these results were not seen on a medical and surgical ward. Also introduction of a computerised prescribing system and a check and control checklist did not result in conclusive results. The introduction of a barcode medication administration system and a preprinted order sheet resulted in a significant decrease in medication errors, but the benefits for paediatric patients in terms of less harm remain unclear.

Despite extensive searching, we identified only seven studies for inclusion. Our assessment of the quality and strength of evidence from these studies is low. This review shows that only a handful of medication safety strategies are studied in robust study designs. When the vulnerability of paediatric patients in hospital is considered, more research of high quality should be included on every research agenda.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Outcomes	Comparison		Effect size (95% CI) or P value	Sample (studies)	GRADE	Comments
Clinical pharmacist vs no clinical pharmacist						
	Pre-intervention	**Post-intervention**				
Serious MEs (ICU)	Intervention wards: 29[a]	Intervention wards: 6[a]	P value <0.01	2967[b] (1 study)	Low	Kaushal 2008; CBA
	Control wards: 20[a]	Control wards: 30[a]				
Serious MEs (medical ward)	Intervention wards: 8[a]	Intervention wards: 9[a]	P value 0.78	3746[b] (1 study)		
	Control wards: 7[a]	Control wards: 8[a]				
Serious MEs (surgical ward)	Intervention wards: 7[a]	Intervention wards: 9[a]	P value 0.89	3672[b] (1 study)		
	Control wards: 8[a]	Control wards: 10[a]				
	Control	**Intervention**				
Length of stay in days (mean and SD)	9.06 (SD ± 5.47)	7.33 (SD ± 3.52)	-1.73 (-3.31 to -0.25) P value 0.02	150[c] (1 study)	Low	Zhang 2012; RCT
Costs of drugs[d] ($: number of participants)	<120: 35 120-360: 26 360-600: 4 > 600: 9	<120: 36 120-360: 24 360-600: 10 > 600: 6	P value 0.945	150[c] (1 study)		

Costs of hospitalisation ($: number of participants)	<240: 15 240-480: 25 480-720: 10 > 720: 24	<240: 18 240-480: 33 480-720: 10 > 720: 15	P value 0.125	150[c] (1 study)			

[a]Per 1000 admission days.
[b]Total number of admission days on intervention and control wards in the pre-intervention and post-intervention periods
[c]Total number of included participants.
[d]American dollars, 1 February 2011: currency exchange rate 1000 Chinese yuan = 120 American dollars

CPOE vs no CPOE

	Pre-intervention	**Post-intervention**					
Non-intercepted serious MEs	23.1[a]	20.6[a]	Change in level: -7%; P value 0.0495 Change in slope: not significant	3234[b] (1 study)	Low	Walsh 2008; ITS	
Preventable ADEs (harm)	7.9[a]	6.5[a]	Change in level: not significant Change in slope: not significant	3234[b] (1 study)			
MEs	Intervention wards: 173; 4.48[a]	Intervention wards: 120; 3.13[a]	Ratio of rate ratios: 1.54 (1.27 to 1.88); P value <0.001	179,183[b] (1 study)	Very low	King 2003; CBA Significant *increase* in potentially harmful ADEs	
	Control wards: 243; 4.80[a]	Control wards: 268; 5.19[a]					
Harmful ADEs	Intervention wards: 6	Intervention wards: 1	Ratio of rate ratios: 1.30 (0.47 to 3.52); P value 0.6	179,183[b] (1 study)			
	Control wards: 9	Control wards: 2					

Potentially harmful ADEs	Intervention wards: 5	Intervention wards: 6	Ratio of rate ratios: 0.24 (0.09 to 0.68); P value <0.001	179,183[b] (1 study)			
	Control wards: 10	Control wards: 3					

[a]Per 1000 admission days.
[b]Admission days on intervention and control wards in the pre-intervention and post-intervention periods

BCMA vs no BCMA

	Pre-intervention	**Post-intervention**					
Targeted preventable ADEs	Intervention beds: 0.86[a]	Intervention beds: 0.43[a]	Unadjusted analysis: P value 0.008 Adjusted RR: 0.53 (0.29 to 0.98); P value 0.044	12,248[b] (1 study)	Low	Morriss 2009; CBA Significant *increase* in MEs	
	Control beds: not reported	Control beds: not reported					
Potential ADEs	Intervention beds: 15.1[a]	Intervention beds: 4.4[a]	Unadjusted analysis: P value <0.001	12,248[b] (1 study)			
	Control beds: not reported	Control beds: not reported					
MEs	Intervention beds: 69.5[a]	Intervention beds: 79.7[a]	Unadjusted analysis: P value <0.001	12,248[b] (1 study			
	Control beds: not reported	Control beds: not reported					

[a]Per 1000 medication doses.
[b]Subject-days on intervention and control wards in the pre-intervention and post-intervention periods

Check and correct checklist vs no check and correct checklist

	Pre-intervention	**Post-intervention**					

Technical prescribing MEs	107.70[a]	73.08[a]	Change in level: -5.02 (-7.09 to -2.95) ; P value <0.0001 Change in slope: -0.21 (-0.41 to - 0.01) ; P value 0.039	30,105[b] (1 study)	Low	Lepee 2012; ITS	
Clinical prescribing MEs	47.18[c]	55.33[c]	Change in level: not significant Change in slope: not significant	1163[d] (1 study)			

[a]Per 1000 opportunities for error.
[b]Opportunities for error on the intervention wards in the pre-intervention and post-intervention periods
[c]Per 1000 medication orders.
[d]Number of medication orders in the pre-intervention and post-intervention periods

Preprinted medication order sheet vs no preprinted medication order sheet

	Control	Intervention					
MEs	68	37	Adjusted OR 0.55 (0.34 to 0.90)	376[a] (1 study)	Low	Kozer 2005; RCT	
Potentially harmful MEs	36	14	Adjusted OR 0.39 (0.21 to 0.77)	411[a] (1 study)			

[a]Prescriptions.

GRADE Working Group grades of evidence.
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

BACKGROUND

An adverse drug event (ADE) is an unwanted occurrence after exposure to a drug that is not necessarily caused by the drug itself (WHO 2009). Adverse drug events include adverse drug reactions (ADRs) and medication errors (MEs). An ADR is defined as any response to a drug that is noxious and unintended and that occurs at doses normally used for prevention, diagnosis or therapy of a disease (WHO 2009). Adverse drug reactions may result from an exaggerated response to a drug (e.g. bronchospasm with beta blockers) or from an idiosyncratic reaction to a drug (e.g. penicillin allergy) (Oren 2003). No uniform definition of an ME is currently being used, despite efforts to develop an international definition (Lisby 2012; Miller 2007; Yu 2005), but most studies use the definition of the US National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) (Lisby 2010). The NCC MERP defines an ME as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient or consumer" (NCC MERP).

Medication errors are one of the most frequent causes of adverse events in hospitalised patients (Tam 2005; Vries de 2008). The Institute of Medicine estimates that, on average, hospitalised patients are subject to at least one ME per day (Aspden 2007). Although human error is often the immediate cause of MEs, most errors are due to system failures precipitated by the increasing complexity of patient care (Davidhizar 2002; Stucky 2003). In fact, ADEs can be described as an emergent property of a particularly complex healthcare system such as a hospital or a paediatric ward within a hospital (Tam 2005). A systematic review of the incidence and nature of MEs in paediatric patients shows a wide distribution in results (Ghaleb 2006). These results might be explained by variation in definitions, choice of denominator, study population or study design and the error detection method used (Franklin 2005; Garfield 2013; Lisby 2010; Meyer-Massetti 2011; Morimoto 2004). Despite variability in the incidence of MEs, children still are considered to be at higher risk of experiencing an ADE. Kaushal et al found that the frequency of potentially harmful MEs was three times higher in paediatric patients than in adults (Kaushal 2001). Pharmacological factors such as age-based variability in absorption, metabolism and excretion of drugs pose special vulnerabilities to the risk of overdosing among children as compared with adults. Dosage calculations in children are much more prone to human error because of the constant need for weight- and surface area-based dosing and unit conversion to reflect the very small doses required (Santell 2003). Therefore, types of paediatric MEs and the interventions necessary to prevent them are different from those involving adults.

In a primary care setting, the processes involved in medication use can be quite different from those seen in a hospital setting. For example, prescribing in primary care may involve diverse personnel operating from different sites with differing accountabilities. This review, therefore, examined MEs in children in a hospital setting only.

OBJECTIVES

To determine the effectiveness of interventions aimed at reducing MEs and related harm in hospitalised children.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs), controlled clinical trials (CCTs), controlled before-after studies (CBAs) and interrupted time series studies (ITSs).

We used the definitions in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins Cochrane Handbook 2011).

Randomised controlled trial (RCT)

A study in which "the author(s) state explicitly (usually by some variant of the term 'random' to describe the allocation procedure used) that the groups compared in the trial were established by random allocation" (Box 6.3.a).

Controlled clinical trial (CCT)

A study in which the intervention's assignment is quasi-random (e.g. when assignment is based on date of birth or medical record number) or a trial that "does not state explicitly that the trial was randomized, but randomization cannot be ruled out" (Box 6.3.a).

Controlled before-after study (CBA)

"A study in which observations are made before and after the implementation of an intervention, both in a group that receives the intervention and in a control group that does not" (Box 13.1.a).

Interrupted time series study (ITS)

"A study that uses observations at multiple time points before and after an intervention (the interruption). The design attempts to detect whether the intervention has had an effect significantly greater than any underlying trend over time" (Box 13.1.a).

We included CBA studies only if they involved contemporaneous data collection, appropriate choice of control site and a minimum of two intervention and two control sites (EPOC 2002). Interrupted time series studies were included only when they described

a clearly defined point in time when the intervention occurred and presented at least three data points before and three data points after the intervention (EPOC 2002). We included unpublished studies, and we imposed no limitations on language or date of publication.

Types of participants

Healthcare professionals

We included studies of healthcare professionals who are authorised to prescribe, dispense or administer medications, and who are involved in the provision of hospital care to children (≤ 18 years). We excluded studies reporting misuse of medication by participants (e.g. suicide with use of medication, compliance issues).

Setting

Studies based in all settings that provide clinical care to children in hospital: inpatient care (in secondary or tertiary units, intensive care units, operation theatres), outpatient care and accident and emergency department care.

Types of interventions

We included interventions applied in hospital care to improve patient safety in terms of MEs. Studies might describe one intervention or a package of interventions that we refer to as multifaceted. We did not include interventions designed solely to change the volume of prescribing (e.g. reducing vancomycin dosage in neonatal units, increasing surfactant dosage in neonatal respiratory distress syndrome). We categorised interventions according to the Cochrane Effective Practice and Organisation of Care Group (EPOC) taxonomy of interventions: professional, financial, organisational or regulatory interventions (EPOC 2002).

Types of outcome measures

Primary outcome measures

- Occurence of MEs as proportions of participants, admission days, prescriptions and administrations.
- Occurrence of (potentially) harmful MEs as proportions of participants, admission days, prescriptions and administrations, defined as categories E t/m I (NCC MERP). MEs can cause serious harm and are potentially lethal (Cousins 2002; Kale 2012). Reduction in (potential) harm is therefore also an important outcome measure for this review.

Secondary outcome measures

- Resource utilisation (costs and length of stay in hospital). Medication errors are associated with extended length of admission and higher associated costs (Hug 2012; Samp 2014; Weingart 2000). We therefore reviewed resource utilisation in terms of length of stay in hospital and costs.
- Unintended consequences of the intervention. It is possible that whilst overall MEs may be reduced by the use of various technological interventions, especially with computerised ordering, serious adverse effects may not be reduced and could even be increased by elimination of the human barrier. Therefore, these outcomes were examined separately.

Comparison groups were given any other intervention, no intervention or usual care. Because different definitions were used to describe MEs, we explicitly cite the definitions used in the studies included in this review.

Search methods for identification of studies

Michelle Fiander, Trials Search Co-ordinator (TSC) for the EPOC Group, developed search strategies in consultation with the review authors. The TSC searched the Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects (DARE) for related systematic reviews, and the databases listed below for primary studies. Searches were conducted in November 2013, and an update of searches in the main databases was conducted in November 2014; exact search dates for each database are included with the search strategies (Appendix 1; Appendix 2; Appendix 3; Appendix 4; Appendix 5; Appendix 6; Appendix 7; Appendix 8). Two methodological search filters were used to limit retrieval to appropriate study designs: the Cochrane Highly Sensitive Search Strategy (sensitivity- and precision-maximising version, 2008 revision) to identify randomised trials, and an EPOC methodology filter to identify non-RCT designs. Neither date nor language restrictions were used. Duplicates were removed from the databases electronically.

Databases

- Evidence-Based Medicine (EBM) Reviews, Cochrane Central Register of Controlled Trials (November 2014), Ovid SP.
- Cochrane Central Register of Controlled Trials (CENTRAL) (2014, Issue 11), Wiley.
- EBM Reviews, Health Technology Assessment (3rd Quarter 2014), Ovid SP.
- EBM Reviews, National Health Service (NHS) Economic Evaluation Database (3rd Quarter 2014), Ovid SP.
- MEDLINE (1947-), In-Process and other non-indexed citations (1946-2014), Ovid SP.
- MEDLINE Daily Update (November 2014), Ovid SP.
- EMBASE (1947 -2014), Ovid SP.

- CINAHL (Cumulative Index to Nursing and Allied Health Literature) (1980-), EbscoHost.
- EPOC Group, Specialised Register.
- ProQuest Dissertations & Theses Full Text.
- ProQuest Nursing & Allied Health database.
- PsycInfo (1806-), Ovid SP.
- Conference Proceedings Citation Index-Science (CPCI-S) (1990-2014), Web of Science.
- Conference Proceedings Citation Index-Social Science & Humanities (CPCI-SSH) (1990-2014), Web of Science.

Searching other resources

Grey literature

We conducted a grey literature search to identify studies not indexed in the databases listed above. Sources included the sites listed below.

- Agency for Healthcare Research and Quality (AHRQ) at www.ahrq.gov/.
- Grey Literature Report (New York Academy of Medicine) at http://greylit.org/.
- Joanna Briggs Institute at http://www.joannabriggs.edu.au/Search.aspx.
- National Institute for Health and Clinical Excellence (NICE) at www.nice.org.uk/.
- National Research Register (NRR) Archive (up to 2007) at http://www.nihr.ac.uk/Pages/NRRArchive.aspx.
- Open Grey at http://www.opengrey.eu/.

Trial registries

We searched the following registries.

- ClinicalTrials.gov, US National Institutes of Health (NIH), at http://clinicaltrials.gov/.
- International Clinical Trials Registry Platform (ICTRP), World Health Organization (WHO), at http://www.who.int/ictrp/en/.

We also:

- handsearched reference lists of all included studies, relevant systematic reviews and other relevant publications; and
- contacted authors of relevant studies or reviews to clarify reported published information and to seek unpublished data.

We present details of these searches in Appendix 9.

Data collection and analysis

Screening

Two review authors (JM and HV) independently screened the search results at three levels: titles, abstracts to assess which studies satisfied the inclusion criteria and full-text copies of papers that were potentially relevant. If we could not assess the paper for relevance based on title or abstract, we obtained the full text. JM and HV also examined grey literature and trial registries independently. We resolved discrepancies in the process of screening by discussion or referred to the arbitrator (AS). Data from research published in duplicate were included only once.

Data abstraction

Two review authors (JM and HV) working independently extracted data from each article using the EPOC data collection checklist (EPOC 2002). We resolved discrepancies by discussion or referred to the arbitrator (AS). We contacted investigators for missing data.

Quality

Assessment of risk of bias in included studies

Quality assessment for included studies was supported by suggested risk of bias criteria for EPOC reviews (EPOC 2014). For included RCTs and CBAs, we used the following criteria: allocation sequence, concealment of allocation, similar baseline outcome measurements, similar baseline characteristics, completeness of outcome data, blinding, protection against contamination, freedom from selective outcome reporting and anything else that might underestimate or overestimate the results. For ITS studies, we used the following criteria: protection against secular changes, prespecification of the shape of the intervention, data collection independent of the intervention, blinding, completeness of the dataset, freedom from selective outcome reporting and any other factors that might have underestimated or overestimated the results (e.g. an explicit rationale for the number and spacing of data points, appropriate time-series analysis) (Ramsay 2003).

For all included studies, we explicitly evaluated the reliability of outcomes. Obtaining reliable outcome measure(s) for medication errors is dependent on the method used. Full review of participant files is considered more sensitive than, for example, voluntary incident reports (Meyer-Massetti 2011; Morimoto 2004). In the literature, a multi-faceted approach is recommended (Olsen 2007). In the included studies, we found full review of participant records, voluntary incident reports and a combination. This might have influenced the study findings. A different way to assess the reliability of the outcome is the inter-rater reliability expressed in kappa's. EPOC defines a threshold of 0.80. In this systematic review, we combined these two elements. When a study reported full review of participant records or a combination of full review and voluntary incident reports, plus a kappa > 0.80, we considered this study as having low risk of bias for this criterion. When a

study reported full review of participant records or a combination of full review and voluntary incident reports, plus a kappa ≤ 0.80, we considered this criterion as showing high risk of bias. When a study used only voluntary incident reports to assess outcome measures, we considered this study always as having high risk of bias for this criterion.

Two review authors (JM and HV) assessed risk of bias independently and resolved discrepancies by discussion. An arbitrator (AS) was available for consultation in the case of persistent disagreement.

Assessment of reporting bias

A thorough search of the grey literature and contact with known experts in the field reduced the influence of publication bias on our review.

Reporting

We tabulated data in natural units for each study. We report (pre-intervention and post-intervention) means or proportions when results were available for both intervention and control groups from RCTs and CBAs. We calculated the absolute change from baseline with the 95% confidence limit. For ITS studies, we report the main outcomes in natural units with two indicators of effects of the intervention: change in the level of outcome immediately after the intervention, and change in the slope of the regression lines.

Analytical approach

Primary analyses

We based the primary analyses on consideration of outcome measures. When studies reported more than one measure for each endpoint, we extracted the outcome measures meeting the aims of our review. We present the results for all comparisons using a standard method of presentation, when possible. For comparisons of RCTs and CBAs, we planned to report for each study design the median, the interquartile range and/or the range of effect sizes across included studies. However, the studies were heterogeneous in terms of methods of analysis used. Therefore, we present the results as presented by study authors. We contacted the first study author for clarification or additional information, when necessary.

Secondary analyses

We planned secondary analyses to explore the consistency of the primary analyses with other types of endpoints. We planned to standardise effect sizes for continuous measures by dividing the difference in mean scores between intervention and control groups in each study through an estimate of the (pooled) standard deviation. However, this was never appropriate in the included studies.

Methods for reanalysis

We aimed to present the results in a comparable way and therefore reanalysed included RCTs and CBAs, when possible, by recalculating results using the appropriate unit of analysis. We contacted the authors of such studies for clarification, when necessary. We reported heterogeneity of included studies in terms of settings, interventions, outcome assessments and outcome measures. We considered statistical meta-analysis only for studies that were similar in these terms. We examined data from ITS studies with unit of analysis errors according to EPOC guidelines.

Summary of findings

We used the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach (Guyatt 2008; Schunemann 2011) to assess the quality of the body of evidence for outcomes, to interpret results and to draw conclusions about the effects (benefits, potential harms and costs) of different interventions, including size of effect and quality of the evidence for outcomes for which evidence was found. We present evidence summaries for the main comparisons of the review in a 'Summary of findings' table.

Ongoing studies

We describe ongoing studies, detailing the primary author, research question(s), methods and outcome measures, and provide an estimate of the reporting date.

RESULTS

Description of studies

Results of the search

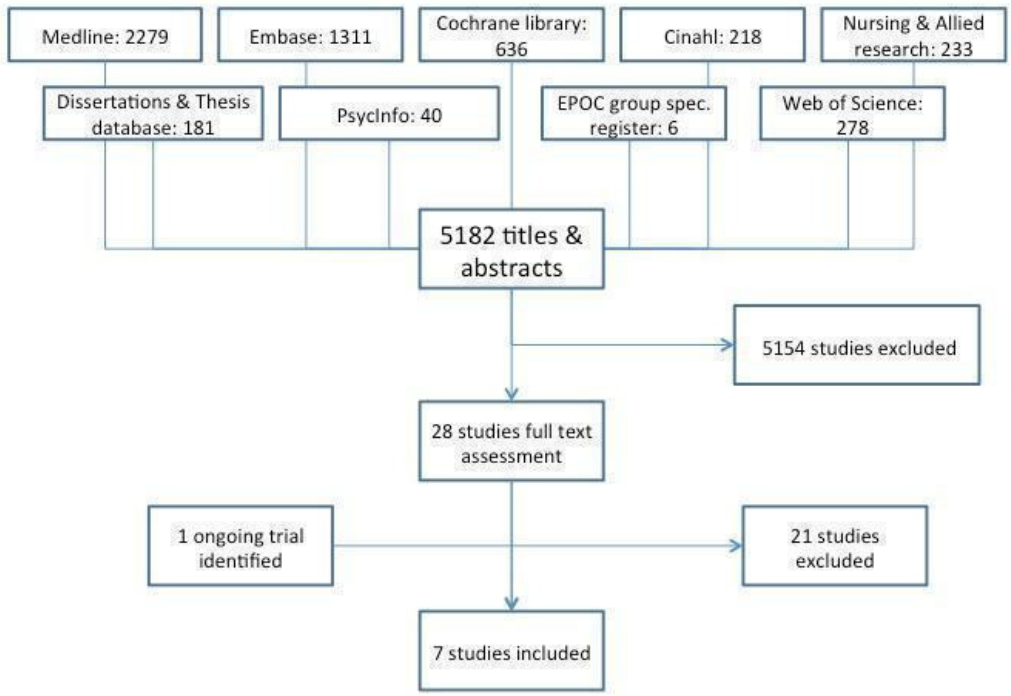
Searches of the main electronic databases led to identification of 5182 titles. After independent examination of titles and abstracts by JM and HV, 90 titles and abstracts were left for further discussion. We decided on 28 articles potentially eligible for the review, given the predefined inclusion criteria. We excluded 18 studies after full-text assessment and found that seven studies met the inclusion criteria of the review and of the Cochrane EPOC group. We contacted the authors of three remaining studies for additional information, resulting in exclusion of all three studies. The full-text studies that were excluded are listed in the Characteristics of excluded studies table.

Handsearching of the references listed in the seven included studies, as well as of systematic reviews, reviews and overviews that we found in searches of the main electronic databases, did not

yield new studies. A search of the grey literature and of trials registries also did not yield new articles, but we included one ongoing study that is potentially eligible for the review in the future (Characteristics of ongoing studies).

We present search strategies for the main databases in Appendix 1. We describe search strategies for the grey literature and for trial registries in Appendix 9. We provide an overview of the selection process in Figure 1.

Figure 1. Study selection process.



Included studies

See Characteristics of included studies.

Methods (design)

We included in this review two RCTs (Kozer 2005; Zhang 2012), two ITS studies (Lepee 2012; Walsh 2008) and three CBAs (Kaushal 2008; King 2003; Morriss 2009).

Participants

All seven included studies were executed in hospitals affiliated with a university or medical school. Five studies included patients admitted to paediatric medical wards (Kaushal 2008; King 2003; Lepee 2012; Walsh 2008; Zhang 2012). One study was executed on paediatric wards and on a paediatric intensive care unit (Kaushal 2008), and another study included paediatric wards, a paediatric intensive care unit and a neonatal intensive care unit (Walsh 2008).

One study was performed on a neonatal intensive care unit only (Morriss 2009), and another study was executed in a paediatric emergency department (Kozer 2005).
Two studies originated from Canada (King 2003; Kozer 2005), three from the United States of America (Kaushal 2008; Morriss 2009; Walsh 2008), one from the United Kingdom (Lepee 2012) and one from China (Zhang 2012).

Interventions

Investigators studied interventions for reducing MEs. Kaushal 2008 and Zhang 2012 studied the effects of including a pharmacist as part of the clinical team. Two studies examined the effects of computerised physician order entry (CPOE) (King 2003; Walsh 2008). One study described the introduction of a barcode medication administration system (BCMA) (Morriss 2009). Lepee 2012 investigated the introduction of a professionally oriented check and control checklist, and Kozer 2005 examined the use of a preprinted order sheet. None of the included studies reported subgroup analyses, neither planned nor post hoc. According to the EPOC taxonomy of interventions (EPOC 2002), the included studies describe professional and organisational interventions. We categorise the check and control checklist and the preprinted order sheet as professional interventions. The clinical pharmacist, CPOE and BCMA are categorised as organisational interventions.

Description of included studies

Clinical pharmacists or unit-based pharmacists were described in a CBA study (Kaushal 2008) and in an RCT (Zhang 2012).
The CBA by Kaushal 2008 was conducted on six units: two general medical units, two surgical units, a paediatric intensive care unit (PICU) and a cardiac intensive care unit (ICU). One of the medical units and one of the surgical units were randomly selected as intervention units, and the others served as controls. The PICU was randomly selected as the intervention unit; the cardiac ICU served as its control. All patients admitted during the study period were included in the study. Demographic characteristics are described in detail. On the intervention units, a pharmacist was added to the team, who provided physicians with timely information and advice, assisted nurses with preparation and provided information on administration and monitoring. In addition, the pharmacist monitored the order transcription process, medication preparation and the storage and distribution system. Serious MEs were chosen as the primary outcome. Data on serious MEs were collected upon review of all clinical data (medication orders, medication administration records and patient charts) and incident reports during six to eight weeks pre-intervention and during a 12-week post-intervention period. A research nurse collected the data. Two physicians rated adverse events on preventability (five categories), severity (four categories) and causality (algorithm of Naranjo). Medication errors were defined as errors in drug ordering, transcribing, dispensing, administering or monitoring. Serious MEs were defined as preventable injuries that resulted from the use of drugs, or non-intercepted near misses. Non-intercepted near misses were defined as MEs with significant potential for injuring patients; they did not cause harm, although they reached the participants.
Zhang 2012 investigated the effects on medication safety of including a clinical pharmacist in an RCT. During a four-month period, paediatric patients with nervous system or respiratory or digestive system diseases were randomly allocated to two groups. In both groups, most patients (70% and 69%) were younger than five years of age. In the intervention group, a clinical pharmacist made rounds together with doctors in charge and provided interventions, which included an assessment of participants' medication, diagnosis and drug treatment. The clinical pharmacist also advised physicians and nurses, monitored MEs and instructed participants. For participants in the control group, the existing medical model was continued, meaning that pharmacists were excluded from the medication process on the ward. Interventions provided by clinical pharmacists, adverse drug reactions (side effects), length of stay and costs of drugs and hospitalisation were chosen as primary outcome measures. For this review, only length of stay and costs were outcomes of interest. This study provided limited information on the data collection process. Length of stay was defined as the number of days from admission to discharge, and costs were defined as total charges for Western and Chinese traditional medicines.
Walsh 2008 evaluated the effects of CPOE on rate of MEs, using an ITS study design. Computerised physician order entry was implemented on the PICU, the NICU and surgical and paediatric medical wards; a paediatric weight-based dosage calculator and medication dosages checks were provided; wrong-dosage alerts, drug-drug interaction alerts and allergy alerts were generated. The primary outcome was the rate of non-intercepted serious MEs. Data on these serious MEs were collected upon review of inpatient records and incident reports over seven months before and nine months after implementation of the CPOE. A random sample of 40 participants per month was selected from all admissions. The median age of participants in the study was four years. Paediatricians made judgements about the preventability (five categories) and severity of MEs (four categories). Between the before and after measurements, six months was used for CPOE system implementation and instruction of professionals. Medication errors were defined as errors in drug ordering, transcribing, dispensing, administering or monitoring. Non-intercepted serious MEs were defined as MEs that caused harm or had substantial potential to cause harm and were not caught by hospital staff before reaching the patient. Preventable ADEs were defined as harm resulting from MEs.
King 2003 reported the effects of CPOE on the number of MEs in a CBA. The intervention group consisted of all patients admitted to two medical paediatric wards on which the CPOE was imple-

mented. The control group consisted of all patients admitted to one medical paediatric and two surgical paediatric wards that continued to use handwritten orders. The average age of study participants was 6.3 years. The CPOE system interfaced with the laboratory system but not with the pharmacy computer and had no clinical decision support. Primary outcomes were MEs and ADEs. Medication errors were defined as any events involving medication prescription, dispensing, administration or monitoring, irrespective of outcome. Adverse drug events were defined as MEs resulting in harm to the participant, and potential ADEs were defined as MEs with the potential for participant injury when no actual harm occurred. Potential ADEs were reported as a secondary outcome. Two physicians accessed the ME database and retrospectively reviewed all incident reports from three years before and three years after implementation of the CPOE. They classified the incidents into ADEs, potential ADEs and others. Data were not collected during the nine-month implementation period.

The CBA by Morriss 2009 investigated the effects of a BCMA on MEs in an NICU. The BCMA supported the process of drug administration by verifying the drug, dose, route, time and frequency and participant identification after scanning the barcode on the participant's wristband and the unit-dose medication. During the first 19 weeks of the study, none of the beds were equipped with a BCMA system. During a second period of 12 weeks, half of randomly chosen beds on two similar units were equipped (two intervention groups), with the other half acting as controls (two control groups). In the last period of the study, lasting 19 weeks, all beds were equipped with the BCMA system. All patients admitted during the study periods were participants. The gestational age of participants was 34.5 (standard deviation (SD) 4.8) weeks. Primary outcomes were targeted preventable ADEs. Effects on MEs and potential ADEs were also reported. Medication errors were defined as errors in drug ordering, transcribing, dispensing, administering or monitoring. A preventable ADE was defined as harm to a participant resulting from an ME. A potential ADE was defined as an ME that could have harmed a participant but did not because it was intercepted, or because the participant did not experience harm. Targeted preventable ADEs were defined as MEs that were expected to be prevented by the BCMA system. Data were collected from medical records and incident reports by two paediatric nurse practitioners. A team that consisted of a neonatologist, two pharmacists and a paediatric clinical pharmacist made final judgements about the preventability and severity of MEs using the classification of the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP). Data were not collected during a four-week implementation period.

Lepee 2012 assessed the effects of a check and control checklist on prescriptions for patients admitted on two paediatric wards, using an ITS study design. This checklist was used in the presence of the patient, during ward rounds. A member of the team reviewed the prescription chart using the check and control checklist and gave immediate feedback on any shortfalls to the other members of the team. Corrections and short teaching comments were made before the end of the round. The study does not report on participant characteristics. The primary outcome was the rate of technical prescribing errors. In addition, data on clinical prescribing errors were collected (secondary outcomes). A technical prescribing error was defined as unclear or missing information on the prescription. A clinical prescribing error was defined as an unintentional significant reduction in the probability that a treatment would be timely and effective, or an increase in risk of harm, when compared with more generally accepted practice, as a result of a prescribing decision or a prescription writing process. To identify technical errors, a student pharmacist screened all inpatient drug charts during two months before and two months after implementation of the checklist. The ward pharmacist identified clinical errors. No data were collected during a one-week implementation period. The quality of documentation in the medical notes was assessed concurrently and acted as a control measurement.

The objective of the RCT conducted by Kozer 2005 was to assess the effects of a structured, pre-printed medication order sheet on prescriptions for paediatric patients visiting an emergency department. The study does not report on participant characteristics. During a one-month period, days were randomly allocated to the intervention group or to the control group. During intervention days, a structured, pre-printed medication order sheet was used for all visiting patients. On control days, the regular blank order sheet was used. Endpoints included the numbers of medication prescribing errors and potentially harmful MEs. Medication errors were defined as a drug regimen different from that recommended (dose difference $\geq$ 20%, deviation $\geq$ 2 hours from the recommended interval between doses and wrong unit or route of administration). Potentially harmful MEs were defined as MEs that could have caused significant or severe harm to participants. To identify these errors, two medical students reviewed all participant charts. After data collection, two paediatric emergency physicians reviewed the database and decided on the severity of the error, using three categories.

Excluded studies

See Characteristics of excluded studies.

We excluded 21 studies that did not meet the inclusion criteria. Ten studies were executed in non-clinical test situations (Balaguer Santamaria 2001; Burgess 2009; Frush 2004; Frush 2006; Hixson 2009; Hohenhaus 2008; Vaidya 2006; Yamamoto 2010; Yin 2008; Yin 2011). We excluded three studies because they investigated MEs in home situations (Frush 2004; Yin 2008; Yin 2011). One study did not specifically aim to prevent MEs (Cunningham 2008). We excluded six studies because they turned out to be CBAs without the required number of intervention or control groups (Burmester 2008; Dehghan-Nayeri 2013; Gazarian 2012; Nguyen 2014; Niemann 2014; Niemann, Bertsche 2014). We excluded three studies because no data on hospitalised children were pre-

sented (Ching 2014; Elsaid 2013; Ramsay 2014). One study was published only in abstract form (Senner 2010).

Risk of bias in included studies

See Characteristics of included studies.

Quality assessment

We report the methodological quality of the included studies in narrative format and in risk of bias summaries and graphs (Figure 2; Figure 3; Figure 4; Figure 5).

Figure 2. Risk of bias graph: RCT and CBA designs.

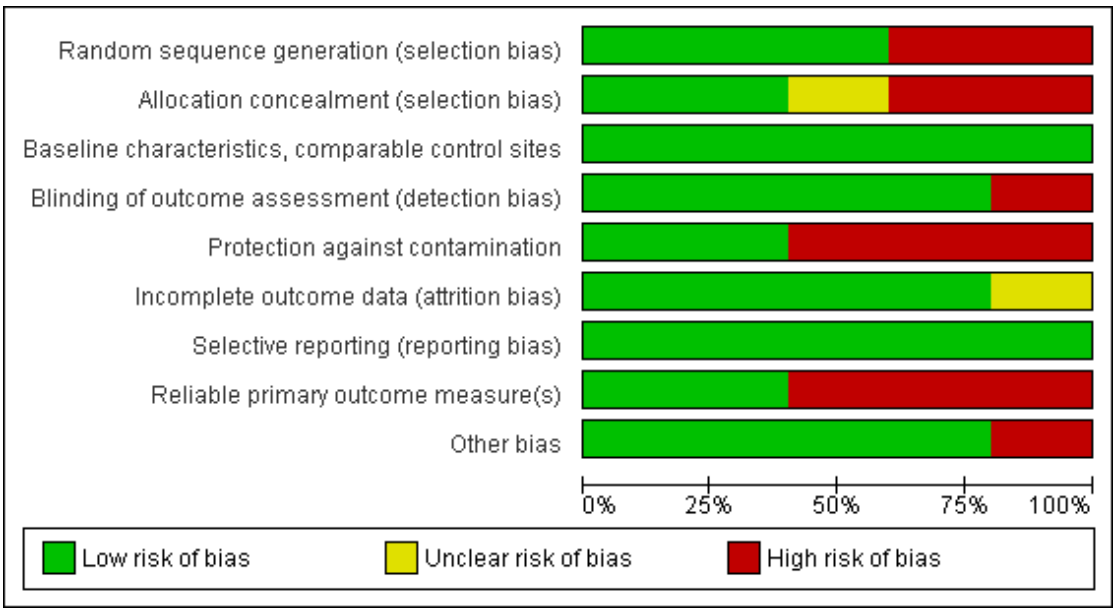


Figure 3. Risk of bias summary: RCT and CBA designs.

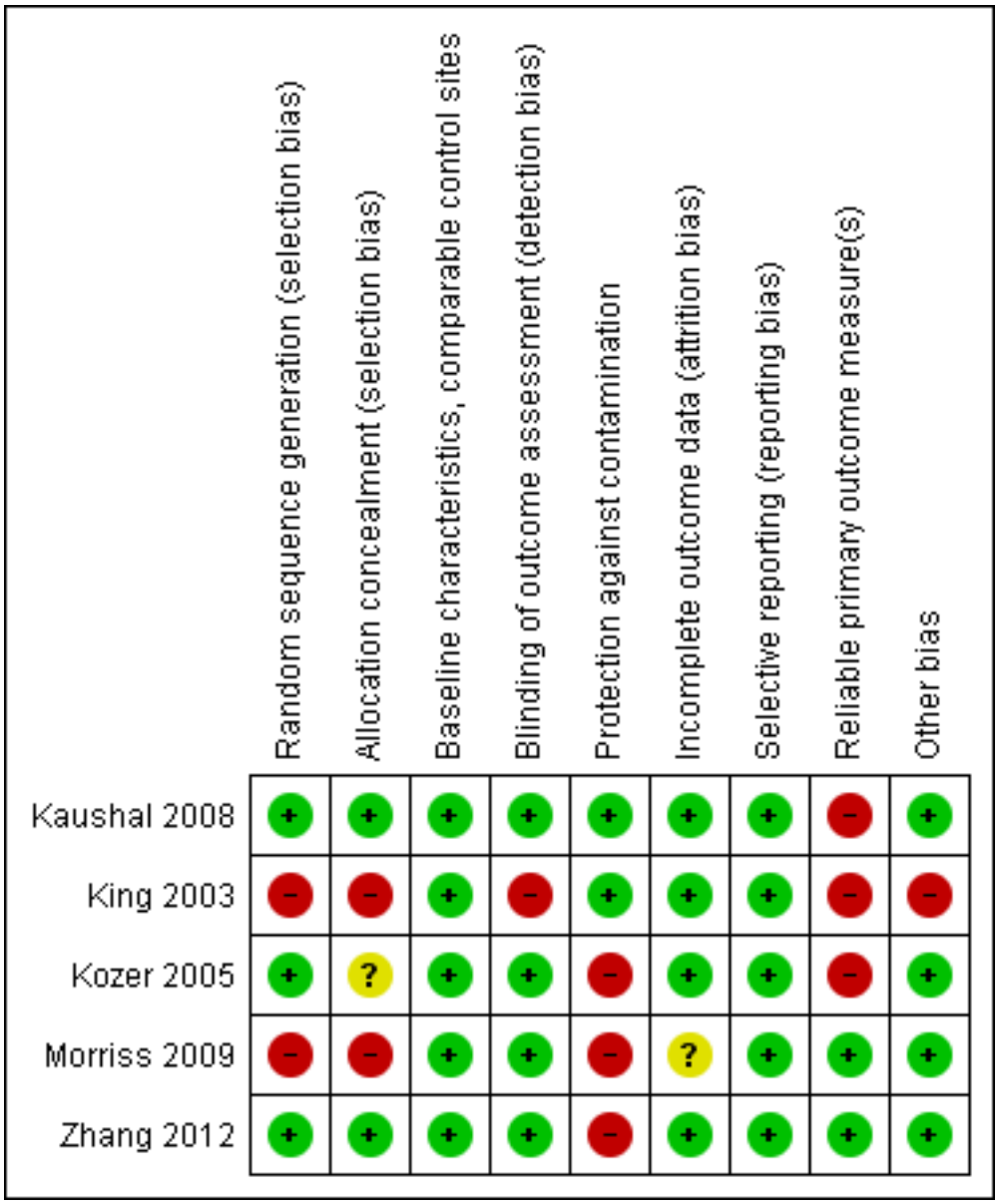


Figure 4. Risk of bias graph: ITS design.

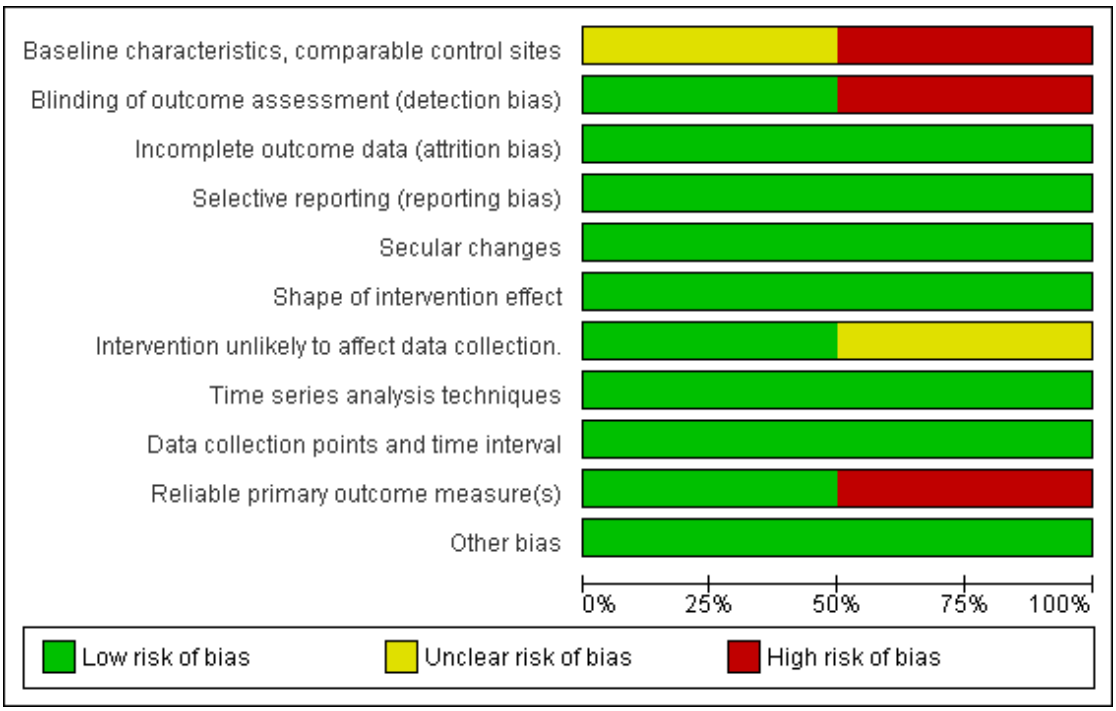
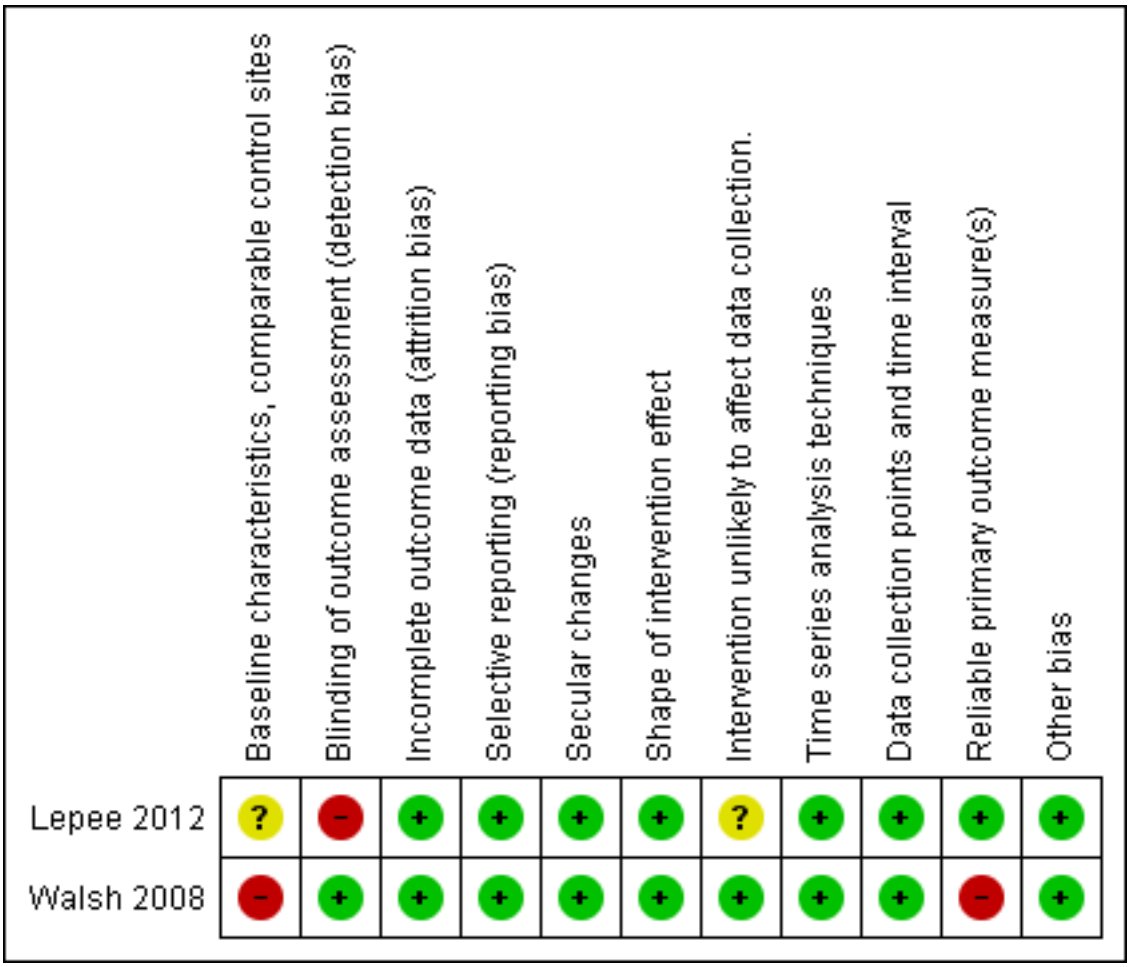


Figure 5. Risk of bias summary: ITS design.



Risk of bias in included studies

The CBA by Kaushal 2008 describes the effects of including a clinical pharmacist. Intervention and control units were randomly selected. Participants in the pre-intervention group were similar to those in the post-intervention group. The process of data collection with blinding was performed accurately and is described in detail. The study was conducted on comparable hospital units with little chance of contamination. Outcome assessment was performed by review of clinical data and incident reports. Study authors report inter-rater reliability of 0.75 for incident classification.

Zhang 2012 studied the effects of including a clinical pharmacist in an RCT. Randomisation, allocation concealment and blinded outcome assessment do not seem to impair the quality of the study. No significant differences were noted between groups at baseline, and missing data were limited and well described. Some contamination between intervention and control groups was noted, as the clinical pharmacists also provided advice for participants in the control group when asked by physicians. This might have led to underestimation of results. Interventions by clinical pharmacists, adverse drug reactions (side effects), length of stay and costs of drugs and hospitalisation were chosen as primary outcome measures. Secondary outcomes included medication compliance rate after discharge and readmission rate. For this review, only length of stay and costs are results of interest.

The ITS study by Walsh 2008 had strengths and limitations. Data collectors were trained paediatric nurses who were unaware of study objectives and paediatricians who were unaware of whether possible errors occurred before or after CPOE. Researchers reported missing data, but the dataset of each time point still covered more than 80%. This study was independent of other changes, meaning that no other major organisational developments during

the study period could have influenced study results. The shape of the intervention effect was prespecified, and identical months were included in the pre-CPOE and post-CPOE periods to control for seasonal effects. Risk of bias regarding whether the intervention affected data collection was low, as methods used for data collection before and after the intervention were the same. Time series analysis techniques were used to correct for changes over time, other than the intervention. Also sufficient numbers of data collection points were chosen (seven before and nine after the intervention). We report two criteria that might cause high risk of bias. Inter-rater reliability for paediatricians' judgements was calculated, resulting in inter-rater reliability for judgements about classification of a possible ME of 0.7, severity of the error of 0.4 and preventability of the error of 0.8. These results might affect the reliability of the primary endpoints. Also, the number of NICU admissions had increased in the post-intervention period, and this might have inflated the effects of CPOE because the rate of MEs in the NICU was less than in other units.

The CBA by King 2003 had strengths and limitations. Participant characteristics were similar in the pre-intervention and post-intervention periods and between intervention and control wards. Each ward was clinically independent, so contamination is not expected. Also, the incident reporting system, which served as the main source of outcomes, was constant during the study period. In this retrospective study, intervention and control wards were not randomly chosen, and no blinding was applied. However, only the incident reporting system was used to collect outcome measures with an inter-rater reliability of 0.64, which might have resulted in less reliable results. In addition, study authors described a decline in ADEs in the pre-intervention period, probably as the result of other interventions provided to increase medication safety.

The CBA by Morriss 2009 had strengths and limitations. Small differences in baseline characteristics were noted in the number of twins and in nursing capacity, but adjustments were made for these in the analyses. Blinded professionals performed outcome assessment. Outcome assessment was performed using a combination of review of medical records and voluntary incident reports, and an inter-rater reliability of 0.82 was reported for detection of MEs. However, intervention and control beds were not randomly selected. Another main threat described in this study is possible contamination: Beds with the BCMA system and beds without the BCMA installed were in the same sections of the NICU. This might have resulted in underestimation of the results.

Lepee 2012 studied the effects of a check and control checklist in an ITS study. Data collection was performed twice a week through review of all inpatient files. The study was independent of other changes; this is shown by the concurrent control variable. The dataset of each time point covered at least 80% of all participants, and the shape of the intervention effect was prespecified. Risk of bias was low regarding whether the intervention affected data collection, as methods used for data collection before and after the intervention were the same. Time series analysis techniques were used to correct for changes over time, other than the intervention. Inter-rater reliability was examined for the primary outcome (technical error), resulting in a kappa of 0.91. Evaluators were not blinded as to whether the data were pre-intervention or post-intervention, but because the endpoint was defined as measurable and objective, there was probably no influence on the results. The number of data points and the time interval chosen in the study were based on maximising the quantity of data that could be collected within available resources (additional information obtained from the study author).

Kozer 2005 studied the effects of a structured order sheet in an RCT. Randomisation and blinded outcome assessment did not seem to impair the quality of the study. Allocation concealment was not described. No significant differences between groups were noted at baseline, and missing data were limited. Possible contamination was noted between intervention and control groups, as the same professionals worked with the structured order sheet on intervention days, as well as with the regular sheet on days chosen as controls. This might have led to underestimation of the results. We also report high risk of bias concerning the reliability of the primary outcomes because only the adverse event reporting system was used. No kappa's were reported.

Effects of interventions

See: **Summary of findings for the main comparison**

Heterogeneity and data synthesis

Five different interventions were evaluated in the seven included studies. Two studies explored the effects of clinical pharmacists (Kaushal 2008; Zhang 2012) but showed clinical and methodological heterogeneity. For example, two different study designs were used; primary endpoints and populations were comparable only in part, and researchers used different methods to obtain primary outcome data. Two studies described the effects of CPOE (King 2003; Walsh 2008). Again, differences in endpoints, methods of data collection, populations and study design were noted. As a result of this heterogeneity, data synthesis was impossible.

Effects of interventions as reported in included studies

The study by Kaushal 2008 described the effects of including a unit-based clinical pharmacist with a CBA study design. During the study period, a total of 4863 admissions with 10,385 admission days were studied in ICU wards, general medical wards and general surgical wards. Serious MEs were chosen as the primary outcome. The baseline rate of serious MEs in the paediatric ICU was 29 per 1000 admission days. After the clinical pharmacist was introduced, the paediatric ICU rate dropped to six per 1000 admission days. Study authors report a statistically significant difference between the paediatric ICU (intervention unit) and the

cardiac ICU (control unit) after the unit-based clinical pharmacist was introduced (P value < 0.01). On the general medical ward and the general surgical wards, results were not significant. See Summary of findings for the main comparison.

The RCT by Zhang 2012 reported on the effects of including a clinical pharmacist. Data on 150 participants were analysed. For this review, only length of stay and costs were results of interest. On the wards where a clinical pharmacist was part of the team, length of stay decreased from 9.06 to 7.33 days (P value 0.02). This reduction was seen mainly in patients with a respiratory system disease. Costs of both drugs and hospitalisation did not change (P value 0.945 and P value 0.125). See Summary of findings for the main comparison.

The ITS study by Walsh 2008 described the effects of CPOE. During the study period, a total of 627 admissions with 3234 admission days and 12,672 medications were analysed. The rate of non-intercepted serious MEs was chosen as the primary outcome. The incidence of non-intercepted serious MEs was 23.1 per 1000 admission days in the pre-intervention period and 20.6 per 1000 admission days in the post-CPOE period. Time series regression analysis indicated a 7% drop in rates of non-intercepted serious MEs (P value 0.0495) after implementation of CPOE. No change was seen in slopes of regression lines before and after the intervention. The incidence of harm as a result of error (preventable ADEs) was 7.9 per 1000 admission days in the pre-intervention period and 6.5 per 1000 admission days in the post-CPOE period. Study authors reported that time series regression analyses showed no differences. The study author when contacted did not reveal additional quantitative information. See Summary of findings for the main comparison.

The CBA study by King 2003 described the effects of CPOE. During the study period, a total of 36,103 participants and 179,183 admission days were studied. Primary outcomes were MEs and ADEs (injuries as a result of error). In the pre-CPOE period, 173 MEs (4.48 per 1000 admission days) were discovered on the intervention wards and 243 (4.80 per 1000 admission days) on the control wards. In the post-CPOE period, the incidence of MEs was 120 (3.13 per 1000 admission days) on the intervention wards and 268 (5.19 per 1000 admission days) on the control wards. The change in rate ratios of MEs after implementation of CPOE is expressed as odds ratio (OR) 1.54 (95% confidence interval (CI) 1.27 to 1.88). Also potential ADEs were reduced after CPOE implementation: OR 0.24, 95% CI 0.09 to 0.68. See Summary of findings for the main comparison.

The study by Morriss 2009 described the effects of BCMA using a CBA study design. During the study period, a total of 958 admissions, representing 12,248 patient-days and 92,398 medication doses, were studied. Primary outcomes were targeted preventable ADEs, and secondary outcomes were potential ADEs and MEs. Unadjusted analysis shows a reduction in targeted preventable ADEs. Potential ADEs were also decreased. In contrast, MEs were increased after implementation of BCMA. Study authors used a generalised estimating equation (GEE) to adjust for non-linearity and additional co-variates. Results of the GEE show a relative risk of targeted preventable ADEs in the intervention group of 0.53 (95% CI 0.29 to 0.98). Adjusted results for MEs are not reported. See Summary of findings for the main comparison.

The study by Lepee 2012 reported on the effectiveness of the check and correct checklist for prescribing errors using an ITS study design. During the study period, a total of 1887 medication orders, comprising 30,105 opportunities for technical errors and 1163 for clinical errors, were studied. Two outcomes were defined: technical prescription writing errors ("technical errors") and prescribing errors involving clinical decision making ("clinical errors"). Data were analysed using segmented regression analysis, corrected for overall documentation quality of medical records, which was chosen as a concurrent control measurement. This analysis revealed a decrease of 5% in the technical error rate (95% CI -7.09% to -2.95%) after the intervention. A decrease in the trend was also reported: -0.21 (95% CI -0.41 to -0.01). Regarding clinical medication errors, study authors reported no effect. See Summary of findings for the main comparison.

The RCT by Kozer 2005 reported on the effects of a structured, pre-printed medication order sheet on prescriptions for patients visiting a paediatric emergency department. During the month of the study, data from 2058 participants were obtained. A total of 411 medications were prescribed on the regular form, and 376 medications were prescribed on the new form. Two outcomes were reported: the total numbers of medication prescribing errors and medication errors that were considered significantly or severely harmful. Medication errors were identified in 68 prescriptions when the regular form was used and in 37 prescriptions on the new form. Analysis revealed a reduction in medication errors: adjusted OR 0.55 (95% CI 0.34 to 0.90). Potentially harmful MEs (significant and severe errors) were reduced from 36 when the regular form was used to 14 on the days when the new form was used. This reduction was substantial: adjusted OR 0.39 (95% CI 0.21 to 0.77). See Summary of findings for the main comparison.

DISCUSSION

Summary of main results

Currently evidence is limited on interventions that are effective in preventing medication errors (MEs) in a paediatric population in hospital. We included seven studies describing five different organisational interventions: a clinical pharmacist, computerised physician order entry (CPOE), a barcode medication administration system (BCMA), a structured prescribing form and a check and control checklist in combination with feedback. Clinical and methodological heterogeneity between studies precluded meta-analyses. Although some interventions described in this review

show a decrease in MEs, results are not consistent, and none of the studies reported a significant reduction in patient harm. Based on the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach, overall quality and strengfh of the evidence are low.

Overall completeness and applicability of evidence

We aimed to create an overview concerning the effectiveness of interventions to reduce medication errors and related harm in children. Because medication safety in paediatric care is different from that in adult care, interventions preferably include components that focus on specific paediatric safety issues, for example, clinical decision support, calculation aids and dosage control. This review describes five different interventions from seven studies, which were evaluated according to the EPOC (Effective Practice and Organisation of Care Group) criteria.

First, a clinical pharmacist might serve as a valuable contribution at different stages of the medication process. Both Kaushal 2008 and Zhang 2012 described the contributions of a clinical pharmacist, for example, in advising doctors on drug selection and dosage, advising nurses on preparation and administration and providing monitoring and education. Kaushal 2008 mentioned the level of education and skills of the clinical pharmacist. Second, information technology might play an important role in medication safety. The recommended system includes CPOE and BCMA, because each system targets specific types of medication errors. In paediatric care, a CPOE is required that is sufficiently flexible to respond to rapid and specific changes that occur in children, and continuous adaptation to weight changes must be possible (Johnson 2013). The CPOE described by Walsh 2008 includes specific paediatric features (e.g. weight-based dosage calculator, automatic dosage checks), but King 2003 describes a CPOE system without clinical decision support and with no interface with the pharmacy. Morriss studied a BCMA system, but it remains unclear whether this was connected with CPOE. Lepee 2012 implemented a check and control checklist to identify technical and clinical errors in prescriptions. Included in this intervention were immediate feedback and instruction to the team during ward rounds. The instruction might have highlighted specific features of paediatric pharmaceutical care, such as weight-based dosages or routes of administration. Structured prescribing forms might improve prescribing practices in general, as shown by Kozer 2005. In conclusion, although all seven studies aimed to improve medication safety for children, not all interventions targeted specific paediatric safety issues.

All studies are coming from North America or Europe, except one that originates from China. Also, all are conducted in tertiary university medical centres, some in highly specialised paediatric wards. This might impact the generalisability of findings.

Other strategies are used to decrease medication errors, such as avoidance of verbal orders, verbal orders read back, medication reconciliation, double check and patient (parent) active participation in care. This review shows that only a handful of medication safety strategies are being studied with robust study designs.

Quality of evidence

Based on study design, we graded the quality of the two included randomised controlled trials (Kozer 2005; Zhang 2012) and four observational studies (Kaushal 2008; Lepee 2012; Morriss 2009; Walsh 2008) as 'low'. We degraded one observational study to 'very low', because results could not be distinguished from other system changes during the study period (King 2003).

Potential biases in the review process

We followed the EPOC Group guidelines for conducting the review, which included performing a very sensitive search of the databases, as well as the grey literature. However, publication bias remains a potential (but unknown) source of bias.

Agreements and disagreements with existing knowledge

We are aware of other reviews that have evaluated the effectiveness of interventions in preventing medication errors in paediatric care. Sanghera 2006 conducted a systematic review examining whether interventions by clinical pharmacists improve medication safety in children, and Chedoe 2007 reviewed the literature to identify strategies to improve medication safety in neonatal intensive care, while including the contribution of a clinical pharmacist. In both reviews, included studies were observational studies without controls (before-after studies or case series). All studies reported significant improvements and concluded that a clinical pharmacist plays an important role in detecting and preventing medication errors. The two studies on this subject included in our systematic review support in part the conclusions based on existing evidence (Kaushal 2008; Zhang 2012). As described before, Kaushal showed a significant decrease in serious MEs with a full-time clinical pharmacist in a paediatric intensive care unit (PICU), but not on paediatric medical wards. Zhang showed a decrease in length of stay, but not in costs; however these results might be underestimated by contamination between intervention and control groups. The effect of CPOE has been summarised in three systematic reviews (Chedoe 2007; Conroy 2007; Rosse van 2009). Again, most of the included studies were observational studies; only the research conducted by King 2003 used a controlled before-after design. Most studies report a beneficial effect of CPOE on MEs, but mixed effects on patient harm are reported. Also new errors (e.g. typographical mistakes, poor design of screens) seemed to appear with the use of CPOE (Cheung 2013; Koppel 2005; Walsh

2006). One study reported an increase in mortality rate after implementation of CPOE in a PICU (Han 2005), but this finding was not confirmed (Del Baccaro 2006; Keene 2007). Computerised clinical decision support as part of CPOE shows multiple functionalities, and the effect on patient care is inconsistent or unknown (Stultz 2012). The two studies on this subject included in our systematic review support the mixed results shown in the existing evidence. Walsh 2008 described a just significant (P value 0.495) decrease in non-intercepted serious MEs but no reduction in preventable harm. King 2003 showed a significant decrease in MEs but no reduction in harmful ADEs and even an increase in potentially harmful ADEs. These results are not surprising, as the constant need for weight- and surface area-based dosing and unit conversion is the key risk for children, and this risk might only be diminished by a CPOE with specific paediatric features, which was the case in only some of the included studies.

Rinke 2014 conducted a systematic review to study interventions to reduce paediatric MEs. Study authors aimed to be as inclusive as possible and therefore used definitions that are broader than the definitions used by the Cochrane EPOC Review Group. This resulted in the inclusion of 63 studies, which the study authors considered as 52 ITS and eight CBA studies. Studies investigated the effects on MEs of the following interventions: CPOE (n = 26), education (n = 20), preprinted order sheets (n = 9), protocol implementation (n = 8), reporting of error rates (n = 7) and pharmacist participation (n = 5). Four studies are included in our systematic review as well (Kaushal 2008; Kozer 2005; Morriss 2009; Walsh 2008). This review shows that multiple interventions revealed statistically significant results, but many studies show high risk of bias. The observations of Rinke et al are congruent with our conclusions, namely, that evidence on preventing paediatric medication errors is seriously hampered by non-uniform definitions, data collection methods and outcome measures.

Manias 2014 published a systematic review to study interventions provided to reduce MEs in PICUs. In total, 34 studies were included. Apart from one study (Kaushal 2008), all were before-after studies without a comparative, concurrent study group. Six types of interventions were studied: CPOE (n = 8), intravenous systems (n = 5), education (n = 11), protocols and guidelines (n = 2), pharmacist involvement (n = 3) and decision support (n = 5). Although the study authors report statistically significant results from meta-analyses for CPOE, intravenous systems and education, they conclude that the evidence remains limited because of variation in definitions and data collection and because of the low quality of the studies. Again, this conclusion is congruent with our observations.

Heterogeneity

Despite efforts toward standardisation (Lisby 2012; Miller 2007; Yu 2005), we found differences in the definitions of an ME and harm (numerator data) and in study populations (denominator data), creating heterogeneity in the results presented in these studies. For example, numerator data are presented as MEs, serious MEs, technical MEs, harmful MEs or potentially harmful MEs, preventable ADEs or potential ADEs. Denominator data are presented as participants, 1000 admission days, 1000 prescriptions or 1000 gifts. Not all studies categorised MEs by severity of outcome for participants, or different scales were used. This variety in definitions and classifications made accurate comparison of results impossible.

AUTHORS' CONCLUSIONS

Implications for practice

Organisations implementing interventions to improve medication safety for hospitalised children must be aware that the evidence endorsing these interventions is limited both in volume and in methodological quality. Although some interventions described in this review show a decrease in MEs, the results are not conclusive, and benefits for patients in terms of less harm remain unclear. The relevance of these results should be weighted in the organisational context.

Implications for research

Evidence

Appropriately powered and methodologically sound studies are needed before evidence-based recommendations can be made. Researchers should use the most robust design possible to minimise bias and maximise generalisability. The standard RCT methodology may not be well suited to answering questions concerning medication safety in the light of social and organisational contexts and their changes over time. Cluster-randomised trials, factorial designs or non-randomised designs like interrupted time series must be considered (Eccles 2003; Fan 2010).

Population

Medication errors are hazardous for all patients, but children are believed to be at exceptionally high risk of harm from such errors. Neonates, infants and surgical paediatric patients are believed to be at higher risk of harm than other children. In addition, medications are very diverse and have a wide range of risk profiles, and MEs do not always cause patient harm. Those with a heightened risk of causing patient harm are known as high-alert medications; their misuse has serious consequences for patients. Therefore it is strongly recommended that research on medication safety should include high-risk populations and high-alert medications. As existing evidence originates from highly specialised pediatric wards

in tertiary university medical centres, research from smaller hospitals with fewer resources is welcome.

Intervention and comparison

To improve medication safety in paediatric care, interventions must include components that focus on specific paediatric safety issues, for example, clinical decision support, calculation aids, alerts in cases of underdosage or overdosage, educational interventions and close monitoring. Apart from technical innovations like CPOE and BCMA, non-technical calculation aids and alerts must be subjects of investigation to support professionals in countries where high-tech applications are not feasible. Attention must be focused on comparable participant groups or study sites.

Outcome

In evaluating safety, patient harm caused by MEs or potentially harmful MEs is more relevant than MEs alone, because errors do not necessarily result in patient harm. Future studies should include (potentially) harmful MEs as main outcome measures. Efforts must be made to ensure uniform definitions of MEs and harm.

Time stamp

Given the vulnerability of paediatric patients in hospital, medication safety should be high on every research agenda.

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REFERENCES

References to studies included in this review

Kaushal 2008 *{published data only}*
Kaushal R, Bates DW, Abramson EL, Soukup JR, Goldmann DA. Unit-based clinical pharmacists' prevention of serious medication errors in pediatric inpatients. *American Journal of Health System Pharmacy* 2008;**65**: 1254–60.

King 2003 *{published data only}*
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.

Kozer 2005 *{published data only}*
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.

Lepee 2012 *{published data only}*
Lepee C, Klaber RE, Benn J, Fletcher PJ, Cortoos P-J, Jacklin A, et al. The use of consultant-led ward round checklist tot improve paediatric prescribing: an interrupted time serie study. *European Journal of Pediatrics* 2012;**171**: 1239–45.

Morriss 2009 *{published data only}*
Morriss FH, Abramowitz PW, Nelson SP, Milavetz G, Michael SL, Gordon SN, 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. *Journal of Pediatrics* 2009;**154**: 363–8.

Walsh 2008 *{published data only}*
Walsh KE, Landrigan CP, Adams WG, Vinci RJ, Chessare JB, Cooper MR, et al. Effect of computer order entry on prevention of serious medication errors in hospitalised children. *Pediatrics* 2008;**121**:e421–7.

Zhang 2012 *{published data only}*
Zhang C, Zhang L, Huang L, Luo R, Wen J. Clinical pharmacists on medical care of pediatric inpatients: a single-center randomized controlled trial. *PLoS ONE* 2001;**7**: e30856.

References to studies excluded from this review

Balaguer Santamaria 2001 *{published data only}*
Balaguer Santamaria JA, Fernandex Ballart JD, Escribano SJ. Usefulness of a software package to reduce medication errors in neonatal care. *Anales Espanoles de Pediatria* 2001; **55**:541–5.

Burgess 2009 *{published data only}*
Burgess CC. Comparison of the effectiveness of traditional nursing medication administration with the Color Coding Kids system in a sample of undergraduate nursing students. Dissertation University of North Carolina 2009.

Burmester 2008 *{published data only}*
Burmester MK, Dionne R, Thiagarajan RR, Laussen PG. Interventions to reduce medication prescribing errors in a paediatric cardiac intensive care unit. *Intensive Care Medicine* 2008;**34**:1083–90.

Ching 2014 *{published data only}*
Ching JM, Williams BL, Idemoto LM, Blackmore CC. Using lean "automation with a human touch" to improve

medication safety: a step closer to the "perfect dose". *Joint Commission Journal on Quality and Patient Safety* 2014;**40**: 341–50.

Cunningham 2008 *{published data only}*
Cunningham S, Logan C, Lockerbie L, Dunn MJG, McMurray A, Prescott R. Effect of an integrated care pathway on acute asthma/wheeze in children attending hospital: cluster randomized trial. *The Journal of Pediatrics* 2008;**152**:315–20.

Dehghan-Nayeri 2013 *{published data only}*
Dehghan-Nayeri N, Bayat F, Salehi T, Faghihzadeh S. The effectiveness of risk management program on pediatric nurses' medication error. *Iranian Journal on Nursing and Midwifery Research* 2013;**18**:371–7.

Elsaid 2013 *{published data only}*
Elsaid K, Truong T, Monckeberg M, McCarthy H, Butera J, Collins C. Impact of electronic chemotherapy order forms on prescribing errors at an urban medical center: results from an interrupted time-series analysis. *International Journal on Quality of Health Care* 2013;**25**:656–63.

Frush 2004 *{published data only}*
Frush KS, Luo XM, Hutchinson P, Higgins JN. Evaluation of a method to reduce over-the-counter medication dosing error. *Archives of Pediatric & Adolescent Medicine* 2004;**158**: 620–4.

Frush 2006 *{published data only}*
Frush K, Hohenhaus S, Luo X, Gerardi M, Wiebe RA. Evaluation of a web-based education program on reducing medication error: a multicenter, randomized controlled trial. *Pediatric Emergency Care* 2006;**22**:62–70.

Gazarian 2012 *{published data only}*
Gazarian M, Graudins LV. Long-term reduction in adverse drug events: an evidence-based improvement model. *Pediatrics* 2012;**129**:e1334–42.

Hixson 2009 *{published data only}*
Hixson R, Gandhi M, Holton F. A randomised trial to evaluate prescribing accuracy when using the Paediatric Analgesia Wheel. *Archives of Disease in Childhood* 2009;**94**: 268–72.

Hohenhaus 2008 *{published data only}*
Hohenhaus SM, Cadwell SM, Stone-Griffith S, Sears-Russell N, Baxter T, Hicks W, et al. Assessment of emergency nursing practice during critical pediatric medication administration in a simulated resuscitation using the "Color Coding Kids Hospital System". *Advanced Nursing Emergency Journal* 2008;**30**:233–41.

Nguyen 2014 *{published data only}*
Nguyen HT, Pham HT, Vo DK, Nguyen TD, van den Heuvel ER, Haaijer-Ruskamp FM, et al. The effect of a clinical pharmacist-led training programme on intravenous medication errors: a controlled before and after study. *BMJ Quality and Safety* 2014;**23**:319–24.

Niemann, Bertsche 2014 *{published data only}*
Niemann D, Bertsche A, Meyrath D, Oelsner S, Ewen AL, Pickardt B, et al. Drug handling in a paediatric intensive care unit: can errors be prevented by a three-step intervention. *Klinische Padiatrie* 2014;**226**:62–7.

Niemann 2014 *{published data only}*
Niemann D, Bertsche A, Meyrath D, Koepf ED, Traiser C, Seebald K, et al. A prospective three-step intervention study to prevent medication errors in drug handling in paediatric care. *Journal of Clinical Nursing* 2014;**June**:doi:10.1111/ jocn.12592 (epub ahead of printing).

Ramsay 2014 *{published data only}*
Ramsay AI, Turner S, Cavell G, Oborne CA, Thomas RE, Cookson G, et al. Governing patient safety: lessons learned from a mixed methods evaluation of implementing a ward-level medication safety scorecard in two English NHS hospitals. *BMJ Quality and Safety* 2014;**23**:136–46.

Senner 2010 *{published data only}*
Senner A, Byrne L, Fischmann A, Daly G, Wright F, Cohn R, et al. A simple intervention targeting patient safety at the bedside. *Journal of Oncology Pharmacy Practice Conference* 2010;**16(2 suppl)**:6–7.

Vaidya 2006 *{published data only}*
Vaidya V, Sowan AK, Mills ME, Soeken K, Gaffoor M, Hilmas E. Evaluating the safety and efficiency of a CPOE system for continuous medication infusions in a pediatric ICU. AMIA Symposium Proceedings, page 1128. 2006.

Yamamoto 2010 *{published data only}*
Yamamoto L, Kanemori J. Comparing errors in ED computer-assisted vs conventional pediatric drug dosing and administration. *American Journal of Emergency Medicine* 2010;**28**:588–92.

Yin 2008 *{published data only}*
Yin HS, Dreyer BP, van Schaick SL, Foltin GL, Dinglas C, Mendelsohn AL. Rndomized controlled trial of a pictogram-based intervention to reduce liquid medication dosing errors and improve adherence among caregivers and young children. *Archives of Pediatrics & Adolescent Medicine* 2008;**162**:814–22.

Yin 2011 *{published data only}*
Yin HS, Medelsohn AL, Fierman A, van Schaick SL, Bazan IS, Dreyer BP. Use of a pictographic diagram to decrease parent dosing errors with infant acetaminophen: a health literacy perspective. *Academic Pediatrics* 2011;**11**:50–7.

References to ongoing studies

Kaushal *{published data only}*
Serious medication errors in paediatrics: evaluation of prevention strategies. Ongoing study February 2000.

Additional references

Aspden 2007
Aspden P, Wolcott JA, Bootman L, Cronenwelt LR. *Prevention Medication Errors: Quality Chasm Series*. Washington DC: The National Academic Press, 2007.

Chedoe 2007
Chedoe I, Molendijk HA, Dittrich ST, Jansman FG, Harting JW, Brouwers JR, et al. Incidence and nature of

medication errors in neonatal intensive care with strategies to improve safety. *Drug Safety* 2007;**30**:503–13.

Cheung 2013
Cheung KC, Veen van der W, Bouvy ML, Wensing M, Bemt van den PM, Smet de PA. Classification of medication incidents associated with information technology. *Journal of the American Medical Informatics Association* 2014;**21**(E1): e63–e70.

Conroy 2007
Conroy S, Sweis D, Planner C, Yeung V, Collier J, Haines L, Wong IC. Interventions to reduce dosing errors in children: a systematic review of the literature. *Drug Safety* 2007;**30**: 1111–25.

Cousins 2002
Cousins D, Clarkson A, Conroy S, Choonara I. Medication errors in children - an eight year review using press reports. *Paediatric and Perinatal Drug Therapy* 2002;**5**:52–8.

Davidhizar 2002
Davidhizar R, Lonser G. Medication errors: what case managers can do. *Hospital Case Management* 2002;**10**: 77–80.

Del Baccaro 2006
Del Baccaro MA, Jeffries HE, Eisenberg MA, Harry ED. Computerized provider order entry implementation: no association with increased mortality rates in an intensive care unit. *Pediatrics* 2006;**118**:290–5.

Eccles 2003
Eccles M, Grimshaw J, Campbell M, Ramsay C. Research designs for studies evaluating the effectiveness of change and improvement strategies. *Quality and Safety in Health Care* 2003;**12**:47–52.

EPOC 2002
The Data Collection Checklist. Cochrane Effective Practice and Organisation of Care Review Group 2002. www.epoc.uottawa.ca/checklist2002.doc (accessed 12 November 2014).

EPOC 2014
Effective Practice, Organisation of Care (EPOC). Suggested risk of bias criteria for EPOC reviews. EPOC Resources for Review Authors. Vol. Oslo: Norwegian Knowledge Centre for the Health Services; 2014. http://epoc.cochrane.org/epoc–specific–resources–review–authors (accessed 12 November 2014).

Fan 2010
Fan E, Laupacis A, Pronovost PJ, Guyatt GH, Needham DM. How to use an article about quality improvement. *Journal of the American Medical Association* 2010;**304**: 2279–87.

Franklin 2005
Franklin B, Vincent C, Schachter M, Barber N. The incidence of prescribing errors in hospital inpatients: an overview of the research methods. *Drug Safety* 2005;**28**: 891–900.

Garfield 2013
Garfield S, Reynolds M, Dermont L, Franklin BD. Measuring the severity of prescribing errors: a systematic review. *Drug Safety* 2013;**36**:1151–7.

Ghaleb 2006
Ghaleb MA, Barber N, Franklin BD, Yeung VW, Khaki ZF, Wong IC. Systematic review of medication errors in pediatric patients. *The Annals of Pharmacotherapy* 2006;**40**: 1766–76.

Guyatt 2008
Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ (Clinical research ed)* 2008;**336**(7650):924–6.

Han 2005
Han YY, Carcillo JA, Venkataraman ST, Clark RS, Watson RS, Nguyen TC, et al. Unexpected increased mortality rate after implementation of a commercially sold computerized physician order entry system. *Pediatrics* 2005;**116**:1506-12 (erratum in Pediatrics 2006;117:594).

Higgins Cochrane Handbook 2011
Higgins J, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions*. New York: Wiley-Blackwell, Version 5.1.0 [updated March 2011].

Hug 2012
Hug BL, Keohane C, Seger DL, Yoon C, Bates DW. The costs of adverse drug events in community hospitals. *Joint Commission Journal on Quality and Patient Safety/Joint Commission Resources* 2012;**38**:120–6.

Johnson 2013
Johnson KB, Lehmann CU, Council on Clinical Information Technology. Electronic prescribing in paediatrics: towards safer and more effective medication management. *Pediatrics* 2013;**131**:1350–6.

Kale 2012
Kale A, Keohane CA, Maviglia S, Gandhi TK, Poon EG. Adverse drug events caused by serious medication administration errors. *BMJ Quality and Safety* 2012;**21**: 933–8.

Kaushal 2001
Kaushal R, Bates DW, Landrigan C, McKenna KJ, Clapp MD, Federico F, et al. Medication errors and adverse drug events in pediatric inpatients. *Journal of the Aerican Medical Association* 2001;**285**:2114–20.

Keene 2007
Keene A, Ashton L, Shure D, Napoleone D, Katyal C, Bellin E. Mortality before and after initiation of a computerized physician order entry system in a critically ill pediatric population. *Pediatric Critical Care Medicine* 2007; **8**:268–71.

Koppel 2005
Koppel R, Metlay JP, Cohen A, Abaluck B, Localio AR, Kimmel SE, et al. Role of computerized physician order entry systems in facilitating medication errors. *Journal of the American Medical Association* 2005;**293**:1197–203.

Lisby 2010
Lisby M, Nielsen LP, Brock B, Mainz J. How are medication errors defined? A systematic literature review of definitions and characteristics. *International Journal for Quality in Health Care (ISQua)* 2010;**22**:507–18.

Lisby 2012
Lisby M, Nielsen LP, Brock B, Mainz J. How should medication errors be defined? Development and test of a definition. *Scandinavian Journal of Public Health* 2012;**40**: 203–10.

Manias 2014
Manias E, Kinney S, Cranswick N, Williams A, Borrott N. Interventions to reduce medication errors in pediatric intensive care. *Annals of Pharmacotherapy* 2014;**48**: 1313–31.

Meyer-Massetti 2011
Meyer-Massetti C, Cheng CM, Schwappach DL, Paulsen L, Ide B, Meier CR, et al. Systematic review of medication safety assessment methods. *American Journal of Health System Pharmacy* 2011;**68**:227–40.

Miller 2007
Miller MR, Robinson KA, Lubomski LH, Rinke ML, Pronovost PJ. Medication errors in paediatric care: a systematic review of epidemiology and an evaluation of evidence supporting reduction strategy recommendations. *Quality and Safety in Health Care* 2007;**16**:116–26.

Morimoto 2004
Morimoto T, Gandhi TK, Seger AC, Hsieh TC, Bates DW. Adverse drug events and medication errors: detection and classification methods. *Quality and Safety in Health Care* 2004;**13**:306–14.

NCC MERP
National Coordinating Council for Medication Error Reporting and Prevention. About medication errors: what is a medication error?. http://www.nccmerp.org/about-medication-errors (accessed 8 March 2012).

Olsen 2007
Olsen S, Neale G, Schwab K, Psaila B, Patel T, Chapman EJ, et al. Hospital staff should use more than one method to detect adverse events and potential adverse events: incident reporting, pharmacist surveillance and local real-time record review may all have a place. *Quality and Safety in Health Care* 2007;**16**:40–4.

Oren 2003
Oren E, Shaffer ER, Guglielmo BJ. Impact of emerging technologies on medication errors and adverse drug events. *Americal Journal of Health System Pharmacology* 2003;**60**: 1447–58.

Ramsay 2003
Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE. Interrupted time series designs in health technology assessment: lessons from two systematic reviews of behavior change strategies. *International Journal of Technology Assessment in Health Care* 2003;**19**:613–23.

Rinke 2014
Rinke ML, Bundy DG, Valesquez CA, Rao S, Zerhouni Y, Lobner K, et al. Interventions to reduce pediatric medication errors: a systematic review. *Pediatrics* 2014;**134**: 338–60.

Rosse van 2009
Rosse van F, Maat B, Rademaker CM, Vlught van AJ, Egberts AC, Bollen CW. The effect of computerized physician order entry on medication prescription errors and clinical outcome in pediatric and intensive care: a systematic review. *Pediatrics* 2009;**123**:1184–90.

Samp 2014
Samp JC, Touchette DR, Marinac JS, Kuo GM, American College of Clinical Pharmacy Practice-Based Research Network Collaborative. Economic evaluation of the impact of medication errors reported by US clinical pharmacists. *Pharmacotherapy* 2014;**34**:350–7.

Sanghera 2006
Sanghera N, Chan P, Khaki ZF, Planner C, Lee KK, Cranswick NE, et al. Interventions of hospital pharmacists in improving drug therapy in children. *Drug Safety* 2006; **29**:1031–47.

Santell 2003
Santell JP. Medication errors: experience of the United States Pharmacopeia (USP) MEDMARX reporting system. *Journal of Medical Pharmacology* 2003;**43**:760–7.

Schunemann 2011
Schunemann H, Hill S, Guyatt G, Akl EA, Ahmed F. The GRADE approach and Bradford Hill's criteria for causation. *Journal of Epidemiology and Community Health* 2011;**65**: 392–5.

Stucky 2003
Stucky ER. Prevention of medication errors in the pediatric inpatient setting. *Pediatrics* 2003;**112**:431–6.

Stultz 2012
Stultz JS, Nahata MC. Computerized clinical decision support for medication prescribing and utilization in pediatrics. *Journal of the American Medical Informatics Association* 2012;**19**:942–53.

Tam 2005
Tam VC. Frequency, type and clinical importance of medication history errors at admission to hospital: a systematic review. *Canadian Medical Association Journal* 2005;**173**:510–5.

Vries de 2008
Vries de EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: a systematic review. *Quality and Safety in Health Care* 2008;**16**:216–23.

Walsh 2006
Walsh KE, Adams WG, Bauchner H, Vinci RJ, Chessare JB, Cooper MR, et al. Medication errors related to computerized order entry for children. *Pediatrics* 2006;**118**: 1872–9.

Weingart 2000

Weingart SN, Wilson R, Gibberd RW, Harrison B. Epidemiology of medical error - education and debate. *BMJ* 2000;**320**:774–7.

WHO 2009

World Health Organization. Conceptial Framework for the International Classification for Patient Safety. Final Technical Report 2009 [Version 1.1]. http://www.who.int/patientsafety/implementation/taxonomy/en/ (accessed 12 November 2014).

Yu 2005

Yu KH, Nation RL, Dooley MJ. Multiplicity of medication safety terms, definitions and functional meanings: when is enough enough?. *Quality and Safety in Health Care* 2005; **14**:358–63.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Kaushal 2008

Methods	Controlled before-after study
Participants	*Setting* Medical, surgical and ICU, as part of a paediatric teaching hospital, USA *Patients* Patients admitted to participating wards. Total number of participants in the study was 4863, of whom less than 5% were adults. Demographic characteristics are described in detail *Professionals* Not reported
Interventions	Clinical pharmacist (full time in the PICU and part time on the medical and surgical wards) compared with no clinical pharmacist
Outcomes	*Primary outcomes* Serious MEs, defined as preventable ADEs (harm to patients as a result of MEs) and non-intercepted near misses (MEs with significant potential for injuring patients) *Secondary outcomes* -
Notes	*Period* Pre-intervention 6 to 8 weeks each ward between March and August 2000 (1576 participants) and post-intervention 3 months each ward between June and November 2000 (3287 patients) *Other* Sample size calculation not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"One of the medical units and one of the surgical units were randomly selected as experimental groups, and the others served as controls. The paediatric ICU was randomly selected as an experimental group; the cardiac ICU served as its control"
Allocation concealment (selection bias)	Low risk	No bias reported
Baseline characteristics, comparable control sites	Low risk	"Pre-intervention patients were generally similar to post-intervention patients in all study units, with most variation occurring in age distribution" "The SMEs/1000 patient days (primary outcome) pre-intervention for the intervention wards and control

Kaushal 2008 (*Continued*)

		wards were not different, as shown in table 2"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Two physicians independently reviewed each suspected ADE and near miss and classified them as ADEs, near misses, or MEs. The reviewers were blinded to the time period (i.e. before or after intervention) and the unit location of events in order to minimize potential bias"
Protection against contamination	Low risk	Allocation was by hospital unit, and it is unlikely that the control group received the intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	"Medication errors, near misses and ADEs were identified through detailed review of all medication orders and patient charts by a nurse data collector randomly assigned to each study unit on a daily basis"
Selective reporting (reporting bias)	Low risk	"We hypothesized that unit-based clinical pharmacists might be able to reduce rates of serious medication errors in paediatric inpatients in both ICU and general care unit settings." Results on this outcome measure are described
Reliable primary outcome measure(s)	High risk	Outcome assessment by review of all clinical data and reports of errors "Measures of inter-rater reliability (before discussion and consensus) were calculated using Kappa statistics, with moderate-to-excellent levels of agreement (0.75 for incident classification)"
Other bias	Low risk	No bias reported

King 2003

Methods	Controlled before-after study
Participants	*Setting* Medical and surgical paediatric wards, as part of a tertiary care paediatric teaching hospital, Canada *Patients* Total number of participants was 36,103. Average age of participants was 6.3 years *Professionals* Intervention wards: a team consisting of paediatric generalists and subspecialists with assistance from paediatric residents, interns and medical students Control wards: not reported
Interventions	CPOE compared with handwritten orders

King 2003 (*Continued*)

Outcomes	*Primary outcomes* MEs, defined as any events involving medication prescription, dispensing, administration or monitoring, irrespective of outcome ADEs, defined as medication errors resulting in injury to the patient *Secondary outcomes* Potential ADEs, defined as medication errors with the potential for patient injury when no actual harm occurred
Notes	*Period* 3 years before (from April 1993 to March 1996; 18,618 participants) and 3 years after (from January 1997 to December 1999; 17,485 participants) implementation of CPOE *Other* Sample size calculation not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	CBA, retrospective design
Allocation concealment (selection bias)	High risk	CBA, retrospective design
Baseline characteristics, comparable control sites	Low risk	Participants: Characteristics of participants (age and gender) are similar in the pre-intervention and post-intervention periods, as well as between intervention and control wards Outcome: "The MERs before the introduction of CPOE for the intervention and control wards were indistinguishable (p=0.5, ratio 0.93, CI 0.76 to 1.13)"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Confirmed by the first study author
Protection against contamination	Low risk	"Each ward is clinically independent with respect to nursing staff"
Incomplete outcome data (attrition bias) All outcomes	Low risk	"Medication errors are reported in a standardized fashion by the adverse event reporting system on all inpatient floors. This is a passive reporting system that was constant throughout the duration of the study"
Selective reporting (reporting bias)	Low risk	"We assessed the impact of a commercially available CPOE system on medication errors and ADEs in paediatric inpatients at a tertiary care paediatric hospital" Results of these outcome measures are described

King 2003 (*Continued*)

Reliable primary outcome measure(s)	High risk	Outcome assessment by adverse event reporting system "Twenty random incident reports were independently rated by each of the 2 reviewers with good agreement (K = 0.64: CI 0.45 - 0.82)"
Other bias	High risk	"... our institution saw a decline in potential ADEs and ADEs in both the intervention (from 11-7) and control wards (from 19-5), perhaps the result of other system changes to reduce medical error, such as ward-based pharmacists"

Kozer 2005

Methods	Randomised controlled trial
Participants	*Setting* Paediatric emergency department, part of a tertiary care paediatric facility, Canada *Patients* All children on participating days (non-urgent, semi-urgent, urgent and emergent/resuscitation). The study does not report on participant characteristics. In total, 2058 participants with 787 orders were included: intervention group 376 orders; control group 411 orders *Professionals* Medical doctors, staff and trainees
Interventions	Structured, pre-printed medication order sheet compared with regular blank order sheets (regular form)
Outcomes	*Primary outcomes* Medication prescribing errors, defined as drug regimen different from recommended (dose difference $\geq$ 20%, deviation $\geq$ 2 hours from the recommended interval between doses and wrong unit or route of administration). Absence of date and unclear signature were not considered errors *Secondary outcomes* Severity of medication prescribing errors
Notes	*Period* July 2001 (1 month) *Other* Sample size calculation not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Eighteen days were selected randomly during July 2001 by a computer-generated random number (block randomization)..."

Kozer 2005 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not reported
Baseline characteristics, comparable control sites	Low risk	"There were no significant differences in the patients' acuity (based on triage category on arrival of the ED) or the time at which the order was given with the regular form compared to the new form" "However, in a multiple logistic regression analysis, the level of training of the prescribing physician did not contribute to the increased risk for error"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Two paediatric emergency physicians, blinded to the form used, reviewed the database and independently decided whether there was an error"
Protection against contamination	High risk	"Before the study commenced, ED staff were oriented to the new forms during research and staff meetings" "Trainees alo attended a short tutorial on the appropriate ordering of drugs before the study commenced"
Incomplete outcome data (attrition bias) All outcomes	Low risk	"In 8 (1%) cases, there was not sufficient information to determine if an error had occurred. These orders were excluded from analysis"
Selective reporting (reporting bias)	Low risk	"The objective of this study was to assess the impact of a structured order sheet on the incidence of medication errors in a paediatric ED" Results on these outcome measures are described
Reliable primary outcome measure(s)	High risk	*Outcome assessment* Incident reporting system "A consensus between reviewers of whether an error had occurred was reached in all but 7 cases. These 7 cases were reviewed by a third paediatrician and the median rank was used"
Other bias	Low risk	No bias reported

Lepee 2012

Methods	Interrupted time series
Participants	*Setting* 2 paediatric wards, together comprising 24 beds, part of an academic health sciences centre, United Kingdom *Patients* The study does not report on participant characteristics *Professionals* Nurses, medical consultants, doctors in training (from 4 months' to over 10 years' expe-

Lepee 2012 (*Continued*)

	rience in paediatrics)
Interventions	Check and correct checklist compared with no such checklist
Outcomes	*Primary outcomes* Technical (prescribing) errors, defined as unclear or missing information on the prescription *Secondary outcomes* Clinical (prescribing) errors, defined as unintentional significant reductions in the probability of treatment being timely and effective, or an increase in the risk of harm when compared with generally accepted practice
Notes	*Period* Pre-intervention from 15 March until 15 May 2011 (2 months, 18 data points) and post-intervention from 23 May until 23 July 2011 (2 months, 18 data points) *Other* Quality of documentation in participants' medical notes as a concurrent control measurement Sample size calculation not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Baseline characteristics, comparable control sites	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	High risk	"A limitation is that the evaluators were not blinded as to whether the data were pre- or post-intervention"
Incomplete outcome data (attrition bias) All outcomes	Low risk	"All patients' drug charts were screened twice weekly during the full study period" "All inpatient drug charts were screened to identify the primary outcome (technical errors)..."
Selective reporting (reporting bias)	Low risk	"The primary outcome was the rate of technical errors" Results on these outcome measures are described
Secular changes	Low risk	"The impact of the intervention was measured using an ITS design, with a concurrent control measurement"
Shape of intervention effect	Low risk	"Our main hypothesis was that the prevalence of the technical errors would be reduced by the implementation of Check and Correct, when compared with any inherent improvement due to increasing prescriber experience"
Intervention unlikely to affect data collection.	Unclear risk	Not reported

Lepee 2012 (*Continued*)

Time series analysis techniques	Low risk	"Error rates for each half-weekly data point were then plotted over time to visually examine temporal trends and formally analyzed using segmented regression analysis whilst adjusting for possible trends in the control data. We checked auto-correlation using the Durban-Watson test and by calculating the (partial) autocorrelation function"
Data collection points and time interval	Low risk	Explained by the corresponding author
Reliable primary outcome measure(s)	Low risk	Outcome assessment by review of all inpatient drug charts "Inter-observer agreement was examined for the primary outcome (technical error), resulting in a Kappa of 0.91, indicating high consistent agreement"
Other bias	Low risk	No bias reported

Morriss 2009

Methods	Controlled before-after study
Participants	*Setting* NICU, part of a university children's hospital, USA *Patients* All 958 patients admitted during the study periods were participants. The gestational age of participants was 34.5 (SD 4.8) weeks *Professionals* Not reported
Interventions	Barcode medication administration system (BCMA, intervention group, 475 participants, 46,308 doses administered) compared with no BCMA (control group, 483 participants, 46,090 doses administered)
Outcomes	*Primary outcomes* Targeted preventable adverse drug events, defined as ADEs that are expected to be prevented by a BCMA system *Secondary outcomes* MEs, defined as errors in ordering, transcribing, dispensing, administering or monitoring a medication Potential MEs, defined as MEs that could have harmed the participant but did not
Notes	*Period* A total of 50 weeks *Other* Researchers calculated that a study during which 92,000 medications were administered could detect a 45% or greater decrease in the primary outcome
Risk of bias	

Morriss 2009 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	"We could not design a blinded, randomized controlled trial of the new medication administration procedure"
Allocation concealment (selection bias)	High risk	"We could not design a blinded, randomized controlled trial of the new medication administration procedure"
Baseline characteristics, comparable control sites	Low risk	"There were small but significant differences only in the proportion of subjects who were twins and in the available nursing/hours/day" "....and we adjusted the analyses for subject and environmental differences that might be confounders"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"....a panel including a neonatologist, 2 pharmacists, and a paediatric clinical pharmacist who were blinded to subject and date identifiers, reviewed out of sequence of all occurrences that the auditors had tentatively designated as either potential ADEs or preventable ADEs"
Protection against contamination	High risk	"The NICU is configured as 2 similar sections; the BCMA system was installed in each room of 1 section for the portion of the study when only some of the beds were BCMA system-equipped"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	Results on targeted preventable ADEs (primary outcome) and MEs (secondary outcome) are reported
Reliable primary outcome measure(s)	Low risk	Outcome assessment by review of the medical records (using triggers) and voluntary incident reports "The inter-observer agreement K calculation was 0.82 for detection of MEs by the 2 auditors"
Other bias	Low risk	No bias reported

Walsh 2008

Methods	Interrupted time series
Participants	*Setting* PICU, NICU and surgical and medical paediatric wards, part of an urban medical centre, United States of America *Patients* A random sample of 627 admissions. Median age of participants was 4 years; participants

	had different racial/ethnic backgrounds and diagnoses, and median length of stay was 3 days *Professionals* Paediatric nurses and paediatricians
Interventions	Computerised physician order entry system (CPOE) compared with handwritten orders
Outcomes	*Primary outcomes* Non-intercepted serious MEs, defined as MEs that caused harm or had substantial potential to cause harm and were not caught by hospital staff *Secondary outcomes* Preventable adverse drug events, defined as MEs that resulted in patient harm
Notes	*Period* Pre-intervention from September 2001 until March 2002 (7 months, 7 data collection points, 275 participants) and post-intervention from September 2002 until May 2003 (9 months, 9 data collection points, 352 participants) *Other* Sample size calculation not reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Baseline characteristics, comparable control sites	High risk	"The number of NICU admissions increased after CPOE implementation, although not statistically significantly. The rate of NICU admissions was smaller than in other units, so this increase would have biased the study toward inflating the effect of CPOE"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"All components of the inpatient record, ..., were reviewed for possible MEs and possible adverse drug events by trained paediatric nurses who were unaware of the study objectives. Nurses then presented a description of possible MEs to 2 paediatricians who were unaware of whether the possible errors occurred before or after CPOE"
Incomplete outcome data (attrition bias) All outcomes	Low risk	"Nine charts before CPOE and 20 charts after CPOE were incomplete (0.3% and 5.7% after, p=.2). An additional 5 charts before CPOE and 8 charts after CPOE were excluded because many parts were missing at the time of the review, making adequate review impossible"
Selective reporting (reporting bias)	Low risk	"The primary study outcome was the rate of non-intercepted serious medication errors per 1000 patient-days" "Time-series regression analysis indicated a statistically significant 7% drop in the level of rates of non-intercepted serious medication errors (p=0.0495) after implementation of CPOE"

Walsh 2008 (*Continued*)

Secular changes	Low risk	"The hospital did not implement any other major systemic change at the time of implementation of CPOE"
Shape of intervention effect	Low risk	"At the time of the study design, we considered it possible that the CPOE system might have more of an effect the longer it was in use or might have a good impact initially with less impact over time"
Intervention unlikely to affect data collection.	Low risk	Data collection was the same in the pre-intervention and post-intervention periods
Time series analysis techniques	Low risk	"We used linear, interrupted time-series analysis to estimate sudden changes in levels or trends in the time series of the study outcome" "We controlled for auto-correlation by assuming the first-order autoregressive process (correlation between 2 consecutive observations), and used residual analysis to test the adequacy of the resulting models"
Data collection points and time interval	Low risk	"Identical months were included in the pre-CPOE and post-CPOE sampling frame to control for seasonal effects on errors rates with two additional months in the post-CPOE period"
Reliable primary outcome measure(s)	High risk	Outcome assessment by review of inpatient records and voluntary incident reports "Inter-rater reliability scores for paediatrician judgments during the review were calculated using K scores. Inter-rater reliability for judgments about the classification of the possible error was 0.7 (95% CI 0.68-0.84), about the severity of the error was 0.4 (95% CI 0.26-0.57) and about the preventability of the error was 0.8 (95% CI 0.67-0.82)"
Other bias	Low risk	No bias reported

Zhang 2012

Methods	Randomised controlled trial
Participants	*Setting* Paediatric wards, part of a university hospital, China *Patients* Children from birth to 18 years old, with nervous system, respiratory system or digestive system diseases. In total, 150 participants were included, 76 in the intervention group and 74 in the control group. In both groups, most participants (70% and 69%) were younger than 5 years of age *Professionals* Not reported

Zhang 2012 (*Continued*)

Interventions	Clinical pharmacist compared with the traditional medical model
Outcomes	*Primary outcomes* Interventions by clinical pharmacists, adverse drug reactions (side effects), length of stay and costs of drugs and hospitalisation *Secondary outcomes* Medication compliance rate after discharge and readmission rate
Notes	*Period* From December 1, 2010, until March 31, 2011 (4 months) *Other* No definitions of outcomes reported Researchers calculated a sample size of 160 participants, with 80 in each group

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Randomization was completed by SPSS 16.0-generated algorithm"
Allocation concealment (selection bias)	Low risk	"Treating assignments, kept in sealed opaque envelopes with only number labeled, were opened after patient gave their informed consents. One of the two clinical pharmacists distributed envelopes and recorded patients in each group enrollment and patient assignment"
Baseline characteristics, comparable control sites	Low risk	"There were no significant differences between the two groups"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Patients and clinical pharmacists were aware of the interventions while the trial research assistants and statisticians responsible for the outcome recording and data analysis, respectively, were blinded to treatment assignment"
Protection against contamination	High risk	"First, clinical pharmacists did not participate in treatment of patients in the control group, but in fact, clinical pharmacists also provided suggestions for patients in the control group when the physicians consulted them, which led to contamination and interference of results of the two groups"
Incomplete outcome data (attrition bias) All outcomes	Low risk	"In the experimental group, after two patients gave up treatment and another two were transferred to another department, only 76 patients received clinical pharmacists' intervention. In the control group, after four patients gave up treatment and another two were transferred

Zhang 2012 (*Continued*)

		to another department, only 74 patients received usual care"
Selective reporting (reporting bias)	Low risk	Primary and secondary outcomes are clearly defined and reported
Reliable primary outcome measure(s)	Low risk	Criteria not used
Other bias	Low risk	No bias reported

ADE: adverse drug event.
BCMA: barcode medication administration.
CBA: controlled before-after study.
CPOE: computerised physician order entry.
ED: emergency department.
ICU: intensive care unit.
ME: medication error.
NICU: newborn intensive care unit.
PICU: paediatric intensive care unit.
SD: standard deviation.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Balaguer Santamaria 2001	Non-clinical, but test situation
Burgess 2009	Non-clinical, but test situation
Burmester 2008	Before-after design without control group
Ching 2014	No data on hospitalised children
Cunningham 2008	Medication safety is not the aim of the intervention
Dehghan-Nayeri 2013	Before-after design without control group
Elsaid 2013	No data on hospitalised children
Frush 2004	Non-clinical, but test situation, no hospital setting
Frush 2006	Non-clinical, but test situation
Gazarian 2012	Before-after design without control group

(*Continued*)

Hixson 2009	Non-clinical, but test situation
Hohenhaus 2008	Non-clinical, but test situation
Nguyen 2014	Controlled before-after design with 1 intervention and 1 control group
Niemann 2014	Before-after design without control group
Niemann, Bertsche 2014	Before-after design without control group
Ramsay 2014	No data on hospitalised children
Senner 2010	Before-after design without control group
Vaidya 2006	Non-clinical, but test situation
Yamamoto 2010	Non-clinical, but test situation
Yin 2008	Non-clinical, but test situation, no hospital setting
Yin 2011	Non-clinical, but test situation, no hospital setting

Characteristics of ongoing studies *[ordered by study ID]*

Kaushal

Trial name or title	Serious medication errors in paediatrics: evaluation of prevention strategies
Methods	Prospective cohort study
Participants	Children admitted to Children's Hospital and Brigham and Women's Hospital
Interventions	The purpose of this study is to determine how effective ward-based clinical pharmacists and computerised physician order entry systems are in reducing serious medication errors (MEs) in paediatric inpatients
Outcomes	Serious medication errors
Starting date	February 2000
Contact information	rkaushal@partners.org http://clinicaltrials.gov/show/NCT00153205
Notes	Estimate of reporting date: unknown

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. MEDLINE search strategy

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>, Ovid MEDLINE(R) Daily Update <October 29, 2013>

1 (preventable adverse drug or medication related adverse event?).ti. [Screen all] (37)
2 Medication errors/ or Inappropriate Prescribing/ (10960)
3 (medication safety or medication incident? or medication error?).ti,ab. (3989)
4 ((pharmacist? or prescrib$ or prescription? or dispens$ or dosing) adj2 (error? or mistake? or miscalculat$)).ti,ab. (1404)
5 (medication? adj2 misadventure?).ti,ab. (40)
6 ((inappropriate adj3 (prescription? or medication?)) or ((appropriat$ or inappropriat$ or optimal) adj2 prescrib$)).ti,ab. (2743)
7 effective prescribing practice?.ti,ab. (6)
8 medication reconciliation/ [...done to avoid medication errors.] (264)
9 (quality improv$ and (prescrib$ or prescript$ or dosing)).ti. (32)
10 ((weight-based or surface-based or weight independent) adj2 (prescrib$ or dose or dosing or dosage?)).ti,ab. and (safety or error?).ti,hw. (59)
11 ((drug? or medication? or medicine? or dose or dosage? or dosing) adj2 wrong$).ti,ab. (402)
12 (medication? adj2 (reconciliation? or audit? or quality improvement)).ti. (269)
13 (accident$ adj2 overdose?).ti,ab. (450)
14 (near miss or near misses).ti,ab. (1266)
15 ((excess$ or inadequat$) adj2 (dosage? or dose? or dosing)).ti,ab. (2207)
16 ("medication related" adj2 (problem? or issue? or hospitali?ation? or mortal$ or morbid$ or illness$ or condition?)).ti,ab. (299)
17 Medical Order Entry Systems/ and (prescript$ or prescrib$).ti,hw. (374)
18 Decision Support Systems, Clinical/ and (prescrib*.ti,hw. or medication?.ti. or *drug therapy/) (327)
19 "Drug Therapy, Computer-Assisted"/ and (safety or error?).ti. (125)
20 Electronic prescribing/ and (safety or error? or improv$).ti. (115)
21 (prevent$ and (error? or (adverse adj2 event?))).ti. and (dosing or drug? or medication? or prescript$ or prescrib$).ti,hw. (505)
22 ((drug? or medication? or prescrib$) adj3 error?).ti. and ((prevent$ or reduce? or reducing).ti. or pc.fs.) (1090)
23 "Pharmaceutical Preparations"/ae and (prevent$.ti. or (prevention or preventing).hw.) (187)
24 (Pharmaceutical preparations/ or Drug Therapy/ or exp Drug Administration Routes/ or exp Drug administration schedule/ or exp drug delivery systems/ or drug dosage calculations/ or exp drug prescriptions/ or exp drug therapy, Combination/ or Drug Therapy, Computer-assisted/) and (error? or mistake or mistakes or prevent$ adverse).ti. (1418)
25 (Medication Systems, Hospital/ or Pharmacy Service, Hospital/) and ((error? or mistake or mistakes or prevent$ adverse).ti. or ((prevent$ or reduce? or reducing) adj2 (error? or adverse event? or adverse drug event? or medication related problem?)).ab.) (921)
26 (exp therapeutic uses/ or exp anti-infective agents/ or exp anti-bacterial agents/) and (((prevent$ or reduce? or reducing) and (error? or (adverse$ adj3 event?))) or (inappropriat$ adj2 "use")).ti. (358)
27 Medical errors/pc and (medication? or drug?).ti,ab. (415)
28 (exp therapeutic uses/ or exp anti-infective agents/ or exp anti-bacterial agents/) and Medical Errors/ (403)
29 (Pharmaceutical preparations/ or Drug Therapy/ or exp Drug Administration Routes/ or exp Drug administration schedule/ or exp drug delivery systems/ or drug dosage calculations/ or exp drug prescriptions/ or exp drug therapy, Combination/ or Drug Therapy, Computer-assisted/) and Medical Errors/ (369)
30 (prevent$ adverse drug or (causes adj2 (prescri$ error? or medication? error?)) or medication related adverse).ti,ab. (396)
31 Medication errors/pc or Inappropriate Prescribing/pc (4775)

32 or/2-31 [Med Errors] (21118)
33 exp Hospitals/ (200382)
34 perioperative care/ or intraoperative care/ or postoperative care/ or perioperative period/ or intraoperative period/ or postoperative period/ or preoperative period/ or Pain, Postoperative/ (140684)
35 exp Hospitalization/ (159154)
36 exp Personnel, Hospital/ (77788)
37 hospital$.ti. or ("in hospital?" or hospitali$).ab. (379338)
38 or/33-37 [Hosptials, Hospitalization General] (753824)
39 Intensive Care Units, Pediatric/ or Intensive Care, Neonatal/ or Intensive Care Units, Neonatal/ or Hospitals, Pediatric/ (25940)
40 Pediatric Nursing/ or Neonatal Nursing/ or Neonatology/ or Perinatology/ (18628)
41 ((p?ediatric? or children? or neonatal or infant?) adj3 (hospital? or ICU or intensive care or care unit or department?)).ti,ab. (53874)
42 or/39-41 [Pediatric Hospitals] (80991)
43 exp child/ or adolescent/ (2429627)
44 (child or children or child? or newborn? or p?ediatric? or infant? or neonate? or teenager? or teens or adolescent? or baby or babies).ti,ab. (1397185)
45 Pediatrics/ or Adolescent Medicine/ (40945)
46 Neonatology/ or Perinatology/ (3531)
47 or/43-46 [Child/Pediatrics] (3004657)
48 exp Adults/ (5618048)
49 exp Residential Facilities/ (43206)
50 (elderly or nursing home?).ti,ab. or geriatric?.ti,ab,hw. or adult?.ti. (456222)
51 or/48-50 [Adults, Elderly, Nursing Homes non-hospital facilities] (5759432)
52 (cocaine or cannabis or marijuana or drug abuse or street drug?).ti,ab,hw. [Terms to exclude] (70327)
53 32 and 38 and 47 [Med Errors & Hospitals & Child/Pediatrics] (761)
54 (32 and 42) not 53 [Med Errors & Pediatric Units/Hospitals] (338)
55 (32 and 38) not 51 not (or/53-54) [Med Errors & Hospitals not Adults] (2471)
56 (or/53-55) not 52 [Results before Filters--illicit drug terms excluded] (3566)
57 (randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti. (897270)
58 exp animals/ not humans.sh. (4055578)
59 57 not 58 [Cochrane RCT Filter 6.4.d Sens/Precision Maximizing--placebo removed] (833187)
60 intervention?.ti. or (intervention? adj6 (clinician? or collaborat$ or community or complex or DESIGN$ or doctor? or educational or family doctor? or family physician? or family practitioner? or financial or GP or general practice? or hospital? or impact? or improv$ or individuali?e? or individuali?ing or interdisciplin$ or multicomponent or multi-component or multidisciplin$ or multi-disciplin$ or multifacet$ or multi-facet$ or multimodal$ or multi-modal$ or personali?e? or personali?ing or pharmacies or pharmacist? or pharmacy or physician? or practitioner? or prescrib$ or prescription? or primary care or professional$ or provider? or regulatory or regulatory or tailor$ or target$ or team$ or usual care)).ab. (166583)
61 (pre-intervention? or preintervention? or "pre intervention?" or post-intervention? or postintervention? or "post intervention?").ti,ab. [added 2.4] (10314)
62 (hospital$ or patient?).hw. and (study or studies or care or health$ or practitioner? or provider? or physician? or nurse? or nursing or doctor?).ti,hw. (721910)
63 demonstration project?.ti,ab. (1989)
64 (pre-post or "pre test$" or pretest$ or posttest$ or "post test$" or (pre adj5 post)).ti,ab. (65937)
65 (pre-workshop or post-workshop or (before adj3 workshop) or (after adj3 workshop)).ti,ab. (610)
66 trial.ti. or ((study adj3 aim?) or "our study").ab. (635247)
67 (before adj10 (after or during)).ti,ab. (363594)
68 ("quasi-experiment$" or quasiexperiment$ or "quasi random$" or quasirandom$ or "quasi control$" or quasicontrol$ or ((quasi$ or experimental) adj3 (method$ or study or trial or design$))).ti,ab,hw. [ML] (104652)
69 ("time series" adj2 interrupt$).ti,ab,hw. [ML] (1192)
70 (time points adj3 (over or multiple or three or four or five or six or seven or eight or nine or ten or eleven or twelve or month$ or hour? or day? or "more than")).ab. (9441)
71 pilot.ti. (40033)
72 Pilot projects/ [ML] (84176)

73 (clinical trial or controlled clinical trial or multicenter study).pt. [ML] (650503)
74 (multicentre or multicenter or multi-centre or multi-center).ti. (29891)
75 random$.ti,ab. or controlled.ti. (781262)
76 (control adj3 (area or cohort? or compare? or condition or design or group? or intervention? or participant? or study)).ab. not (controlled clinical trial or randomized controlled trial).pt. [ML] (413431)
77 "comment on".cm. or review.ti,pt. or randomized controlled trial.pt. [ML] (2964738)
78 (rat or rats or cow or cows or chicken? or horse or horses or mice or mouse or bovine or animal?).ti. (1370441)
79 exp animals/ not humans.sh. [ML] (4055578)
80 (or/60-76) not (or/77-79) [EPOC Methods Filter 2.4 Medline] (2156894)
Results from search conducted 29 October 2013
81 56 and 59 [RCT Results] (182)
82 (56 and 80) not 81 [EPOC Filter Results] (2131)
83 ((1 and (or/42,47)) or (1 not 51)) not (or/81-82) [KW Results] (11)
84 "2013".ep,ed,yr. (789818)
85 ("201211$" or "201212$").ed,ep. [Nov-Dec 2012] (259202)
86 (or/81-83) and (or/84-85) [Update results Nov 2012 to Oct 29, 2013] (144)
Results from search conducted October 2012
81 56 and 59 [RCT Results] (145)
82 (56 and 80) not 81 [EPOC Filter Results] (1837)
83 ((1 and (or/42,47)) or (1 not 51)) not (or/81-82) [KW Results] (13)

Appendix 2. EMBASE strategy

EMBASE Classic + EMBASE <1947 to 29 October 2013>
1 (preventable adverse drug or medication related adverse event?).ti. (50)
2 effective prescribing practice?.ti,ab. (8)
3 medication related adverse.ti. (10)
4 or/1-3 [KW] (59)
5 medication error/ (12229)
6 inappropriate prescribing/ (897)
7 (medication safety or medication incident? or medication error?).ti,ab. (5767)
8 "inappropriate use".ti. and (drug?.hw,ti. or medication?.ti.) (147)
9 ((pharmacist? or prescrib$ or prescription? or dispens$ or dosing) adj2 (error? or mistake? or miscalculat$)).ti,ab. (2096)
10 (medication? adj2 misadventure?).ti,ab. (65)
11 ((inappropriate adj3 (prescription? or medication?)) or ((appropriat$ or inappropriat$ or optimal) adj2 prescrib$)).ti,ab. (3904)
12 medication therapy management/ [includes med reconciliation] (1975)
13 (quality improv$ and (prescrib$ or prescript$ or dosing)).ti. (36)
14 ((weight-based or surface-based or weight independent) adj2 (prescrib$ or dose or dosing or dosage?)).ti,ab. and (safety or error?).ti,hw. (187)
15 ((drug? or medication? or medicine? or dose or dosage? or dosing) adj2 wrong$).ti,ab. (675)
16 (medication? adj2 (reconciliation? or audit? or quality improvement)).ti. (428)
17 (accident$ adj2 overdose?).ti,ab. (545)
18 (near miss or near misses).ti,ab. (1721)
19 ((excess$ or inadequat$) adj2 (dosage? or dose? or dosing)).ti,ab. (3594)
20 ("medication related" adj2 (problem? or issue? or hospitali?ation? or mortal$ or morbid$ or illness$ or condition?)).ti,ab. (419)
21 ("drug use"/ or prescription/) and medical error/ [EM] (544)
22 hospital pharmacy/ and (medical error/ or error?.ti. or preventable.ti. or preventing.ti.) [EM] (403)
23 Decision Support System/ and "drug use"/ [EM] (79)
24 decision support system/ and (prescrib$.ti,hw. or medication?.ti.) (429)
25 computer assisted drug therapy/ and (safety or error?).ti. [EM] (66)
26 Electronic prescribing/ and (safety or error? or improv$).ti. [EM] (168)
27 (prevent$ and (error? or (adverse adj2 event?))).ti. and (dosing or drug? or medication? or prescript$ or prescrib$).ti,hw. (750)

28 ((drug? or medication? or prescrib$) adj3 error?).ti. and ((prevent$ or reduce? or reducing).ti. or pc.fs.) (1087)
29 drug/ and (error? or mistake or mistakes or prevent$ adverse).ti. (270)
30 drug/ and inappropriat$.ti. (48)
31 drug/ae and prevent$.ti. (106)
32 decision support system/ and drug/ (55)
33 drug/ and medical error/ (54)
34 exp drug/ and medical error/ (184)
35 medication? related adverse.ab. (104)
36 (prescrib$ or drug therapy or medication management).ti. and patient safety.ti,hw. (344)
37 or/5-36 [Med Errors] (28760)
38 *medication therapy management/ or (quality improv$ and (prescrib$ or prescript$ or dosing)).ti. (1021)
39 ((weight-based or surface-based or weight independent) adj2 (prescrib$ or dose or dosing or dosage?)).ti,ab. and (safety or error?).ti,hw. (187)
40 ((drug? or medication? or medicine? or dose or dosage? or dosing) adj2 wrong$).ti,ab. (675)
41 ((excess$ or inadequat$) adj2 (dosage? or dose? or dosing)).ti,ab. and (prevent$.ti. or prevent?ble.ab.) (83)
42 ("medication related" adj2 (problem? or issue? or hospitali?ation? or mortal$ or morbid$ or illness$ or condition?)).ti,ab. (419)
43 ((*"drug use"/ or *prescription/) and *medical error/) or (*hospital pharmacy/ and (*medical error/ or error?.ti. or preventable.ti. or preventing.ti.)) or (*Decision Support System/ and *"drug use"/) or (*decision support system/ and (prescrib$.ti,hw. or medication? .ti.)) or (*computer assisted drug therapy/ and (safety or error?).ti.) or (*Electronic prescribing/ and (safety or error? or improv$).ti.) or ((prevent$ and (error? or (adverse adj2 event?))).ti. and (dosing or drug? or medication? or prescript$ or prescrib$).ti,hw.) or (((drug? or medication? or prescrib$) adj3 error?).ti. and ((prevent$ or reduce? or reducing).ti. or pc.fs.)) or (exp *drug/ and (error? or mistake or mistakes or prevent$ adverse).ti.) or (*drug/ and inappropriat$.ti.) or (*drug/ae and prevent$.ti.) (2145)
44 (*decision support system/ and exp *drug/) or (exp *drug/ and *medical error/) or medication? related adverse.ab. or ((prescrib$ or drug therapy or medication management).ti. and patient safety.ti,hw.) (480)
45 medication error/ and (patient safety/ or accident prevention/) (1450)
46 ((medication safety or medication error?) adj4 (improv$ or reduce? or reducing or implement$ or prevent$)).ab. (1319)
47 (medication? adj2 misadventure?).ti,ab. (65)
48 (accident$ adj2 overdose?).ti,ab. (545)
49 (medication? adj2 (reconciliation? or audit? or quality improvement)).ti. (428)
50 (near miss or near misses).ti,ab. and ((prevent$ or reduc$ or improv$).ti. or pc.fs.) (334)
51 *medication error/ (6397)
52 (medication safety or medication incident? or medication error?).ti,ab. and ((improv$ or reduc$ or implement$ or prevent$).ti. or pc.fs.) (1951)
53 or/38-52 [Med Errors focussed] (12390)
54 hospital/ or community hospital/ or general hospital/ or geriatric hospital/ or hospital building/ or "hospital subdivisions and components"/ or magnet hospital/ or mental hospital/ or non profit hospital/ or private hospital/ or public hospital/ or exp teaching hospital/ (429959)
55 hospital$.ti. or hospitali$.ab. (455496)
56 hospital patient/ (72915)
57 inpatient?.ti,ab. (88179)
58 or/54-57 [Hospital] (829280)
59 adult/ or exp aged/ or middle aged/ or geriatrics/ (5637241)
60 (adult? or elder$ or geriatric$).ti. (400955)
61 or/59-60 [Adult] (5748674)
62 hospitalized adolescent/ (371)
63 pediatric hospital/ (12115)
64 or/62-63 [Pediatric hospital] (12484)
65 pediatrics/ or child psychiatry/ or child urology/ or exp neonatology/ (83610)
66 *adolescent/ or juvenile/ (53036)
67 exp child/ or embryo/ or fetus/ or exp newborn/ (2634785)
68 (child$ or infant? or baby or neonat$ or preschool$ or pre-school$ or fetus or fetal or newborn?).ti. (1145250)
69 or/65-68 [Child/pediatrics] (2905568)
70 37 and 58 and 69 [Med Errors & Hosp & Child] (574)

71 (37 and 64) not 69 [Med Errors & Pediatric Hospitals] (60)
72 (37 and 58) not 61 not (or/70-71) [Med Errors & Hospitals not Adult] (3642)
73 controlled clinical trial/ or controlled study/ or randomized controlled trial/ [EM] (4248126)
74 (book or conference paper or editorial or letter or review).pt. not randomized controlled trial/ [Per BMJ Clinical Evidence filter] (4037268)
75 (random sampl$ or random digit$ or random effect$ or random survey or random regression).ti,ab. not randomized controlled trial/ [Per BMJ Clinical Evidence filter] (54329)
76 (animal$ not human$).sh,hw. (3916035)
77 73 not (or/74-76) [Trial filter per BMJ CLinical Evidence] (2804210)
78 intervention?.ti. or (intervention? adj6 (clinician? or collaborat$ or community or complex or DESIGN$ or doctor? or educational or family doctor? or family physician? or family practitioner? or financial or GP or general practice? or hospital? or impact? or improv$ or individuali?e? or individuali?ing or interdisciplin$ or multicomponent or multi-component or multidisciplin$ or multi-disciplin$ or multifacet$ or multi-facet$ or multimodal$ or multi-modal$ or personali?e? or personali?ing or pharmacies or pharmacist? or pharmacy or physician? or practitioner? or prescrib$ or prescription? or primary care or professional$ or provider? or regulatory or regulatory or tailor$ or target$ or team$ or usual care)).ab. (201883)
79 (pre-intervention? or preintervention? or "pre intervention?" or post-intervention? or postintervention? or "post intervention?").ti,ab. [added 2.4] (12654)
80 (hospital$ or patient?).hw. and (study or studies or care or health$ or practitioner? or provider? or physician? or nurse? or nursing or doctor?).ti,hw. (1626348)
81 demonstration project?.ti,ab. (2362)
82 (pre-post or "pre test$" or pretest$ or posttest$ or "post test$" or (pre adj5 post)).ti,ab. (93606)
83 (pre-workshop or post-workshop or (before adj3 workshop) or (after adj3 workshop)).ti,ab. (809)
84 trial.ti. or ((study adj3 aim?) or "our study").ab. (840342)
85 (before adj10 (after or during)).ti,ab. (474598)
86 (time points adj3 (over or multiple or three or four or five or six or seven or eight or nine or ten or eleven or twelve or month$ or hour? or day? or "more than")).ab. (11772)
87 pilot.ti. (49865)
88 (multicentre or multicenter or multi-centre or multi-center).ti. (39260)
89 random$.ti,ab. or controlled.ti. (934044)
90 review.ti. (313223)
91 (animal$ not human$).sh,hw. (3916035)
92 *experimental design/ or *pilot study/ or quasi experimental study/ (7012)
93 ("quasi-experiment$" or quasiexperiment$ or "quasi random$" or quasirandom$ or "quasi control$" or quasicontrol$ or ((quasi$ or experimental) adj3 (method$ or study or trial or design$))).ti,ab. (128839)
94 ("time series" adj2 interrupt$).ti,ab. (1127)
95 (or/78-89,92-94) not (or/90-91) [EPOC Methods Filter 2.4 EMBASE] (3328457)
96 (or/70-72) and 79 [RCT] (69)
97 (53 and 58 and 95) not 61 not (or/70-71,96) [Med Errors Focussed & Hospitals (not Adult) & EPOC Filter] (1362)
98 4 not (or/96-97) [KW] (48)
99 (201244$ or 201245$ or 201246$ or 201247$ or 201248$ or 201249$ or 20125$ or 2013$).em. (1534962)
100 (or/96-98) and 99 [Update results October 30-2013] (226)

EMBASE Classic + EMBASE <1947 to 1 November 2012>

1 (preventable adverse drug or medication related adverse event?).ti. (43)
2 effective prescribing practice?.ti,ab. (8)
3 medication related adverse.ti. (7)
4 or/1-3 [KW] (52)
5 medication error/ (11044)
6 inappropriate prescribing/ (522)
7 (medication safety or medication incident? or medication error?).ti,ab. (5045)
8 "inappropriate use".ti. and (drug?.hw,ti. or medication?.ti.) (131)
9 ((pharmacist? or prescrib$ or prescription? or dispens$ or dosing) adj2 (error? or mistake? or miscalculat$)).ti,ab. (1835)
10 (medication? adj2 misadventure?).ti,ab. (57)
11 ((inappropriate adj3 (prescription? or medication?)) or ((appropriat$ or inappropriat$ or optimal) adj2 prescrib$)).ti,ab. (3387)

12 medication therapy management/ [includes med reconciliation] (1178)
13 (quality improv$ and (prescrib$ or prescript$ or dosing)).ti. (28)
14 ((weight-based or surface-based or weight independent) adj2 (prescrib$ or dose or dosing or dosage?)).ti,ab. and (safety or error?).ti,hw. (157)
15 ((drug? or medication? or medicine? or dose or dosage? or dosing) adj2 wrong$).ti,ab. (596)
16 (medication? adj2 (reconciliation? or audit? or quality improvement)).ti. (341)
17 (accident$ adj2 overdose?).ti,ab. (485)
18 (near miss or near misses).ti,ab. (1480)
19 ((excess$ or inadequat$) adj2 (dosage? or dose? or dosing)).ti,ab. (3403)
20 ("medication related" adj2 (problem? or issue? or hospitali?ation? or mortal$ or morbid$ or illness$ or condition?)).ti,ab. (351)
21 ("drug use"/ or prescription/) and medical error/ [EM] (484)
22 hospital pharmacy/ and (medical error/ or error?.ti. or preventable.ti. or preventing.ti.) [EM] (380)
23 Decision Support System/ and "drug use"/ [EM] (73)
24 decision support system/ and (prescrib$.ti,hw. or medication?.ti.) (366)
25 computer assisted drug therapy/ and (safety or error?).ti. [EM] (61)
26 Electronic prescribing/ and (safety or error? or improv$).ti. [EM] (113)
27 (prevent$ and (error? or (adverse adj2 event?))).ti. and (dosing or drug? or medication? or prescript$ or prescrib$).ti,hw. (701)
28 ((drug? or medication? or prescrib$) adj3 error?).ti. and ((prevent$ or reduce? or reducing).ti. or pc.fs.) (1002)
29 drug/ and (error? or mistake or mistakes or prevent$ adverse).ti. (264)
30 drug/ and inappropriat$.ti. (41)
31 drug/ae and prevent$.ti. (99)
32 decision support system/ and drug/ (49)
33 drug/ and medical error/ (46)
34 exp drug/ and medical error/ (158)
35 medication? related adverse.ab. (89)
36 (prescrib$ or drug therapy or medication management).ti. and patient safety.ti,hw. (286)
37 or/5-36 [Med Errors] (25204)
38 *medication therapy management/ or (quality improv$ and (prescrib$ or prescript$ or dosing)).ti. (652)
39 ((weight-based or surface-based or weight independent) adj2 (prescrib$ or dose or dosing or dosage?)).ti,ab. and (safety or error?).ti,hw. (157)
40 ((drug? or medication? or medicine? or dose or dosage? or dosing) adj2 wrong$).ti,ab. (596)
41 ((excess$ or inadequat$) adj2 (dosage? or dose? or dosing)).ti,ab. and (prevent$.ti. or prevent?ble.ab.) (80)
42 ("medication related" adj2 (problem? or issue? or hospitali?ation? or mortal$ or morbid$ or illness$ or condition?)).ti,ab. (351)
43 ((*"drug use"/ or *prescription/) and *medical error/) or (*hospital pharmacy/ and (*medical error/ or error?.ti. or preventable.ti. or preventing.ti.)) or (*Decision Support System/ and *"drug use"/) or (*decision support system/ and (prescrib$.ti,hw. or medication? .ti.)) or (*computer assisted drug therapy/ and (safety or error?).ti.) or (*Electronic prescribing/ and (safety or error? or improv$).ti.) or ((prevent$ and (error? or (adverse adj2 event?))).ti. and (dosing or drug? or medication? or prescript$ or prescrib$).ti,hw.) or (((drug? or medication? or prescrib$) adj3 error?).ti. and ((prevent$ or reduce? or reducing).ti. or pc.fs.)) or (exp *drug/ and (error? or mistake or mistakes or prevent$ adverse).ti.) or (*drug/ and inappropriat$.ti.) or (*drug/ae and prevent$.ti.) (1965)
44 (*decision support system/ and exp *drug/) or (exp *drug/ and *medical error/) or medication? related adverse.ab. or ((prescrib$ or drug therapy or medication management).ti. and patient safety.ti,hw.) (401)
45 medication error/ and (patient safety/ or accident prevention/) (1199)
46 ((medication safety or medication error?) adj4 (improv$ or reduce? or reducing or implement$ or prevent$)).ab. (1147)
47 (medication? adj2 misadventure?).ti,ab. (57)
48 (accident$ adj2 overdose?).ti,ab. (485)
49 (medication? adj2 (reconciliation? or audit? or quality improvement)).ti. (341)
50 (near miss or near misses).ti,ab. and ((prevent$ or reduc$ or improv$).ti. or pc.fs.) (280)
51 *medication error/ (5854)
52 (medication safety or medication incident? or medication error?).ti,ab. and ((improv$ or reduc$ or implement$ or prevent$).ti. or pc.fs.) (1743)
53 or/38-52 [Med Errors focussed] (10856)

54 hospital/ or community hospital/ or general hospital/ or geriatric hospital/ or hospital building/ or "hospital subdivisions and components"/ or magnet hospital/ or mental hospital/ or non profit hospital/ or private hospital/ or public hospital/ or exp teaching hospital/ (380626)
55 hospital$.ti. or hospitali$.ab. (419860)
56 hospital patient/ (61124)
57 inpatient?.ti,ab. (78306)
58 or/54-57 [Hospital] (747481)
59 adult/ or exp aged/ or middle aged/ or geriatrics/ (5279904)
60 (adult? or elder$ or geriatric$).ti. (370800)
61 or/59-60 [Adult] (5385621)
62 hospitalized adolescent/ (342)
63 pediatric hospital/ (10365)
64 or/62-63 [Pediatric hospital] (10705)
65 pediatrics/ or child psychiatry/ or child urology/ or exp neonatology/ (78627)
66 *adolescent/ or juvenile/ (47978)
67 exp child/ or embryo/ or fetus/ or exp newborn/ (2510845)
68 (child$ or infant? or baby or neonat$ or preschool$ or pre-school$ or fetus or fetal or newborn?).ti. (1088180)
69 or/65-68 [Child/pediatrics] (2766254)
70 37 and 58 and 69 [Med Errors & Hosp & Child] (485)
71 (37 and 64) not 69 [Med Errors & Pediatric Hospitals] (55)
72 (37 and 58) not 61 not (or/70-71) [Med Errors & Hospitals not Adult] (3102)
73 controlled clinical trial/ or controlled study/ or randomized controlled trial/ [EM] (3975625)
74 (book or conference paper or editorial or letter or review).pt. not randomized controlled trial/ [Per BMJ Clinical Evidence filter] (3833563)
75 (random sampl$ or random digit$ or random effect$ or random survey or random regression).ti,ab. not randomized controlled trial/ [Per BMJ Clinical Evidence filter] (47298)
76 (animal$ not human$).sh,hw. (3769775)
77 73 not (or/74-76) [Trial filter per BMJ CLinical Evidence] (2608907)
78 intervention?.ti. or (intervention? adj6 (clinician? or collaborat$ or community or complex or DESIGN$ or doctor? or educational or family doctor? or family physician? or family practitioner? or financial or GP or general practice? or hospital? or impact? or improv$ or individuali?e? or individuali?ing or interdisciplin$ or multicomponent or multi-component or multidisciplin$ or multi-disciplin$ or multifacet$ or multi-facet$ or multimodal$ or multi-modal$ or personali?e? or personali?ing or pharmacies or pharmacist? or pharmacy or physician? or practitioner? or prescrib$ or prescription? or primary care or professional$ or provider? or regulatory or regulatory or tailor$ or target$ or team$ or usual care)).ab. (175395)
79 (pre-intervention? or preintervention? or "pre intervention?" or post-intervention? or postintervention? or "post intervention?").ti,ab. [added 2.4] (10256)
80 (hospital$ or patient?).hw. and (study or studies or care or health$ or practitioner? or provider? or physician? or nurse? or nursing or doctor?).ti,hw. (1445318)
81 demonstration project?.ti,ab. (2221)
82 (pre-post or "pre test$" or pretest$ or posttest$ or "post test$" or (pre adj5 post)).ti,ab. (80422)
83 (pre-workshop or post-workshop or (before adj3 workshop) or (after adj3 workshop)).ti,ab. (682)
84 trial.ti. or ((study adj3 aim?) or "our study").ab. (725507)
85 (before adj10 (after or during)).ti,ab. (439104)
86 (time points adj3 (over or multiple or three or four or five or six or seven or eight or nine or ten or eleven or twelve or month$ or hour? or day? or "more than")).ab. (9904)
87 pilot.ti. (44135)
88 (multicentre or multicenter or multi-centre or multi-center).ti. (34482)
89 random$.ti,ab. or controlled.ti. (840955)
90 review.ti. (286121)
91 (animal$ not human$).sh,hw. (3769775)
92 *experimental design/ or *pilot study/ or quasi experimental study/ (5335)
93 ("quasi-experiment$" or quasiexperiment$ or "quasi random$" or quasirandom$ or "quasi control$" or quasicontrol$ or ((quasi$ or experimental) adj3 (method$ or study or trial or design$))).ti,ab. (119894)

94 ("time series" adj2 interrupt$).ti,ab. (911)
95 (or/78-89,92-94) not (or/90-91) [EPOC Methods Filter 2.4 EMBASE] (2981054)
96 (or/70-72) and 79 [RCT] (51)
97 (53 and 58 and 95) not 61 not (or/70-71,96) [Med Errors Focussed & Hospitals (not Adult) & EPOC Filter] (1167)

Appendix 3. Cochrane Library strategy

EBM Reviews - Cochrane Central Register of Controlled Trials <September 2013>, EBM Reviews - Health Technology Assessment <3rd Quarter 2013>, EBM Reviews - NHS Economic Evaluation Database <3rd Quarter 2013>
--
1 (preventable adverse drug or medication related adverse event?).ti. [Screen all] (1)
2 Medication errors/ or Inappropriate Prescribing/ (172)
3 (medication safety or medication incident? or medication error?).ti,ab. (109)
4 ((pharmacist? or prescrib$ or prescription? or dispens$ or dosing) adj2 (error? or mistake? or miscalculat$)).ti,ab. (89)
5 (medication? adj2 misadventure?).ti,ab. (5)
6 ((inappropriate adj3 (prescription? or medication?)) or ((appropriat$ or inappropriat$ or optimal) adj2 prescrib$)).ti,ab. (165)
7 effective prescribing practice?.ti,ab. (0)
8 medication reconciliation/ [...done to avoid medication errors.] (10)
9 (quality improv$ and (prescrib$ or prescript$ or dosing)).ti. (4)
10 ((weight-based or surface-based or weight independent) adj2 (prescrib$ or dose or dosing or dosage?)).ti,ab. and (safety or error?).ti,hw. (14)
11 ((drug? or medication? or medicine? or dose or dosage? or dosing) adj2 wrong$).ti,ab. (11)
12 (medication? adj2 (reconciliation? or audit? or quality improvement)).ti. (8)
13 (accident$ adj2 overdose?).ti,ab. (8)
14 (near miss or near misses).ti,ab. (12)
15 ((excess$ or inadequat$) adj2 (dosage? or dose? or dosing)).ti,ab. (187)
16 ("medication related" adj2 (problem? or issue? or hospitali?ation? or mortal$ or morbid$ or illness$ or condition?)).ti,ab. (25)
17 Medical Order Entry Systems/ and (prescript$ or prescrib$).ti,hw. (14)
18 Decision Support Systems, Clinical/ and (prescrib*.ti,hw. or medication?.ti. or *drug therapy/) (27)
19 "Drug Therapy, Computer-Assisted"/ and (safety or error?).ti. (7)
20 Electronic prescribing/ and (safety or error? or improv$).ti. (2)
21 (prevent$ and (error? or (adverse adj2 event?))).ti. and (dosing or drug? or medication? or prescript$ or prescrib$).ti,hw. (14)
22 ((drug? or medication? or prescrib$) adj3 error?).ti. and ((prevent$ or reduce? or reducing).ti. or pc.fs.) (26)
23 "Pharmaceutical Preparations"/ae and (prevent$.ti. or (prevention or preventing).hw.) (0)
24 (Pharmaceutical preparations/ or Drug Therapy/ or exp Drug Administration Routes/ or exp Drug administration schedule/ or exp drug delivery systems/ or drug dosage calculations/ or exp drug prescriptions/ or exp drug therapy, Combination/ or Drug Therapy, Computer-assisted/) and (error? or mistake or mistakes or prevent$ adverse).ti. (26)
25 (Medication Systems, Hospital/ or Pharmacy Service, Hospital/) and ((error? or mistake or mistakes or prevent$ adverse).ti. or ((prevent$ or reduce? or reducing) adj2 (error? or adverse event? or adverse drug event? or medication related problem?)).ab.) (19)
26 (exp therapeutic uses/ or exp anti-infective agents/ or exp anti-bacterial agents/) and (((prevent$ or reduce? or reducing) and (error? or (adverse$ adj3 event?))) or (inappropriat$ adj2 "use")).ti. (33)
27 Medical errors/pc and (medication? or drug?).ti,ab. (0)
28 (exp therapeutic uses/ or exp anti-infective agents/ or exp anti-bacterial agents/) and Medical Errors/ (7)
29 (Pharmaceutical preparations/ or Drug Therapy/ or exp Drug Administration Routes/ or exp Drug administration schedule/ or exp drug delivery systems/ or drug dosage calculations/ or exp drug prescriptions/ or exp drug therapy, Combination/ or Drug Therapy, Computer-assisted/) and Medical Errors/ (8)
30 (prevent$ adverse drug or (causes adj2 (prescri$ error? or medication? error?)) or medication related adverse).ti,ab. (31)
31 Medication errors/pc or Inappropriate Prescribing/pc (25)
32 or/2-31 [Med Errors] (764)
33 exp Hospitals/ (2504)
34 perioperative care/ or intraoperative care/ or postoperative care/ or perioperative period/ or intraoperative period/ or postoperative period/ or preoperative period/ or Pain, Postoperative/ (15863)

35 exp Hospitalization/ (10135)
36 exp Personnel, Hospital/ (684)
37 hospital$.ti. or ("in hospital?" or hospitali$).ab. (43791)
38 or/33-37 [Hosptials, Hospitalization General] (61491)
39 Intensive Care Units, Pediatric/ or Intensive Care, Neonatal/ or Intensive Care Units, Neonatal/ or Hospitals, Pediatric/ (885)
40 Pediatric Nursing/ or Neonatal Nursing/ or Neonatology/ or Perinatology/ (241)
41 ((p?ediatric? or children? or neonatal or infant?) adj3 (hospital? or ICU or intensive care or care unit or department?)).ti,ab. (3005)
42 or/39-41 [Pediatric Hospitals] (3576)
43 exp child/ or adolescent/ (91053)
44 (child or children or child? or newborn? or p?ediatric? or infant? or neonate? or teenager? or teens or adolescent? or baby or babies).ti,ab. (65038)
45 Pediatrics/ or Adolescent Medicine/ (414)
46 Neonatology/ or Perinatology/ (28)
47 or/43-46 [Child/Pediatrics] (126443)
48 exp Adults/ (319983)
49 exp Residential Facilities/ (1122)
50 (elderly or nursing home?).ti,ab. or geriatric?.ti,ab,hw. or adult?.ti. (26282)
51 or/48-50 [Adults, Elderly, Nursing Homes non-hospital facilities] (329749)
52 (cocaine or cannabis or marijuana or drug abuse or street drug?).ti,ab,hw. [Terms to exclude] (3529)
53 32 and 38 and 47 [Med Errors & Hospitals & Child/Pediatrics] (34)
54 (32 and 42) not 53 [Med Errors & Pediatric Units/Hospitals] (2)
55 (32 and 38) not 51 not (or/53-54) [Med Errors & Hospitals not Adults] (65)
56 (or/53-55) not 52 [Results before Filters--illicit drug terms excluded] (100)
57 from 56 keep 1-92 [CRCT export no date limits October 2013] (92)

Cochrane Library via Wiley (2012 strategy)

Search conducted: 8/11/2012 16:05:15.736

#1(preventable adverse drug or medication related adverse event?):ti
#2MeSH descriptor: [Medication Errors] this term only
#3MeSH descriptor: [Inappropriate Prescribing] this term only
#4(medication safety or medication incident? or medication error?):ti,ab
#5((pharmacist? or prescrib* or prescription? or dispens* or dosing) near/2 (error? or mistake? or miscalculat*)):ti,ab
#6(medication? near/2 misadventure?):ti,ab
#7((inappropriate near/3 (prescription? or medication?)) or ((appropriat* or inappropriat* or optimal) near/2 prescrib*)):ti,ab
#8effective prescribing practice?:ti,ab
#9MeSH descriptor: [Medication Reconciliation] this term only
#10(quality improv* and (prescrib* or prescript* or dosing)):ti
#11((weight-based or surface-based or weight independent) near/2 (prescrib* or dose or dosing or dosage?)):ti,ab and (safety or error?):ti,kw
#12((drug? or medication? or medicine? or dose or dosage? or dosing) near/2 wrong*):ti,ab
#13(medication? near/2 (reconciliation? or audit? or "quality improvement")):ti
#14(accident* near/2 overdose?):ti,ab
#15("near miss" or "near misses"):ti,ab
#16((excess* or inadequat*) near/2 (dosage? or dose? or dosing)):ti,ab
#17("medication related" near/2 (problem? or issue? or hospitali?ation? or mortal* or morbid* or illness* or condition?)):ti,ab
#18MeSH descriptor: [Medical Order Entry Systems] this term only
#19(prescript* or prescrib*):ti,kw
#20#18 and #19
#21MeSH descriptor: [Decision Support Systems, Clinical] this term only
#22prescrib*:ti,kw or medication?:ti
#23MeSH descriptor: [Drug Therapy] this term only
#24#21 and (#22 or #23)
#25MeSH descriptor: [Drug Therapy, Computer-Assisted] this term only

#26(safety or error?):ti or error?:ab
#27#25 and #26
#28MeSH descriptor: [Electronic Prescribing] this term only
#29(safety or improv*):ti,kw or error?:ti,ab,kw
#30#28 and #29
#31(prevent* and (error? or (adverse near/2 event?))):ti and (dosing or drug? or medication? or prescript* or prescrib*):ti,kw or (prevent* near/3 (error? or (adverse drug event?) or (adverse medication event?))):ab,kw
#32((drug? or medication? or prescrib*) near/3 error?):ti and (prevent* or reduce? or reducing):ti,kw or (((drug? or medication? or prescrib*) near/3 error?) near/4 (prevent* or reduce? or reducing or reduction)):ab,kw
#33MeSH descriptor: [Pharmaceutical Preparations] this term only and with qualifiers: [Adverse effects - AE]
#34(prevent*:ti or ("prevention" or "preventing"):kw)
#35#33 and #34
#36MeSH descriptor: [Pharmaceutical Preparations] this term only
#37MeSH descriptor: [Drug Administration Routes] explode all trees
#38MeSH descriptor: [Drug Administration Schedule] explode all trees
#39MeSH descriptor: [Drug Delivery Systems] explode all trees
#40MeSH descriptor: [Drug Dosage Calculations] this term only
#41MeSH descriptor: [Drug Prescriptions] explode all trees
#42MeSH descriptor: [Drug Therapy, Combination] explode all trees
#43(error? or mistake or mistakes or prevent* adverse):ti or error?:ab
#44(#23 or #25 or #36 or #37 or #38 or #39 or #40 or #41 or #42) and #43
#45MeSH descriptor: [Medication Systems, Hospital] this term only
#46MeSH descriptor: [Pharmacy Service, Hospital] this term only
#47((error? or mistake or mistakes or prevent* adverse):ti or ((prevent* or reduce? or reducing) near/2 (error? or adverse event? or adverse drug event? or medication related problem?)):ab) or ERROR?:ab
#48(#45 or #46) and #47
#49MeSH descriptor: [Therapeutic Uses] explode all trees
#50MeSH descriptor: [Anti-Infective Agents] explode all trees
#51MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#52(((prevent* or reduce? or reducing or PRESCRIB*) and (error? or (adverse* near/3 event?))) or (inappropriat* near/2 "use")):ti or ERROR?:ab
#53(#49 or #50 or #51) and #52
#54MeSH descriptor: [Medical Errors] explode all trees
#55(medication? or drug?):ti,ab,kw
#56#54 and #55
#57MeSH descriptor: [Medical Errors] this term only
#58(#49 or #50 or #51) and #57
#59(#23 or #25 or #36 or #37 or #38 or #39 or #40 or #41 or #42) and #57
#60(prevent* adverse drug or (causes near/2 (prescri* error? or medication? error?)) or medication related adverse):ti,ab
#61MeSH descriptor: [Medication Errors] explode all trees and with qualifiers: [Prevention & control - PC]
#62MeSH descriptor: [Inappropriate Prescribing] this term only and with qualifiers: [Prevention & control - PC]
#63#2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #20 or #24 or #27 or #30 or #31 or #32 or #35 or #44 or #48 or #53 or #56 or #58 or #59 or #60 or #61 or #62
#64MeSH descriptor: [Hospitals] explode all trees
#65MeSH descriptor: [Perioperative Care] this term only
#66MeSH descriptor: [Intraoperative Care] this term only
#67MeSH descriptor: [Postoperative Care] this term only
#68MeSH descriptor: [Perioperative Period] this term only
#69MeSH descriptor: [Intraoperative Period] this term only
#70MeSH descriptor: [Postoperative Period] this term only
#71MeSH descriptor: [Preoperative Period] this term only
#72MeSH descriptor: [Pain, Postoperative] this term only
#73MeSH descriptor: [Hospitalization] explode all trees

#74MeSH descriptor: [Personnel, Hospital] explode all trees
#75hospital*:ti or ("in hospital?" or hospitali*):ab
#76#64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75
#77MeSH descriptor: [Intensive Care Units, Pediatric] this term only
#78MeSH descriptor: [Intensive Care, Neonatal] this term only
#79MeSH descriptor: [Intensive Care Units, Neonatal] this term only
#80MeSH descriptor: [Hospitals, Pediatric] this term only
#81MeSH descriptor: [Pediatric Nursing] this term only
#82MeSH descriptor: [Neonatal Nursing] this term only
#83MeSH descriptor: [Neonatology] this term only
#84MeSH descriptor: [Perinatology] this term only
#85((p?ediatric? or children? or neonatal or infant?) near/3 (hospital? or ICU or intensive care or care unit or department?)):ti,ab
#86#77 or #78 or #79 or #80 or #81 or #82 or #83 or #84 or #85
#87MeSH descriptor: [Child] explode all trees
#88MeSH descriptor: [Adolescent] this term only
#89(child or children or child? or newborn? or p?ediatric? or infant? or neonate? or teenager? or teens or adolescent? or baby or babies):ti,ab
#90MeSH descriptor: [Pediatrics] this term only
#91MeSH descriptor: [Adolescent Medicine] this term only
#92#83 or #84 or #87 or #88 or #89 or #90 or #91
#93MeSH descriptor: [Adult] explode all trees
#94MeSH descriptor: [Residential Facilities] explode all trees
#95(elderly or nursing home?):ti,ab or geriatric?:ti,ab,kw or adult?:ti
#96#93 or #94 or #95
#97(cocaine or cannabis or marijauna or drug abuse or street drug?):ti,ab,kw
#98#63 and #76 and #92
#99(#63 and #86) not #98
#100(#63 and #76) not #96
#101(#98 or #99 or #100)

Appendix 4. CINAHL strategy

	#	Query
Results		S88 or s89 or S90 and Published Date: 20121001-20131031 [October 2013 update]
37	S90	((S1 and (S39 or S44)) or (S1 not S48)) NOT (S88 or S89) [November 6, 2012]
17	S89	(S53 and S87) NOT S88 [November 6, 2012]
297	S88	S53 and S62 [November 6, 2012]
72	S87	S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70 or S71 or S72 or S73 or S74 or S75 or S76 or S77 or S78 or S79 or S80 or S81 or S82 or S83 or S84 or S85 or S86
378026	S86	TI ((time points n3 over) or (time points n3 multiple) or (time points n3 three) or (time points n3 four) or (time points n3 five) or (time points n3 six) or (time points n3 seven) or (time points n3 eight) or (time points n3 nine) or (time points n3 ten) or (time points n3 eleven) or (time points n3 twelve) or (time points n3 month*) or (time points n3 hour*) or (time points n3 day*) or (time points n3 "more than")) or AB ((time points n3 over) or (time

(*Continued*)

		points n3 multiple) or (time points n3 three) or (time points n3 four) or (time points n3 five) or (time points n3 six) or (time points n3 seven) or (time points n3 eight) or (time points n3 nine) or (time points n3 ten) or (time points n3 eleven) or (time points n3 twelve) or (time points n3 month*) or (time points n3 hour*) or (time points n3 day*) or (time points n3 "more than"))
1346	S85	TI ((control w3 area) or (control w3 cohort*) or (control w3 compar*) or (control w3 condition) or (control w3 group*) or (control w3 intervention*) or (control w3 participant*) or (control w3 study)) or AB ((control w3 area) or (control w3 cohort*) or (control w3 compar*) or (control w3 condition) or (control w3 group*) or (control w3 intervention*) or (control w3 participant*) or (control w3 study))
41092	S84	TI (multicentre or multicenter or multi-centre or multi-center) or AB random*
88053	S83	TI random* OR controlled
29899	S82	TI (trial or (study n3 aim) or "our study") or AB ((study n3 aim) or "our study")
73171	S81	TI (pre-workshop or preworkshop or post-workshop or postworkshop or (before n3 workshop) or (after n3 workshop)) or AB (pre-workshop or preworkshop or post-workshop or postworkshop or (before n3 workshop) or (after n3 workshop))
281	S80	TI (demonstration project OR demonstration projects OR preimplement* or pre-implement* or post-implement* or postimplement*) or AB (demonstration project OR demonstration projects OR preimplement* or pre-implement* or post-implement* or postimplement*)
1189	S79	(intervention n6 clinician*) or (intervention n6 community) or (intervention n6 complex) or (intervention n6 design*) or (intervention n6 doctor*) or (intervention n6 educational) or (intervention n6 family doctor*) or (intervention n6 family physician*) or (intervention n6 family practitioner*) or (intervention n6 financial) or (intervention n6 GP) or (intervention n6 general practice*) Or (intervention n6 hospital*) or (intervention n6 impact*) Or (intervention n6 improv*) or (intervention n6 individualize*) Or (intervention n6 individualise*) or (intervention n6 individualizing) or (intervention n6 individualising) or (intervention n6 interdisciplin*) or (intervention n6 multicomponent) or (intervention n6 multi-component) or (intervention n6 multidisciplin*) or (intervention n6 multi-disciplin*) or (intervention n6 multifacet*) or (intervention n6 multi-facet*) or (intervention n6 multimodal*) or (intervention n6 multi-modal*) or (intervention n6 personalize*) or(intervention n6 personalise*) or (intervention n6 personalizing) or (intervention n6 personalising) or (intervention n6 pharmaci*) or (intervention n6 pharmacist*) or (intervention n6 pharmacy) or (intervention n6 physician*) or (intervention n6 practitioner*) Or (intervention n6 prescrib*) or (intervention n6 prescription*) or (intervention n6 primary care) or (intervention n6 professional*) or (intervention* n6 provider*) or (intervention* n6 regulatory) or (intervention n6 regulatory) or (intervention n6 tailor*) or (intervention n6 target*) or (intervention n6 team*) or (intervention n6 usual care)
36531	S78	TI (collaborativ* or collaboration* or tailored or personalised or personalized) or AB (collaborativ* or collaboration* or tailored or personalised or personalized)
33670	S77	TI pilot
10254	S76	(MH "Pilot Studies")
26470	S75	AB "before-and-after"
15258	S74	AB time series

(*Continued*)

1564	S73	TI time series
218	S72	AB (before* n10 during or before n10 after) or AU (before* n10 during or before n10 after)
28931	S71	TI ((time point*) or (period* n4 interrupted) or (period* n4 multiple) or (period* n4 time) or (period* n4 various) or (period* n4 varying) or (period* n4 week*) or (period* n4 month*) or (period* n4 year*)) or AB ((time point*) or (period* n4 interrupted) or (period* n4 multiple) or (period* n4 time) or (period* n4 various) or (period* n4 varying) or (period* n4 week*) or (period* n4 month*) or (period* n4 year*))
44078	S70	TI ((quasi-experiment* or quasiexperiment* or quasi-random* or quasirandom* or quasi control* or quasicontrol* or quasi* W3 method* or quasi* W3 study or quasi* W3 studies or quasi* W3 trial or quasi* W3 design* or experimental W3 method* or experimental W3 study or experimental W3 studies or experimental W3 trial or experimental W3 design*)) or AB ((quasi-experiment* or quasiexperiment* or quasi-random* or quasirandom* or quasi control* or quasicontrol* or quasi* W3 method* or quasi* W3 study or quasi* W3 studies or quasi* W3 trial or quasi* W3 design* or experimental W3 method* or experimental W3 study or experimental W3 studies or experimental W3 trial or experimental W3 design*))
10858	S69	TI pre w7 post or AB pre w7 post
7993	S68	MH "Multiple Time Series" or MH "Time Series"
1198	S67	TI ((comparative N2 study) or (comparative N2 studies) or evaluation study or evaluation studies) or AB ((comparative N2 study) or (comparative N2 studies) or evaluation study or evaluation studies)
9367	S66	MH Experimental Studies or Community Trials or Community Trials or Pretest-Posttest Design + or Quasi-Experimental Studies + Pilot Studies or Policy Studies + Multicenter Studies
30633	S65	TI (pre-test* or pretest* or posttest* or post-test*) or AB (pre-test* or pretest* or posttest* or "post test*) OR TI (preimplement*" or pre-implement*) or AB (pre-implement* or preimplement*)
6192	S64	TI (intervention* or multiintervention* or multi-intervention* or postintervention* or post-intervention* or preintervention* or pre-intervention*) or AB (intervention* or multiintervention* or multi-intervention* or postintervention* or post-intervention* or preintervention* or pre-intervention*)
131264	S63	(MH "Quasi-Experimental Studies")
5226	S62	S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61
136507	S61	TI controlled AND TI (trial or trials or study or experiment* or intervention)
15711	S60	AB ((multicent* n2 design*) or (multicent* n2 study) or (multicent* n2 studies) or (multicent* n2 trial*)) or AB ((multi-cent* n2 design*) or (multi-cent* n2 study) or (multi-cent* n2 studies) or (multi-cent* n2 trial*))
5820	S59	TI multicentre or multicenter or multi-centre or multi-center
3835	S58	TI (cluster N2 trial* or cluster N2 study or cluster N2 group or cluster N2 groups or cluster N2 cohort or cluster N2 design or cluster N2 experiment*) OR AB (cluster N2 trial* or cluster N2 study or cluster N2 group or cluster N2 groups or cluster N2 cohort or cluster N2 design or cluster N2 experiment*)

(*Continued*)

1437	S57	TI (control group or control groups OR control* experiment* or control* design or controlled study) OR AB (control group OR control groups or control* cohort* or controlled experiment* controlled design or controlled study)
44417	S56	TI random* or AB random*
97077	S55	TI ("clinical study" or "clinical studies") or AB ("clinical study" or "clinical studies")
6259	S54	(MM "Clinical Trials+")
7510	S53	(S50 or S51 or S52) NOT S49
1605	S52	(S29 and S35) NOT S48 NOT (S50 or S51)
1136	S51	(S29 and S39) NOT S50
184	S50	S29 and S35 and S44
285	S49	TI (cocaine or cannabis or marijauna or drug abuse or street drug#) OR AB (cocaine or cannabis or marijauna or drug abuse or street drug#) OR MW (cocaine or cannabis or marijauna or drug abuse or street drug#)
11583	S48	S45 or S46 or S47
659369	S47	(TI (elderly or nursing home#) OR AB (elderly or nursing home#)) OR (TI (geriatric#) OR AB (geriatric#) OR MW (geriatric#)) OR TI adult#
101606	S46	(MH "Residential Facilities+")
17635	S45	(MH "Adult+")
631032	S44	S40 or S41 or S42 or S43
414718	S43	MH neonatology OR MH perinatology
423	S42	MH pediatrics OR MH adolescent medicine
5788	S41	TI (child or children or child# or newborn# or p#ediatric# or infant# or neonate# or teenager# or teens or adolescent# or baby or babies) OR AB (child or children or child# or newborn# or p#ediatric# or infant# or neonate# or teenager# or teens or adolescent# or baby or babies)
224131	S40	(MH "Child+") OR (MH "Adolescence")
366722	S39	S36 or S37 or S38
25827	S38	TI ((p#ediactric# or children# or neonatal or infant) N3 (hospital# or ICU or intensive care or care unit or department#)) OR AB ((p#ediactric# or children# or neonatal or infant) N3 (hospital# or ICU or intensive care or care unit or department#))

(*Continued*)

6914	S37	MH pediatric nursing OR MH neonatal nursing OR MH neotalogy OR MH perinatology
10767	S36	(MH "Intensive Care Units, Pediatric") OR (MH "Intensive Care Units, Neonatal") OR (MH "Intensive Care, Neonatal") OR (MH "Hospitals, Pediatric")
12821	S35	S30 or S31 or S32 or S33 or S34
170323	S34	TI hospital* OR AB (("in hospital#" or hospitali*))
77174	S33	(MH "Personnel, Health Facility+")
18851	S32	(MH "Hospitalization+")
31178	S31	(MH "Perioperative Care") OR (MH "Intraoperative Care") OR (MH "Postoperative Care") OR (MH "Intraoperative Period") OR (MH "Postoperative Period") OR (MH "Preoperative Period") OR (MH "Postoperative Pain")
22902	S30	(MH "Hospitals+")
54736	S29	S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28
11019	S28	(MH "Medication Errors/PC")
3771	S27	TI (prevent# adverse drug OR (causes N2 (prescri# error? or medication? error?)) OR medication related adverse) or AB (prevent# adverse drug OR (causes N2 (prescri# error? or medication? error?)) OR medication related adverse)
116	S26	(MH "Drug therapy" or MH "Drug administration routes+" or MH "drug administration schedule+" or MH "drug delivery systems+" or MH "drug prescriptions+" or MH "drug therapy, Combination+" or MH "drug therapy, computer-assisted+") AND MH "Treatment Errors"
58	S25	(MH "Antiinfective Agents+") AND MH Treatment Errors
24	S24	(MH "Treatment Errors/PC") AND (TI (medication# or drug#) OR AB (medication# or drug#))
66	S23	(MH "Antiinfective Agents+") AND (TI ((prevent* or reduce# or reducing) and (error# or (adverse* N3 event#))) or (inappropriat* N2 "use"))
132	S22	(MH "Drug Therapy" OR MH "Drug Administration Routes+" OR MH "Drug administration schedule+" OR MH "drug delivery systems+" OR MH "drug prescriptions+" OR MH "drug therapy, Combination+" AND MH "Drug Therapy, Computer-assisted+") AND (TI error# or mistake or mistakes or prevent* adverse)
454	S21	TI ((drug# or medication# or prescrib*) N3 error#) AND TI (prevent* or reduce# or reducing)
451	S20	TI (prevent* and (error# or (adverse N2 event#))) AND (TI (dosing or drug# or medication# or prescript* or prescrib*) or MW (dosing or drug# or medication# or prescript* or prescrib*))
422	S19	MH "Drug Therapy, Computer Assisted" AND TI (safety or error#)

(*Continued*)

37	S18	MH Drug Therapy, Computer-Assisted AND TI (safety or error#)
0	S17	MH Decision Support Systems, Clinical AND (((TI (prescrib*) or MW (prescrib*)) or TI medication# or MH drug therapy))
113	S16	TI ("medication related" N2 (problem# or issue# or hospitali#ation# or mortal* or morbid* or illness* or condition#)) OR AB ("medication related" N2 (problem# or issue# or hospitali#ation# or mortal* or morbid* or illness* or condition#))
89	S15	TI ((excess* or inadequat*) N2 (dosage# or dose# or dosing)) OR AB ((excess* or inadequat*) N2 (dosage# or dose# or dosing))
170	S14	TI (near miss or near misses) OR AB (near miss or near misses)
416	S13	TI accident* N2 overdose# OR AB accident* N2 overdose#
82	S12	TI medication# N2 (reconciliation# or audit# or quality improvement)
185	S11	TI ((drug# or medication# or medicine# or dose or dosage# or dosing) N2 wrong*) OR AB ((drug# or medication# or medicine# or dose or dosage# or dosing) N2 wrong*)
177	S10	(TI ((weight-based or surface-based or weight independent) N2 (prescrib* or dose or dosing or dosage#)) OR AB ((weight-based or surface-based or weight independent) N2 (prescrib* or dose or dosing or dosage#))) AND (TI (safety or error#) OR MW (safety or error#))
25	S9	TI quality improv* and (prescrib* or prescript* or dosing)
26	S8	MH medication reconciliation
294	S7	TI effective prescribing practice# OR AB effective prescribing practice#
13	S6	TI ((inappropriate N3 (prescription# or medication#)) or ((appropriat* or inappropriat* or optimal) N2 prescrib*)) OR AB ((inappropriate N3 (prescription# or medication#)) or ((appropriat* or inappropriat* or optimal) N2 prescrib*))
865	S5	TI medication# N2 misadventure# OR AB medication# N2 misadventure#
11	S4	TI ((pharmacist# or prescrib* or prescription# or dispens* or dosing) N2 (error# or mistake# or miscalculat*)) OR AB ((pharmacist# or prescrib* or prescription# or dispens* or dosing) N2 (error# or mistake# or miscalculat*))
470	S3	TI (medication safety or medication incident# or medication error#) OR AB (medication safety or medication incident# or medication error#)
3617	S2	MH Medication errors
7741	S1	TI preventable adverse drug or medication related adverse event#

(*Continued*)

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Appendix 5. PsycInfo strategy

PsycINFO <1806 to October Week 5 2012> & PsycINFO <1806 to October Week 4 2013>

1 (preventable adverse drug or medication related adverse event?).ti. [Screen all] (3)
2 (Medication errors or Inappropriate Prescribing).ti,ab,id. (344)
3 (medication safety or medication incident? or medication error?).ti,ab. (341)
4 ((pharmacist? or prescrib$ or prescription? or dispens$ or dosing) adj2 (error? or mistake? or miscalculat$)).ti,ab. (102)
5 (medication? adj2 misadventure?).ti,ab. (4)
6 ((inappropriate adj3 (prescription? or medication?)) or ((appropriat$ or inappropriat$ or optimal) adj2 prescrib$)).ti,ab. (447)
7 effective prescribing practice?.ti,ab. (2)
8 (quality improv$ and (prescrib$ or prescript$ or dosing)).ti. (2)
9 ((drug? or medication? or medicine? or dose or dosage? or dosing) adj2 wrong$).ti,ab. (53)
10 (medication? adj2 (reconciliation? or audit? or quality improvement)).ti. (19)
11 (accident$ adj2 overdose?).ti,ab. (72)
12 (near miss or near misses).ti,ab. (246)
13 ((excess$ or inadequat$) adj2 (dosage? or dose? or dosing)).ti,ab. (169)
14 ("medication related" adj2 (problem? or issue? or hospitali?ation? or mortal$ or morbid$ or illness$ or condition?)).ti,ab. (53)
15 decision support systems/ and (prescrib*.ti,hw. or medication?.ti. or *drug therapy/) (21)
16 Electronic prescribing.ti,ab,id. and (safety or error? or improv$).ti. (4)
17 (prevent$ and (error? or (adverse adj2 event?))).ti. and (dosing or drug? or medication? or prescript$ or prescrib$).ti,hw. (12)
18 (((drug? or medication? or prescrib$) adj3 error?) and (prevent$ or reduce? or reducing)).ti. (18)
19 (drug therapy/ or exp drug administration routes/ or (drug administration schedule or drug delivery systems or drug dosage calculations or drug prescriptions or combination drug therapy or computer-assisted drug therapy).ti,ab,id.) and (error? or mistake or mistakes or prevent$ adverse).ti. (138)
20 (hospital medication systems or hospital pharmacy service).ti,ab,id. and ((error? or mistake or mistakes or prevent$ adverse).ti. or ((prevent$ or reduce? or reducing) adj2 (error? or adverse event? or adverse drug event? or medication related problem?)).ab.) (1)
21 medical errors.ti,ab,id. and (medication? or drug?).ti,ab. (49)
22 (drug therapy/ or exp drug administration routes/ or (pharmaceutical preparations or drug administration schedule or drug delivery systems or drug dosage calculations or drug prescriptions or combination drug therapy or computer-assisted drug therapy).ti,ab,id.) and medical errors.ti,ab,id. (12)
23 (prevent$ adverse drug or (causes adj2 (prescri$ error? or medication? error?)) or medication related adverse).ti,ab. (42)
24 or/2-23 [Med errors] (1524)
25 exp hospitals/ (14703)
26 (perioperative care or intraoperative care or postoperative care or perioperative period or intraoperative period or postoperative period or preoperative period or postoperative pain).ti,ab,id. (1175)
27 exp hospitalization/ (16534)
28 hospital personnel.ti,ab,id. (413)
29 hospital$.ti. or ("in hospital?" or hospitali$).ab. (48251)
30 or/25-29 [Hosptials, Hospitalization General] (63084)
31 (pediatric intensive care units or neonatal intensive care units or pediatric hospitals).ti,ab,id. or neonatal intensive care/ (781)
32 (Pediatric Nursing or Neonatal Nursing or Neonatology or Perinatology).ti,ab,id. (262)
33 ((p?ediatric? or children? or neonatal or infant?) adj3 (hospital? or ICU or intensive care or care unit or department?)).ti,ab. (4370)
34 or/31-33 [Pediatric Hospitals] (4722)
35 (child or adolescent).ti,ab,id. (249289)
36 (child or children or child? or newborn? or p?ediatric? or infant? or neonate? or teenager? or teens or adolescent? or baby or babies).ti,ab. (558383)

37 pediatrics/ or adolescent medicine.ti,ab,id. (12518)
38 (neonatology or perinatology).ti,ab,id. (126)
39 or/35-38 [Child/Pediatrics] (565768)
40 adults.ti,ab,id. (176810)
41 exp residential care institutions/ (28594)
42 (elderly or nursing home?).ti,ab. or geriatric?.ti,ab,hw. or adult?.ti. (116898)
43 or/40-42 [Adults, Elderly, Nursing Homes non-hospital facilities] (265885)
44 (cocaine or cannabis or marijauna or drug abuse or street drug?).ti,ab,hw. [Terms to exclude] (53408)
45 24 and 30 and 39 [Med Errors & Hospitals & Child/Pediatrics] (21)
46 (24 and 34) not 45 [Med Errors & Pediatric Units/Hospitals] (11)
47 (24 and 30) not 43 not (or/45-46) [Med Errors & Hospitals not Adults] (80)
48 (or/45-47) not 44 [Results before Filters--illicit drug terms excluded] (106)
49 double-blind.tw. (16397)
50 random$ assigned.tw. (21826)
51 control.tw. (283286)
52 or/49-51 [RCT Filter per J Clin Epidemiol. 2008 January; 61(1): 34-40] (309846)
53 intervention?.ti. or (intervention? adj6 (clinician? or collaborat$ or community or complex or DESIGN$ or doctor? or educational or family doctor? or family physician? or family practitioner? or financial or GP or general practice? or hospital? or impact? or improv$ or individuali?e? or individuali?ing or interdisciplin$ or multicomponent or multi-component or multidisciplin$ or multi-disciplin$ or multifacet$ or multi-facet$ or multimodal$ or multi-modal$ or personali?e? or personali?ing or pharmacies or pharmacist? or pharmacy or physician? or practitioner? or prescrib$ or prescription? or primary care or professional$ or provider? or regulatory or regulatory or tailor$ or target$ or team$ or usual care)).ab. (75950)
54 (pre-intervention? or preintervention? or "pre intervention?" or post-intervention? or postintervention? or "post intervention?").ti,ab. [added 2.4] (4141)
55 (hospital$ or patient?).hw. and (study or studies or care or health$ or practitioner? or provider? or physician? or nurse? or nursing or doctor?).ti,hw. (39422)
56 demonstration project?.ti,ab. (893)
57 (pre-post or "pre test$" or pretest$ or posttest$ or "post test$" or (pre adj5 post)).ti,ab. (32125)
58 (pre-workshop or post-workshop or (before adj3 workshop) or (after adj3 workshop)).ti,ab. (371)
59 trial.ti. or ((study adj3 aim?) or "our study").ab. (60657)
60 (before adj10 (after or during)).ti,ab. (45884)
61 ("quasi-experiment$" or quasiexperiment$ or "quasi random$" or quasirandom$ or "quasi control$" or quasicontrol$ or ((quasi$ or experimental) adj3 (method$ or study or trial or design$))).ti,ab,hw. (39916)
62 ("time series" adj2 interrupt$).ti,ab,hw. (376)
63 (time points adj3 (over or multiple or three or four or five or six or seven or eight or nine or ten or eleven or twelve or month$ or hour? or day? or "more than")).ab. (1789)
64 pilot.ti. (9209)
65 (multicentre or multicenter or multi-centre or multi-center).ti. (1572)
66 random$.ti,ab. or controlled.ti. (118983)
67 (control adj3 (area or cohort? or compare? or condition or design or group? or intervention? or participant? or study)).ab. not (controlled clinical trial or randomized controlled trial).pt. (77108)
68 "comment on".cm. or review.ti,pt. or randomized controlled trial.pt. (97596)
69 review.ti. (97596)
70 (rat or rats or cow or cows or chicken? or horse or horses or mice or mouse or bovine or animal?).ti. (96983)
71 (or/53-67) or experimental design/ or between groups design/ or quantitative methods/ or quasi experimental methods/ (409712)
72 exp animals/ or animal?.ti,id,hw. (271628)
73 71 not (or/69-70,72) [EPOC Methods Filter 2.4 PsycInfo] (373217)
74 48 and 52 [RCT Results] (9)
75 (48 and 73) not 74 [EPOC Filter Results] (43)

3 October 2013

74 48 and 52 [RCT Results] (10)
75 (48 and 73) not 74 [EPOC Filter Results] (51)
76 (201211$ or 201212$).up. or 2013$.up,dp. (189306)

77 (or/74-75) and 76 (9)

Appendix 6. ProQuest Dissertations & Theses strategy

13 November 2012 Results: 175
3 October 2013: Results: 15

(ti,ab("medication safety" OR "medication incident?" OR "medication error?") OR ti,ab((pharmacist? OR prescrib* OR prescription? OR dispens* OR dosing) NEAR/2 (error? OR mistake? OR miscalculat*)) OR ti,ab((inappropriate NEAR/3 (prescription? OR medication?)) OR ((appropriat* OR inappropriat* OR optimal) NEAR/2 prescrib*)) OR ti,ab,if,su("Medication errors" OR "Inappropriate Prescribing") OR ti,ab,if,su("medication reconciliation") OR ti,ab((drug? OR medication? OR medicine? OR dose OR dosage? OR dosing) NEAR/2 wrong*) OR ti,ab(accident* NEAR/2 overdose?) OR ti,ab("near miss" OR "near misses") OR ti,ab((excess* OR inadequat*) NEAR/2 (dosage? OR dose? OR dosing)) OR ti,ab("medication related" NEAR/2 (problem? OR issue? OR hospitali?ation? OR mortal* OR morbid* OR illness* OR condition?)) OR (ti,ab,if,su("Electronic prescribing") AND ti(safety OR error? OR improv*)) OR (ti,ab,if,su("Pharmaceutical preparations" OR "Drug Therapy" OR "Drug Administration Routes" OR "Drug administration schedule" OR "drug delivery systems" OR "drug dosage calculations" OR "drug prescriptions" OR "drug therapy, Combination" OR "Drug Therapy, Computer-assisted") AND ti(error? OR mistake OR mistakes OR "prevent* adverse")) OR (ti,ab,if,su("Pharmaceutical preparations" OR "Drug Therapy" OR "Drug Administration Routes" OR "Drug administration schedule" OR "drug delivery systems" OR "drug dosage calculations" OR "drug prescriptions" OR "drug therapy, Combination" OR "Drug Therapy, Computer-assisted") AND ti,ab,if,su(Medical Errors))) AND ((child OR children OR toddler* OR adolescent OR adolescents OR pediatric* OR paediatric* OR neonat* OR perinatal* OR infant OR infants OR newborn*) NOT ti(nursing home OR nursing homes OR elderly OR "old* adults" OR "old* adult"))

Appendix 7. ProQuest Nursing & Allied Health strategy

Please note: Other search strateigies were used in this database, but copies were not saved. However results from those searches yielded 515 citations gross; 233 after removal of duplicates. Searches were conducted 3 October 2013.
(intervention* or pre-intervention* or post-intervention* or team* or collaborat* or interdisciplin*) OR TITLE(chang* or impact or implement* or improv*) AND (((medication pre/3 error?) OR (medication? w/3 miscalculat*) or (drug? w/3 miscalculat*) or (dosing w/3 error?) or (dose w/3 error?) or (dosage w/3 error?)) OR (MESH(Medication errors))) AND (((child* or teen* or p?edatric? or infant* or infancy or adolescent?)) OR (MESH(child) or MESH(infant) or MESH(adolescent) or MESH(Infant, Premature) or MESH(Infant, Postmature))) [25 citations]
Database: ProQuest Nursing & Allied Health Source
Look for terms in: citation and abstract
Publication type: all publication types
(random* or (before w/3 after) or (interrupted time series) or control* or quasiexperiment* or quasi-experiment* or experiment*) AND (((medication pre/3 error?) OR (medication? w/3 miscalculat*) or (drug? w/3 miscalculat*) or (dosing w/3 error?) or (dose w/3 error?) or (dosage w/3 error?)) OR (MESH(Medication errors))) AND (((child* or teen* or p?edatric? or infant* or infancy or adolescent?)) OR (MESH(child) or MESH(infant) or MESH(adolescent) or MESH(Infant, Premature) or MESH(Infant, Postmature))) [49 citations]
Database: ProQuest Nursing & Allied Health Source
Look for terms in: citation and abstract
Publication type: all publication types

Appendix 8. Web of Science strategy

We identified 337 (2012) + 64 (2013) citations in our searches of Web of Science databases, specifically Science Citation Index (SCI-EXPANDED); Conference Proceedings, Science (CPCI-S); Social Sciences Citation Index (SSCI); and Social Sciences Conference Proceedings Indices (CPCI-SSH). However, we do not have copies of the search strategies as run.

Appendix 9. Other resources search strategies

Open Grey	
Date of search	10 February 2013
Search terms	"medication safety" OR "ME*" OR "medication incident*" OR "drug safety" OR "drug error*" OR "drug incident*" OR "adverse drug event*"
Results of the search	54
Results after screening titles (and abstracts)	0

Grey literature report	
Date of search	10 February 2013
Search terms: results of the search	"medication safety", results of the search: 3 "ME(s)" , results of the search: 69 (69) "medication incident(s)", results of the search: 1 (1) "drug safety" , results of the search: 18 "drug error(s)", results of the search: 0 (0) "drug incident(s)", results of the search: 0 (0) "adverse drug event(s)", results of the search: 4 (4)
Results after screening titles (and abstracts)	Results after screening titles (and abstracts): 0

AHRQ	
Date of search	10 February 2013
Search terms	Advanced search → all in title "medication safety" OR "ME*" OR "medication incident*" OR "drug safety" OR "drug error*" OR "drug incident*" OR "adverse drug event*"
Results of the search	84

(*Continued*)

Results after screening titles (and abstracts)	0

NRR	
Date of search	31 January 2013
Search terms: results of the search	Advanced search → the exact phrase medication safety, results of the search: 1 ME(s), results of the search: 0 (1) medication incident(s), results of the search: 0 (1) drug safety, results of the search: 4 drug error(s), results of the search: 0 (0) drug incident(s), results of the search: 0 (0) adverse drug event(s), results of the search: 6 (0)
Results after screening titles (and abstracts)	0

Joanna Briggs Institute	
Date of search	10 February 2013
Search terms: results of the search	medication safety, results of the search: 1 ME(s) , results of the search: 0 (1) medication incident(s), results of the search: 0 (1) drug safety , results of the search: 0 drug error(s), results of the search: 0 (0) drug incident(s), results of the search: 0 (0) adverse drug event(s), results of the search: 0 (0)
Results after screening titles (and abstracts)	0

NICE	
Date of search	31 January 2013
Search terms	"medication safety" OR "ME*" OR "medication incident*" OR "drug safety" OR "drug error*" OR "drug incident*" OR "adverse drug event*"

(*Continued*)

Results of the search	11
Results after screening titles (and abstracts)	0

ICTRP (WHO)	
Date of search	31 January 2013
Search terms	Search for trials, advanced search: clinical trials in children Search terms: medication safety OR ME OR medication incident OR drug safety OR drug error OR drug incident OR adverse drug event
Results of the search	4
Results after screening titles (and abstracts)	1

Clinical Trials	
Date of search	31 January 2013
Search terms	Advanced search: search terms met additional criteria child (0-17) Search terms: “medication safety” OR “ME*” OR “medication incident*” OR “drug safety” OR ”drug error*” OR “drug incident*” OR “adverse drug event*”
Results of the search	129
Results after screening titles (and abstracts)	1

HISTORY

Protocol first published: Issue 4, 2006

Review first published: Issue 3, 2015

Date	Event	Description
22 January 2013	New citation required and major changes	New authors added
22 January 2013	Amended	New authors added, methods updated

CONTRIBUTIONS OF AUTHORS

The review authors made substantial contributions to the design of the review (JM, HV, BA, BF, MG, AN, ST, AS), acquisition of data (JM, HV, AS), analysis of data (JM, HV, AS) or drafting of the review (JM, HV, BA, BF, MG, AN, ST, AS). All review authors approved the final version to be submitted (JM, HV, BA, BF, MG, AN, ST, AS).

DECLARATIONS OF INTEREST

None.

SOURCES OF SUPPORT

Internal sources

- Medway Maritime Hospital, UK.
- Academic Medical Center, Amsterdam, Netherlands.

External sources

- Cochrane Child Health Field, Canada.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the protocol, we defined two primary outcomes: MEs and patient harm as a result of MEs. During the review, we found that in several included studies, harm was expressed as potentially harmful MEs. We considered this information valuable for this review and report potentially harmful MEs as well.

The review authors' sequence and position have changed.

INDEX TERMS

Medical Subject Headings (MeSH)

*Child, Hospitalized; Automatic Data Processing; Checklist; Drug Prescriptions; Medical Order Entry Systems [organization & administration]; Medication Errors [*prevention & control]; Pharmacists; Randomized Controlled Trials as Topic

MeSH check words

Adolescent; Child; Humans